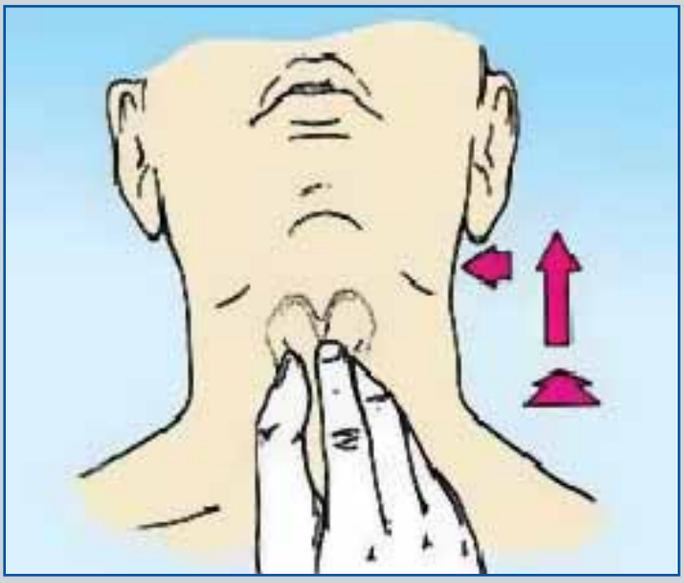
ISSN 2222-9442

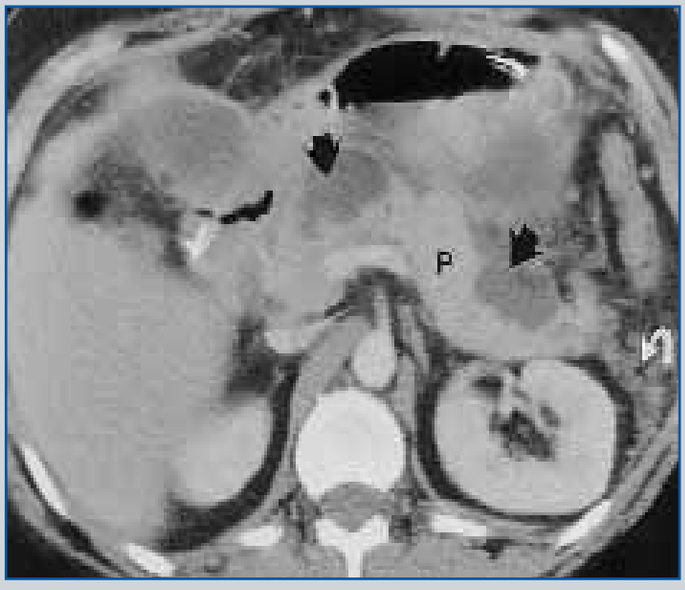
MJEM

MED EMERGENCY/URGENCE

Revue Méditerranéenne de Médecine d´Urgence

Mediterranean Journal of Emergency Medicine





PERCEPTION OF ORGAN DONATION IN ETHNIC MINORITIES IN SPAIN

TWO YEARS OF EXPERIENCE WITH PROPOFOL IN AN ED IN FRANCE

FIRE SMOKE INHALATION

TEST YOUR KNOWLEDGE IN TOXICOLOGY

SÉDATION ET ANESTHÉSIE DU PATIENT EN ÉTAT DE CHOC

IMAGING IN ACUTE PANCREATITIS

Trimestriel

Endorsed by Lebanese Resuscitation Council

March 2013-N°14

C-MAC® for Airway Management – a Sophisticated System

Pocket Monitor

C-MAC®

FIVE

C-HUB™*

* Image output for S-Video and USB, compatible with Philips IntelliVue MX 800 for Airway Cockpit as well as other, non-medical grade monitors

STORZ
KARL STORZ — ENDOSKOPE
THE DIAMOND STANDARD

AN 40 08/2012/A-LB

KARL STORZ GmbH & Co. KG, Mittelstraße 8, 78532 Tuttlingen/Germany Telephone: +49 (0)7461 708-0, Fax: + 49 (0)7461 708-105, E-Mail: info@karlstorz.de
KARL STORZ Endoskope – East Mediterranean and Gulf S.A.L., Block M, 3rd Floor, Beirut Souks, Weygand Street, 2012 3301 Beirut/Lebanon,
Phone: +961 (1) 999390, Fax: +961 (1) 999391, E-mail: info@karlstorz-emg.com
www.karlstorz.com

When there is a will,
there is a way ..

MED Emergency, MJEM
Mediterranean Journal of Emergency Medicine
Publication of the Lebanese Resuscitation Council
By New Health Concept
P.O.Box 90.815 Jdeideh - Lebanon
Tel: 00961.1.888921 Fax: 00.961.1.888922
Email: info@newhealthconcept.net
Website: www.newhealthconcept.net

Med Emergency, MJEM
New look, same mission, vision and value

Since its creation in 2009 Med Emergency MJEM adopted as a mission to be a platform of scientific and cultural exchange between the Arab Mediterranean countries and the rest of the world. Emergency medicine is certainly a scientific and medical discipline but its exercise is subject to traditions and to the culture of every region. Edited in the Levant with a global reach, the specificity of Med Emergency, MJEM resides in its rich content that is not limited to one category of articles to satisfy a readership that wants to know everything about our discipline but is rather filling a void in our region. We publish original research articles that remain for us the basis but also continuous formation articles, clinical cases, and experiences coming from various parts of the world thus giving the publication its value in daily practice.

Our vision has always been to be a reference in a discipline as vast as Emergency medicine. The recent evaluation of our publication by our peers of the National Library of Medicine in the US and their qualification of our journal as important have comforted us in our mission. Amongst the Journal Strengths as cited by the Literature Selection Technical Review Committee were the work of the Editorial board as well as the Journal's content including « research reports, case reports, technical papers, clinical overview and education » as well as the high level of ethics policies and the high level of field experience of the authors. As for areas for improvement they are mostly pertaining to the articles layout. Such comments and suggestions prompt us to do a relooking of our Journal by improving the design and restructuring the layout while pursuing our policy based on quality and ethics.

Last but not least, our primary value remains the team work and vast experience of the members of the editorial board as well as opening to diverse disciplines which renders the journal a « Global Emergency Medicine » publication. The series of editorials published in this issue reflects our attachment to this opening. In the name of the editorial board members and in my name I would like to extend my thanks to all those who contributed to the success of this initiative.

Nagi Souaiby, MD, MPH, MHM
Chief Editor

CONTENTS

Editorials and Special Features

Research / Original Articles

Continuous Education

General informations

The Global Network on Emergency Medicine Concept
An active role for European Emergency Medicine.

The definition of Emergency Medicine (EM) provided by the International Federation for Emergency Medicine is "Emergency medicine is a field of practice based on the knowledge and skills required for the prevention, diagnosis and management of acute and urgent aspects of illness and injury affecting patients of all age groups with a full spectrum of episodic undifferentiated physical and behavioral disorders; it further encompasses an understanding of the development of pre-hospital and in-hospital emergency medical systems and the skills necessary for this development". The European Society for Emergency Medicine (EuSEM) adds some specific elements pertinent to Europe: "… It is a specialty in which time is critical. The practice of Emergency Medicine encompasses the pre-hospital and in-hospital triage, resuscitation, initial assessment and management of undifferentiated urgent and emergency cases until discharge or transfer to the care of another physician or health care professional." The World Health Assembly Resolution 60.22 states that emergency care is an essential part of the public health, and calls upon governments to establish comprehensive Emergency Health Care Systems (EMHCS) which integrate pre-hospital care with triage, stabilization, immediate care, and in-hospital care. Conceptually, emergency care contains pre hospital emergency medicine services (PHEMS) and in-hospital emergency medical services (IHEMS), which must be integrated for a complete EMHCS. The relative importance of the pre-hospital versus the in-hospital emergency care, the staffing, and location of in-hospital care systems have developed very differently in parts of Europe compared to North America. Regardless of which model of emergency care is practiced, increasingly, there is recognition that when a patient is met by a physician skilled in emergency medicine, the patient receives better care. In many countries, financial aspects guide significantly the choice of a system that is non doctor-based rather than a doctor-based system namely Franco-German model. In the European Union (EU) countries, 60 to 70% of PHEMS use a doctor-based model. This does not mean that for each emergency a doctor is systematically sent to the scene. The decision is made by the dispatching center according to the type of emergencies. To date, there are no convincing level I studies showing that an emergency doctor-based EMS compared to a non-doctor-based EMS leads to a decrease in overall mortality or morbidity. Methodological, legal and ethical issues make such studies difficult.

Emergency Medicine has developed along many separate trajectories, buffeted by widely varying political requirements and different entrenched special interests in each country. EM in Europe has variously been the domain of anaesthesiologists and/or intensive care specialists, trauma surgeons, internists and sometimes just new trainees. It has been the fuel for many battles. Still, there are broad common aspects and trends which can be highlighted. One goal of the EU is standardization, or "harmonization." The EU decided to open borders to the free flow of goods and services, including medical personnel. Theoretically, European physicians are free to seek employment in countries other than that in which they qualified. One of its stated objectives was to set minimum training requirements for physicians, nurses, midwives, dentists, pharmacists. Additionally, for a limited number of professions, the EU Directive allows for automatic recognition of qualifications. By 2012, three out of five EU countries have recognised EM as a specialty, making EM an official specialty throughout all EU countries. Since November 2012, the Union of European Medical Specialists (UEMS) webpage lists the specialty as "Emergency Medicine" rather than as "Accident & Emergency Medicine" as it had previously. At the meeting of the Council of UEMS in October 2011, the Section of Emergency Medicine was created by the majority of voting members. This means that Emergency Medicine is clearly recognized as a primary specialty in the EU. All members of this Section are emergency physicians, each delegated by his or her National Medical Association based on a proposal by the national EM society, and each EU country has representation. The recognition of EM in the EU as a whole has been the culmination of many years of work, and encourages all EU countries to create the primary specialty of emergency medicine with a 5-years training period, as recommended by the Council of UEMS.

The development of EM as a primary specialty in Europe will increase the European influence in the world and balance the relationship with North America by giving a great opportunity for sharing and elaborating together Guidelines in all fields of EM. A group of European emergency physicians decided to build the concept of a Global Network on Emergency Medicine Conference to increase relationships between developing, emerging, and developed countries. One of the goals is to implement a network at the Global level involving all emergency physicians who work actively in all settings (pre hospital and/or in hospital). This network has the objective to share knowledge and expertise in 3 domains: Systems and Organisations, Education, and Research. The experience started with the 1st Global Network Conference on Emergency Medicine held in Dubai in January 2012. This first conference was successful and confirmed that the project will continue indeed with the second conference that will be held on May 2-6, 2013 in Dubai. High level speakers involved in this conference will come from different part of the world (Europe, North America, Asia, MENA region, and Australasia). The 2nd conference will be organised in association with the 1st national congress of the Emirati Emergency Medicine Society (ESEM) recently created and will be supported by the International Federation for Emergency Medicine (IFEM) and many scientific EM societies.
We are delighted to welcome all professionals, doctors and non doctors involved in EM to this great event that will be a great opportunity for networking and sharing experiences in EM along with enjoying fantastic activities in this fascinating Emirate, Dubai.

Abdelouahab Bellou, Professor, MD, PhD
President of the 2nd Global Network Conference on Emergency Medicine
Current President of the European Society for Emergency Medicine

The Global Emergency Medicine Literature Review
The best EM articles screened for you

The body of published literature relevant to Global Emergency Medicine (GEM) continues to grow. As busy clinicians and academicians, most of us find it difficult to keep up with the many journals and publications and to read articles published in languages other than our own. In addition, the wide range of both research and policy development undertaken by governments, intergovernmental organizations, and NGOs never makes it to publication and thus remains inaccessible. The Global Emergency Medicine Literature Review (GEMLR) was developed to help EM providers navigate the growing abundance of GEM literature. Now in its 8th year, the GEMLR highlights and disseminates high quality GEM research in the fields of system development, disaster and humanitarian response, and emergency care in resource-limited settings.

Each year, GEMLR conducts a search for articles published in that calendar year, utilizing a set of international and EM search terms and a manual search of journals that have produced large numbers of international emergency medicine articles for past reviews. The search produces about 7000 articles, which are divided among reviewers who screen them using established inclusion/exclusion criteria to select relevant articles.

GEMLR is overseen by an editorial board composed of a diverse group of highly experienced GEM physicians from all over the world. The review is published annually in Academic Emergency Medicine and online with universal access: http://www.gemlr.org. Each year, the articles selected by the GEMLR represent high quality international emergency medicine research that is currently ongoing in high, middle, and low-income countries. GEMLR is not intended to be a systematic review, but it is instead meant to be a selection of current high-quality global EM literature, and strives to foster further growth in the field and highlight evidence-based practice.

Please email gemlrgroup@gmail.com to be considered for a position as a Reviewer for the 2013 GEMLR.

Gabrielle A. Jacquet, MD, MPH and Adam C. Levine, MD, MPH

Foundation of the Lebanese Society for Quality and Patient safety in Healthcare

As Medicine is progressing with massive leaps in technology and management, we are witnessing great steps of improvement in the health care field manifested by setting standardized accreditation standards, and conduction of Performance Improvement activities in the health care organizations all over the world. As a result societies targeting the improvement of health care have been created in different countries as USA, Europe, Ireland, UK, Australia, etc.

As we see Lebanon a leading country in healthcare, and as we need always to improve in order to provide the best possible care and reduce harm, we have founded a society to follow up Quality and Safety issues in Lebanon, composed of quality professionals and expert physicians that can compete with the most successful societies in the world.

Our mission is to improve healthcare quality through education, raising public awareness, promoting, fostering communication and collaboration between professionals about Quality and patient Safety in Lebanon. This will be achieved through the organization of regional meetings, conferences and seminars, through research and training of healthcare professionals. We will be providing support to providers working in all regions concerning issues related to quality of health care or patient safety.

Emergency medicine is a domain that might suffer incidents, adverse events and medication errors. Those need to be thoroughly reported and used to improve the care provided in emergency departments and ensure patient safety throughout the whole care process.

Quality circle consists on identifying problems, planning changes, standardizing protocols, measuring performance by specific indicators and designing action plans to follow up and monitor healthcare systems.

Each trimester, we will be posting ideas related to the implementation of those topics in ER… Read us next edition as we will be speaking about Patient Safety in ER.

Rola Hammoud, MD, DA, MHM
Medical Quality Director, Clemenceau Medical Center- Lebanon
President, Lebanese Society for Quality and Patient Safety

PERCEPTION of ORGAN DONATION in ETHNIC MINORITIES in SPAIN. Perception de la Donación de órganos en las minorías étnicas en España

ARAIZ BURDIO J.J, GUTIEREZ ROMERO M.T, PARACUELLOS M.J, ROYO PUERTO M, SANCHEZ MIRET J.I. Perception of organ donation in ethnic minorities in Spain. Med Emergency, MJEM 2013; 14: 5-12
Keywords: Donation, Survey, Opinion, Minorities

ABSTRACT

Aim: To discover the social perception of ethnic minorities, detect areas of improvement and establish possible measures of action specifically aimed at these groups with regard to organ donation and transplants.

Design: A cross-sectional study using stratified, proportional random sampling based on a personal survey carried out on members of different minorities over the age of 16, and subsequently performing a bivariate descriptive statistical study.

Results: 561 surveys were carried out: 313 (56%) on women and 248 (44%) on men. The mean age of respondents was 34.7 ± 11 years and the mean global time of residence in Spain for foreign minorities was 6.9 years. 68% of respondents expressed a favourable attitude to organ donation, within a range of between 25%-79% depending on the minority group ($p<0.0001$). The three reasons that were most frequently given for being in favour of organ donation were: to save someone's life (60%), because a relation/friend needs it (40%) and out of solidarity (35%), self-interested reasons (social opinion, economic motives) were scarcely valued (2%). The reasons indicated for being against organ donation were different depending on the groups. To obtain more information on donation and transplants most of the respondents (56%) indicated that they would turn to health professionals. It was observed that there is a greater predisposition towards donation the longer the person has resided in our country, from 25% to 82% ($p<0.05$). Most respondents indicated their willingness to receive an organ transplant, with percentages that varied from 48% (those who would not be donors) and 93% (those that would be donors) ($p<0.0001$).

Conclusions: With regard to donation, willingness to donate organs amongst the minorities studied, when considered as whole, does not differ significantly from the opinion of the Spanish population. However, it is important to underline that certain minorities show a less favourable attitude towards organ donation. There is thus a need to increase the level of information; this information must be given by health professionals and must be oriented and specifically directed at each ethnic group.

Authors' affiliation:
Juan José Araiz Burdio
Transplant Coordinator. Intensive Medicine Service. Hospital Clínico Universitario "Lozano Blesa". Zaragoza
María Teresa Gutiérrez Romero; María Jesús Paracuellos Paracuellos; Milagros Royo Puerto.
Graduate in Nursing. Intensive Medicine Service. Hospital Clínico Universitario "Lozano Blesa". Zaragoza
Correspondant autor: José Ignacio Sánchez Miret
Regional Coordinator for Transplants. Aragon Provincial Council. Autonomous Region of Aragon. Transplant Coordinator Expert from DTI Foundation.

Article history / info:
Category: Original article
Received: Dec, 1st 2012
Revised: Feb. 14, 2013
Original in Spanish: published online.

Conflict of interest statement:
There is no conflict of interest to declare

José Ignacio Sánchez Miret

RESUMEN

Objetivo: Conocer la percepción social de las minorías étnicas, detectar puntos de mejora y establecer las posibles medidas de acción específicamente dirigidas, respecto de la donación y trasplante de órganos.

Diseño: Estudio transversal mediante un muestreo estratificado, proporcional y aleatorizado, basado en una encuesta personal dirigida a integrantes de las distintas minorías mayores de 16 años, realizándose posteriormente un estudio estadístico-descriptivo bivariante.

Resultados: Se han realizado 561 encuestas: 313 (56%) mujeres y 248 (44%) hombres. La edad media de los encuestados fue de 34,7 + 11 años y la media global de residencia en España para las minorías extranjeras fue de 6,9 años. El 68% declaraba una actitud favorable hacia la donación, con un rango entre 25%-79% según grupo minorías ($p < 0,0001$). Las tres razones más frecuentemente esgrimidas a favor de la donación fueron: salvar una vida (60%), porque algún familiar/amigo lo necesite (40%) y por solidaridad (35%), las razones interesadas (opinión social, razones económicas) fueron poco valoradas (2%). Respecto de las razones aducidas para oponerse a la donación fueron distintas según los grupos. Para ampliar sus conocimientos sobre donación y trasplante la mayoría (56%) acudiría a los profesionales sanitarios. Se observa una mayor predisposición a donar a mayor tiempo de residencia en nuestro país desde el 25% al 82% ($p < 0,05$). La mayoría estaría dispuesto a recibir un trasplante, con porcentajes que oscilan entre el 48% de los que no serían donantes y el 93% de los que si serian ($p < 0,0001$).

Conclusiones: En materia de donación, la disposición a donar de las minorías estudiadas al considerarlas de una forma global no difiere de forma significativa con la opinión de la población española, pero debemos incidir en determinadas minorías que muestran una actitud menos favorable. Hace falta pues, incrementar los niveles de información, esta información debe estar liderada por los profesionales sanitarios y debe ser orientada y específicamente dirigida a cada grupo étnico.

Palabras Clave: Donación, Encuesta, Opinión, Minorías.

INTRODUCTION

The model of the Spanish National Transplant Organisation (Organización Nacional de Trasplantes – ONT) serves as an example for other countries, with consistently high donation rates, above 30 donations per million people (pmp) since 1998. These are the highest figures of any country in the world. However, in recent years a drop in the rate of donors has been observed, essentially due to epidemiological changes regarding encephalic death: there are fewer traffic and work accidents, lower cerebrovascular mortalities, better checks on cardiovascular risk factors, etc.

However, the main reason for the decline in potential donors is the refusal to donate; either by the deceased patient while alive or by the family during discussion.

Because of this fall in donor numbers, the Spanish National Transplant Organisation has drawn up what it calls the 40 Donation Plan which aims to raise the donor rate in Spain to 40 donors pmp. One of the recommendations set out by the 40 Plan is the implementation of measures aimed at minorities: informational campaigns, training of cultural mediators, collaboration with associations and opinion polls.

In recent years, Spain's population has undergone a significant sociodemographic change, essentially due to immigration that has led to the arrival of individuals of different cultures and faiths. It is calculated that 10% of the Spanish population comprises residents born outside the country.

In order to identify how these minorities perceive organ donation and thereby outline potential plans of action and/or improvements that specifically target different groups, we have conducted the following study in the Autonomous Region of Aragon.

1. MATERIALS AND METHOD

This study is based on opinion polls addressed at different ethnic minority groups; both residents born outside Spain and members of the Gypsy community (the main Spanish ethnic minority).

The design of the survey took into account previous studies with similar characteristics[1,2,3]. The idea was to create a simple survey not requiring external monitors in a concise and well-structured format. It was aimed at members of different minority groups over the age of 16 residing in the Autonomous Region of Aragon.

The survey was neither validated nor published and consisted of 5 open and 27 closed questions (of which 3 allowed for multiple responses) that were intended to provide information on:

- The demographic profile of the respondent.
- How the respondent uses the national health system and his or her opinion of it.
- Personal attitude, opinions and intentions when it comes to organ donation and transplants, in relation to him or herself and his or her family members/friends/acquaintances.
- Reasons for being for or against donation.
- Opinion of/expectations of the survey.

To determine the sample size for the research, the following formula, commonly used in studies defining parameters to make inferences on population figures [4,5], was used:

$$n = \frac{NK^2pq}{e^2(N-1) + K^2pq}$$

A bivariate analysis of the statistical/descriptive data was conducted.

2. RESULTS

2.1. Profile of Respondents

A total of 561 were completed of which 10% required some assistance from the interviewer. In all groups, the percentage of men and women was around 60% and 40% respectively, except in the African group, where this ratio was inverted. The average age of respondents was 34.7 + 11 years and the average time in Spain for foreign-born minority groups was 6.9 years, with no differences between the groups.

The most common family situation was that of married with children. This was most frequent in the Latin-American minority group, in which 74% had children. By contrast, in the Asian minority, 53% were single and only half had children.

Around 60% of respondents had a middle or high level of education. This was the case for all foreign-born groups, but markedly different from the Gypsy community, where 62% only had a basic level of education.

Regarding religious faith, a total of 10 different faiths were recorded, as well as the non-confessional group. Most were Catholics (49%), followed by Muslims (21%), Orthodox (18%) and Evangelists (8%); although, naturally, this range varied greatly from one group to another. Eighty-one percent of the respondents claimed that religion was very or quite important in their lives. The group that placed least importance on religious faith was the Asian minority.

2.2. Contact with and Opinion of the Health System

Ninety-four percent of respondents had some contact with the Spanish health system in the past, with the Asian group recording the lowest level of contact with it (82%). In most groups, the most common experience was contact at various levels of the system or with primary care centres.

Only an average of 23% had any contact with Intensive Care Units (ICU), but this percentage covered statistically significant differences between groups, with the highest figure recorded in the Gypsy community (53%) and the lowest recorded in the Asian minority (6%).

On average, and in most groups, around 80% of opinions regarding the Spanish health system were that of good or very good, as were specific opinions on the intensive care units. This percentage was lower (59%) in the Asian minority, where 35% of respondents had a fair opinion of the system and 50% had a fair opinion of the intensive care units.

2.3. Knowledge of Organ Donation

An average of 70% of respondents had prior knowledge of organ donation, but this figure showed statistically significant differences between groups: it was lower for the Asian (65%) and African (59%) minority ($p < 0.001$). In all foreign-born groups, initial awareness of organ donation was acquired in their country of origin (55%), and only a third became aware of it for the first time in Spain.

Although the vast majority of respondents claim to have some knowledge of organ donation, when asked where organ donors are usually found, only 10% of any group place them in intensive care units and between 30% and 59% do not know or do not answer the question.

Fourteen percent of respondents claim to have direct knowledge of organ donation from a family member/friend/acquaintance, with the highest percentage in the Gypsy community (24%) and the lowest in the Asian minority (6%).

2.4. Personal Attitudes, Opinions and Intentions Regarding Organ Donation and Transplants.

In our study, when asked what position you take regarding organ donation, 50% of respondents answer that they would be willing to be a donor, 2% say they carry a donor card, 16% clearly express that they would not be a donor and 32% do not know or do not answer the question.

However, there are significant differences between the minority groups: the European and American groups are even more favourable to donation and the African group is slightly less favourable. The Asian and Gypsy communities are least open to donation, with a higher percentage of undecided respondents (47 and 37%, respectively) and a higher percentage against donation (29% and 31%, respectively).

The purpose of questions 11 and 12 was to analyse to what extent organ donation is discussed in family and social environments. Both questions display similar results which could be summarised as follows: only half the respondents expressed their opinion on the matter in the family and social environment and the other half did not. There were no significant differences between the groups in this regard.

When asked if they would respect the wishes of a deceased person to donate, the vast majority say they would (86%), with little variation between the groups. However, when asked, if they were charged with the decision of whether or not to donate the organs of a deceased person, the percentage of positive responses is lower (68%).

With regard to who should give permission for an organ donation, almost all groups agree that it should be a close family member (81-90%), except for the African minority, where there is a significant difference: 62% answer that it should in fact be a close family member, but a considerable percentage (21%) claim that it should be a leader: whether it be areligious (16%) or community (5%) leader.

In terms of the opinions and intentions regarding possible transplants, approximately one in four respondents (26%) have direct awareness of a transplant given to someone they know. Three quarters of them would be willing to receive a transplant if they needed it (only one in ten would refuse one); this is a similar trend in all groups. Only in the Asian minority is the percentage of those refusing transplants significantly higher (23%) ($p< 0.001$).

2.5. Reasons For and Against Organ Donation

In order of importance, the three arguments most frequently put forward in favour of donation are: saving a life (60%), because a family member/friend needs it (40%), out of solidarity (35%). The more self-interested or less altruistic reasons (social expectations, financial reasons) were not highly valued (2%).

Most of the minority groups presented quite similar arguments in favour of donation, although there are some significant differences. In the African minority, one in three respondents refer to arguments we might call mystical or religious: living on after death (27%, NS), religious reasons (10%, $p < 0.01$). More than one in three respondents chose solidarity as a reason for donation, this percentage being lower among respondents in the Gypsy community (14%) ($p< 0.001$).

When it comes to reasons for opposing donation and the responses from various minority groups are compared, interesting results are observed. In the Gypsy and Asian groups, the most important reason for opposing donation is preservation of wholeness of the corpse (32 and 41%, respectively, $p < 0.01$), for the African minority it is the premature certification of death (29%, NS) and in the Latin-American group, there are three reasons for distrusting donation: the possibility of unfair use of organs (33%, $p < 0.001$), mistrust of healthcare staff (23%, $p < 0.0001$) and if they certify my death too soon(33%, NS).

2.6. Opinion / Expectations for Obtaining Information

Regarding the choice of resources to be used for expanding knowledge of donation and transplants, there are no significant differences between the groups studied. It is worth highlighting that they all feel that the best option is approaching healthcare professionals (56%); with the internet (24%) being the second preferred resource.

2.7. Specific Analyses

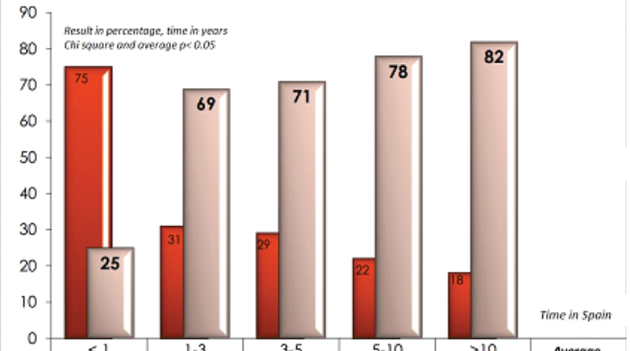
In our search for sociodemographic factors that may lead to a positive or negative attitude regarding organ donation, we have not found a profile leaning more to one side rather than the other: neither age, civil status nor parental status were significantly influential in relation to the questions analysed. Only women show a slightly higher predisposition to donation ($p < 0.05$), while those without an education display a lower predisposition ($p < 0.0001$). This last figure could be swayed by a specific minority group and not in itself be a predisposing factor.

The questions on predisposition to donating were also linked to religious faith and to the importance of religion expressed by each respondent. Here, there are significant differences ($p < 0.0001$): Catholics are the religious group that has the greatest predisposition to donating (67% would donate their own organs and 82% would donate the organs of someone they know if they had to decide). In the Orthodox group, these percentages drop to 46% and 63% respectively. In Muslims they decrease to 32% and 55%, and finally it is the Evangelists who are least predisposed to donation: 27% and 41%, respectively. This last figure may also be swayed by a specific minority group.

For the minority groups born outside of Spain, we observed the relationship between predisposition to organ donation and length of time in the country **(figure 1)**. Here, we can see low predisposition in the first year followed by an increasing predisposition over time ($p < 0.05$): respondents who have lived in Spain for less than a year would
donate the organs of a family member in 25% of cases. This figure gradually reaches 82% for those who have lived in the country for over 10 years. The difference between the average length of time in Spain for those who would donate (7.3 years) and for those who would not (5.7 years) is also statistically significant ($p < 0.05$).
We also studied the relationship between predisposition to organ donation and views on the health system and ICUs. It is worth highlighting that the percentage of predisposition to donate falls as the opinion of the health system worsens. The predisposition is also lower for respondents who are unaware of the opinions of others in their family and social circles.

Figure 1: Evolution of behavior toward organ donation in Spain

If you had to decide, would you agree to donate the organs of a deceased member of your family, a friend or a person you know?



	< 1	1-3	3-5	5-10	>10	Average
No	75	31	29	22	18	5,7 years
Yes	25	69	71	78	82	7,3 years

Finally, we felt it would be interesting to look at the relationship between predisposition to organ donation and predisposition to receiving a transplant, should one be needed. On this point, regardless of personal opinions on donation, most respondents would be willing to receive a transplant, with percentages between 48% for those who would not be donors and 93% for those who would ($p < 0.0001$).

3. DISCUSSION

In the majority of western nations, generating organs for transplant ultimately comes down to personal and/or family choice[6] -- consent to donation. The decision to donate is a psychosocial one that depends on a multitude of factors (family, work, social, economic and healthcare environments), this decision being the start of a long chain eventually leading to a transplant.

Currently, the main reason for losing potential donors identified by the hospital liaison teams is refusal to donate, either expressed by the deceased while alive or by the family during discussions with liaison experts. This is why we felt it was important to investigate the public perception of donation among minorities directly involved in our health system and who could therefore also contribute to generating organs for transplant.

The main result that we can highlight in this study is that overall predisposition to organ donation among minority groups surveyed does not differ significantly from the opinions reflected in the UAM/ONT study of the Spanish population as a whole2. While the UAM/ONT study selected a subgroup of foreign-born residents, this sample was not deemed large enough to draw such conclusions. To the question "what is your attitude to organ donation?" 58.6% of this subgroup was in favour while 20.7% was not. These percentages were similar to those recorded for the Spanish population as a whole.

Predisposition to donating is closely related to conversations held in family and social circles on this issue. We can summarise by saying that no more than 50% of respondents had discussed it. In a separate publication about the national study conducted by the UAM/ONT in 1999 and 2006, an increase was observed in the percentage of respondents who have talked about the issue in the family environment, from 49.9% to 57.4% ($p < 0.05$)[7]. In the 2009 Eurobarometer, willingness to donate increased to 77% among those who had discussed the matter with family members, although only 40% had done so. The impact of family interactions on willingness to donate has been analysed in a recent study[8], and the two most important factors in decision-making are knowledge of the deceased individual's wishes and the decision-makers' attitude to donation. When there is any discrepancy between these two processes, it is safe to conclude that the role of transplant liaison specialists and healthcare staff play an extremely important role in the family decision-making process.

Regarding who should give permission for a donation, there is quite unanimous agreement that it should be a direct family member (ranging from 81-90%), but 1 in 5 of the African minority would consider it necessary to consult a religious and/or community leader. There is also a very high level of respect for the wishes of the deceased (overall 86%; range between 69-97%).

If we observe reasons given by respondents in favour of donation, they can be grouped as follows:
• Bioethical: these were the main reasons given overall in our study and in most of the subgroups (saving a life 60%, out of solidarity 35%).
• Mystical/Religious: These reasons (living on after death, religious reasons) were given in 1 in 3 respondents from the African minority.
• Socio-economic: The less altruistic reasons (financial motivations, desire for public prestige) were not highly valued by any of the groups studied. In a telephone survey of Afro-Americans in Ohio, 45.6% of respondents presented financial reasons for consenting to organ donation[9].

Regarding reasons for not being donors, respondents who have a negative attitude to donation can be grouped as follows:
• Health factors: these motivations were particularly prevalent among respondents from the Latin-American minority (fear of premature certification of death, mistrust of health professionals, doubts about organ distribution). We feel that these reasons are fairly logical given the frequent stories on illegal trafficking of organs featured in the media of those countries.
• Mystical/religious beliefs: these reasons are more prevalent among members of the Gypsy and Asian minorities (wholeness of the corpse) and the African community (religious reasons) and are based on traditional funeral rites, beliefs in resurrection, reincarnation, etc. These reasons were given similar levels of importance in the population survey conducted by the ONT in 2009[10] .

In terms of prior knowledge of the subject of organ donation, we feel that our study highlights certain contradictions in the opinions given by respondents. The vast majority of respondents claimed to know about donation (range: 59-80%). This figure is similar to that recorded in the UAM/ONT[2] study, in which almost 70% of respondents felt they had sufficient information regarding donation and transplants. Despite this, when asked, "where they thought organ donors were normally found" only 10% of them answered: intensive care units; and, even more significantly, between 30 and 59% did not answer the question.

However, when asked where they would go for further information on donation and transplants, the unanimous answer was: healthcare professionals. The internet was the second most preferred option. We feel, then, that levels of information on donation and transplants need to be increased in these groups, although previous studies seem to conclude that, particularly in health matters, information alone has a limited impact when it comes to changing behaviours[2].

All of this leads us to three important conclusions:
• We need to increase the amount of information that these groups have on donation and transplants.
• Healthcare professionals must play an important role in this, leading and coordinating these flows of information.
• Bearing in mind the differences observed in our study between the various minorities groups, when it comes to reasons or concerns that make them less favourable to donation, this information must be targeted. In this respect, disseminating general messages, leaflets and adverts does not seem effective. The information must be shaped and fine-tuned in accordance with the group that is to receive it.

We agree with other authors claiming that intervention measures designed to improve public attitudes to donation should firstly be based on prior knowledge of the perceptions generally found among the targeted population group[11]; and that direct actions must be adapted to the social characteristics of individual communities[12].

In relation to certain individual factors that may create a particular attitude to donation, in our study neither age, civil status nor parenthood revealed any significant differences. We do find that women and individuals with a high level of education are more favourable. In previous studies[11,13], ,greater

predisposition in individuals with higher education and in young people was observed. There have generally been no differences found regarding gender[18], although some studies have observed a difference[14,15].

Another aspect was religious faith. Here we do find significant differences between the various minorities groups studied, although no great difference was observed when exploring the importance of religion in the respondents' lives. Because this study covered groups from four different continents, the differences may be influenced by other, not exclusively religious factors. Once again, it must be stressed that, to date, we are unaware of any religion that is against donation or that opposes it in any way.

In the group of residents born outside Spain, we observed the predisposition to donation in relation to the time lived in the country, as we have not found this aspect published in any similar study. Here we found an initial inverse relationship and then a gradual increase of predisposition as more time is spent in Spain. We believe that this data, together with the excellent opinion on the health system as reflected in our study, is an example of the benefits of a system based on universality, equity and fairness.

One aspect that continues to surprise those of us who work directly in the area of organ donation and transplants is that now and again we find individuals and families who refuse to donate organs, but we have never or almost never come across an individual or family that refuses a transplant if it is needed. This fact is also borne out by this study, where we see that regardless of willingness to donate, the majority of respondents would be willing to receive a transplant if they needed it. We believe that this should be an argument in favour of donation that we need to increasingly convey to the public and local communities.

CONCLUSIONS

The main conclusions that we can highlight in this study are the following:

- Overall, willingness to donate among the minority groups surveyed does not differ significantly from the opinions reflected in other national surveys, but we must emphasise that some minority groups show a less favourable attitude to organ donation.
- The level of information must be increased in these groups when it comes to donation and transplants.
- This information must be led and coordinated by health professionals, who, in the eyes of the respondents, are the most reliable sources of information.
- This information also needs to be specifically targeted, bearing in mind the differences identified in our study between different minority groups regarding reasons or concerns that create a less favourable attitude to donation.

REFERENCES

1. Rodríguez F, Monteon I. Encuesta de opinión sobre la donación de órganos. Acta Medica Grupo Angeles 2004; 2(1): 7-12.
2. López JS, Martínez JM, Scandroglio B, Martin MJ, San José MC. Análisis de las actitudes de la población española hacia la donación y el trasplante de órganos. Revisión 2006. Publicación de la Universidad Autónoma de Madrid, 2007.
3. Martínez JM, Martín A, López JS. La opinión pública española ante la donación y el trasplante de órganos. Medicina Clínica 1995; 105: 401-406.
4. Dawson-Saunders B, Trapp RG. Bioestadística Médica. 2ª ed. México: Editorial el Manual Moderno; 1996.
5. Milton JS, Tsokos JO. Estadística para biología y ciencias de la salud. Madrid: Interamericana McGraw Hill; 2001
6. Matesanz R. Cadaveric organ donation.Comparison of legislation in various countries of Europe.Nephrology, Dialysis and Transplantation 1998; 13: 1632-1635.
7. Dominguez-Gil B, Martín MJ, Valentín MO, Scandroglio B, Coll E, Lopez JS, Martinez JM, Miranda B, Matesanz R. Decrease in refusals to donate in Spain despite no substantial change in the population's attitude towards donation. Organs, tissues &cells 2010; 13:17-24.
8. López JS, Martín MJ, Scandroglio B, Martínez JM. Family perception of the process of organ donation.Qualitative psychosocial analysis of the subjective interpretation of donor and nondonor families. The Spanish Journal of Psychology 2008, 11(1): 125-136.
9. Siminoff LA, Burant CJ, Ibrahim SA. Racial disparities in preferences and perceptions regarding organ donation.J Gen Intern Med 2006; 21(9): 995-1000.
10. Valentín M, Coll E & cols. Encuesta poblacional 2009. Actitudes frente a la donación. XXV Congreso Nacional de Coordinadores de Trasplantes. Barcelona 2009. Availableon: http://www.gencat.cat.
11. Shanteau J, Harris RJ. VandenBos G. Psychosocial and behavioral factors in organ donation.Hosp Community Psychiatry 1992; 43:211-214.
12. Martínez JM, López JS, Martín A. Percepción social de la donación en España tras la década de los trasplantes. Nefrología 2001; 21:45-48.
13. Sanner M. A comparison of public attitudes toward autopsy, organ donation, and anatomic dissection.A Swedish survey.JAMA 1994; 271:284-288.
14. Östergren PO, Gäbel H. Influence of social support and study course on attitudes of 18-year-old students toward cadaveric organ donation and transplantation.Transplantation Proceedings 1993; 25:1702-1703.
15. Rando B, Blanca MJ, de Frutos MA. La toma de decisión sobre donación de órganos en la población andaluza. Psicothema 2002; 14:300-309.

ANNEXE

Aragon Transplant Coordination: Opinion Poll

Hospital Clínico Universitario "Lozano Blesa"

Introduction
Good morning/afternoon,
We are carrying out a study to learn more about your thoughts on organ donation and transplants. Your participation is extremely important and useful for us. We would be really grateful if you could answer all our questions. This questionnaire is completely ANONYMOUS. Thank you.

Respondent profile
Age: ..... years Gender: Male ☐ Female ☐
Country of birth: ..... How long have you lived in Spain? ..... Years
Civil status:
☐ Married ☐ Single ☐ Widowed ☐ Separated ☐ Other
Number of children: ☐ 1-2 ☐ 3-4 ☐ More than 4 ☐ None
Level of education: ☐ No education ☐ Basic ☐ Medium ☐ University
Give qualification: (optional) .....
Religion: .....
How important is religion in your life?
☐ Very important ☐ Quite important ☐ Not very important ☐ Not at all

Opinion on the Spanish Health System
1. Have you had any contact with the Spanish health system? ☐ YES ☐ NO
(Have you ever needed to visit doctors and/or nurses in the public health system?)

2. What services in the system have you needed?
☐ Health centres ☐ Specialists ☐ Hospitals ☐ None

3. What is your opinion of the Spanish health system?
☐ Very Good ☐ Good ☐ Fair ☐ Poor ☐ Very Poor

4 - Have you had any contact with Intensive Care Units? ☐ YES ☐ NO
(Have you or a family member/friend/acquaintance ever been hospitalized in an Intensive Care Unit, UCI, CCU or ITU?)

5. What is your opinion of the Intensive Care Units?
☐ Very Good ☐ Good ☐ Fair ☐ Poor ☐ Very Poor
Opinion of organ donation

6. Do you know anything about organ donation? ☐ YES ☐ NO

7. Where did you first find out about organ donation?
(In which country did you hear of, have experience of or learn about organ donation?)
☐ In your country ☐ In Spain ☐ In another country ☐ Nowhere

8. Where do you think one would find patients who could become organ donors?
(People who die and can become organ donors are usually found...?)
☐ At home ☐ At A&E/the E.R. ☐ In any hospital department
☐ In an ICU/CCU/ITU ☐ In theatre ☐ Don't know / no answer

9. Have any of your family members/friends/acquaintances been organ donors?
☐ YES ☐ NO

10. As regards organ donation, what is your current situation?
☐ I have a donor card ☐ I am not a donor, but am willing to be one
☐ I am not a donor and would not be willing to be one ☐ Don't know/No answer

11. Do your family members/friends/acquaintances know your views on donation?
☐ YES ☐ NO

12. Do you know your family members'/friends'/acquaintances' views on donation?
☐ YES ☐ NO

13. If a family member/friend/acquaintance had expressed his or her wish to be an organ donor, would you respect that wish? ☐YES ☐ NO

14. If it were you who had to decide, would you give permission to donate the organs of a family member/friend/acquaintance who had died? ☐ YES ☐ NO

15. Who do you think should give or refuse permission for an organ donation?
(If someone dies and a decision must be made on organ donation, who, in your opinion, should sign the necessary documents?)
☐ Direct family members: parents, children, partner/spouse... ☐ Any family member
☐ Ethnic or cultural community leaders ☐ Religious leader
☐ Others ☐ Don't know/no answer

16. What would be your opinion if you knew that a family member/friend/acquaintance of yours had been an organ donor?
☐ Agree ☐ Don't care ☐ Disagree ☐ Don't know/no answer

17. How do you think hospital staff treats organ donors and their families?
☐ Better than other patients ☐ The same as other patients
☐ Worse than other patients ☐ Don't know/no answer

18. Why would you become an organ donor? (Tick a maximum of 3 options)
(What is/are the most important reason/s for being or becoming an organ donor?)
☐ For living on after death ☐ To avoid a pointless waste of organs
☐ Out of solidarity ☐ For religious reasons
☐ Because of social expectations ☐ Because I might need an organ
☐ Because a family member/friend may need it ☐ To save a life
☐ For financial reasons ☐ Don't know/no answer

19. Why would you NOT be an organ donor? (Tick a maximum of 3 options)
(What is/are the most important reason/s for NOT being an organ donor?)
☐ In case they certify me as dead too soon ☐ Mistrust of healthcare staff
☐ Because they might be used unfairly ☐ For religious reasons
☐ Because I want to keep my body whole ☐ Don't know/no answer
Opinion on organ transplants

20. Do you have any family members/friends/acquaintances who need or have received an organ transplant?
(Is there anyone important to you in need of a transplant, on a waiting list for a transplant or who has received an organ transplant?)
☐ YES ☐ NO

21. If, due to illness, your life depended on a transplant, would you be willing to receive an organ transplant?
☐ YES ☐ NO ☐ Don't know/no answer

22. In order to broaden your knowledge of organ donation and transplants, you go to
☐ Healthcare staff ☐ Associations ☐ Family members
☐ Books/magazines ☐ The internet ☐ Friends/acquaintances
☐ TV/radio programmes ☐ Other ☐ Don't know/no answer

Do you have any comments or suggestions?

Thank you very much for taking the time to answer this survey

TWO YEARS OF EXPERIENCE WITH PROPOFOL IN AN EMERGENCY DEPARTMENT IN FRANCE.

Deux années d'expérience du propofol dans un service d'urgences en France

ROCHE V, LEGAUT C, LUCAS-AMICHI A, ABOUASSAF N, ANDRONIKOF M. Two years of experience with propofol in an emergency department in France. Med Emergency, MJEM 2013; 14: 13-19
Keywords: propofol, emergency, conscious sedation protocol, painful procedures

ABSTRACT

Introduction:The use of conscious sedation protocols (CSP) before painful procedures in the emergency medicine is a new trend in the last few years. Of all the short acting and ultra-short acting sedatives that are used nowadays in France, propofol is the least studied in conscious sedation in the emergency in France whereas it is well used in the Americas for adults and pediatric emergency procedures. It is imperative to evaluate its use in the emergency department in France.

Objectives: Evaluate the efficacy and tolerance of propofol pre painful procedures in the emergency medicine in France

Methods: It's a prospective study over two years for the use of propofol as conscious sedation before painful procedures in the adult emergency medicine. A bolus dose of propofol of 1mg/kg was given, followed by lower doses of maintenance until the desired level off sedation was obtained for the procedure. An analgesic was given as per emergency protocol before the procedure. All patients were tightly monitored in the emergency procedure room for 30minutes. A physician and a registered nurse were responsible for the conscious sedation. Another physician was responsible for the painful procedure where propofol was indicated,

Results:In two years, 50 patients received propofol for conscious sedation pre procedure, 46 entered the study. 30 males and 16 females with average age 53, 5 (S.D. 21.6 [19-94]) average weight 72,8 (S.D. 13.4; [48-110]). The average total dose of propofol was 122mg (S.D. 66.3 [30-370]) the average dose per weight was 1.67 mg/kg (S.D 0.73 [0.5-3.5]). The indications for conscious were: dislocated shoulder (19), dislocated hip prosthesis (15), dislocated ankle (5), dislocated to dislocated elbow (4), dislocated toe (1), dislocated jaw (1), and lumbar puncture (1). The painful procedure was successful in 100% of cases. Six patients (13%) had hypoventilation requiring bag ventilation for less than 5 minutes. 100% of patients were fully awake and stable after 30 minutes. None had any vomiting or undesirable side effect.

Discussion:Conscious sedation is very useful in the emergency medicine. Propofol is a good choice with an onset of 30 seconds, half life of 1-3 minutes and with a titrated dose dependent. The major side effects include hypotension and respiratory depression .The handling and management of possible side effects of propofol sedation depends on the emergency physician skills. In our series, we didn't have any complication that will question its use in the emergency room.

Conclusion: Propofol is an effective drug for a conscious sedation before painful procedures in the emergency medicine.

Authors' affiliation:

Adult Emergency Medicine Dept
Hôpital Antoine Béclère - Clamart, France.
Correspondent author : Dr M. Andronikof
Emergency Medicine,
Hôpital Antoine Béclère (APHP), 157 rue de la Porte de Trivaux, 92140 Clamart, France
E.mail: marc.andronikof@abc.aphp.fr

Article history / info:

Category: Original article
Received: Jan 2010 (Urgence Pratique)
Revised: Feb. 1st, 2013
Original in French: Published online

Conflict of interest statement:

There is no conflict of interest to declare

Valérie Roche

RÉSUMÉ

Introduction: L'utilisation de protocoles de sédation analgésie avant procédure douloureuse (SAP) dans les services d'urgences est une avancée majeure des dernières années. Sédatif hypnotique de délai et de durée d'action ultra courts, utilisé jusqu'à présent en France principalement en anesthésie et en réanimation, le propofol y est peu connu aux urgences alors qu'il est largement utilisé pour les SAP aux urgences adultes et pédiatriques outre-Atlantique. L'évaluation de son utilisation aux urgences dans un environnement français paraissait indispensable.

Objectif: Evaluer l'efficacité et la tolérance du propofol dans un service d'urgences adultes en France.

Méthode: Etude prospective sur deux ans de l'utilisation du propofol pour les SAP dans un service d'urgences adultes. Le propofol était injecté en bolus de 1 mg/kg, suivi éventuellement de réinjections de doses inférieures, jusqu'à l'obtention ou le maintien de l'effet sédatif désiré afin de permettre une procédure douloureuse. Une antalgie préalable était administrée suivant un protocole de service. Tous les malades étaient étroitement surveillés en box d'urgences pendant 30 minutes. Un médecin et une infirmière étaient responsables de la SAP, un autre médecin était chargé de la procédure douloureuse pour laquelle le propofol était indiqué.

Résultats: En deux ans, 50 malades ont eu une SAP par propofol, 46 dossiers sont exploitables, soit 30 hommes et 16 femmes d'âge moyen, 53,5 ans (écart type 21,6 ; extrêmes 19-94), de poids moyen 72,8 Kg (écart type 13,4 ; extrêmes 48-110). La dose totale moyenne de propofol était de 122 mg (écart type 66,3 ; extrêmes 30-370). La dose moyenne/Kg de poids était de 1,67 mg/Kg (écart type 0,73 ; extrêmes 0,5-3,5). Les indications de la SAP étaient : luxation d'épaule (19), luxation de prothèse de hanche (15), luxation de cheville (5), luxation de coude (4), luxation d'orteil (1), luxation de mandibule (1), ponction lombaire (1). Dans 100% des cas, le geste douloureux a pu être réalisé avec succès. Six patients (13%) ont eu une hypoventilation ayant nécessité une ventilation au ballon (< 5 minutes). Six patients (13%) ont eu une hypotension artérielle transitoire s'amendant spontanément en moins de 5 minutes. 100% des patients étaient parfaitement réveillés et stables à 30 minutes. Aucun patient n'a présenté de vomissement ni d'autres effets indésirables.

Discussion: La sédation profonde est très utile aux urgences, et n'a souvent besoin d'être que de courte durée. Le propofol constitue pour cela une molécule de choix : délai d'action de 30 s, demi-vie de 1 à 3 min, effet clinique dose dépendante. Les effets secondaires principaux sont l'hypotension et la dépression respiratoire. Le maniement et la prise en charge des éventuels effets secondaires du propofol lors d'une sédation courte, font partie des compétences de l'urgentiste. Dans notre série, nous n'avons eu aucune complication qui remettrait en cause son utilisation aux urgences.

Conclusion:Le Propofol répond efficacement aux besoins de sédation analgésie avant procédure douloureuse dans un service d'urgences.

Mots Clés: Propofol, urgences, sédation analgésie, procédures douloureuse.

INTRODUCTION

The use of analgesics and sedatives in the emergency room is an emerging revision for patient care in the last few decades. Pain control, whether acute or chronic is a major public health issue. Pain is one of the major complaints to which patient present to the emergency room to seek medical advice after a trauma. Most procedures in the emergency room necessitate patient's relaxation and cooperation for a short duration not longer than few minutes. These procedures are by themselves extremely painful. Patients' cooperation is impossible to obtain in case of pain, agitation or anxiety. Physicians, in addition to patients, are in need of conscious sedation for procedure. As example for painful procedures where conscious sedation is indicated or needed, we have: suturing for pediatric age group, painful suturing for adults such as in-growing toe nail, reduction of a dislocated joint, lumbar puncture, chest tube insertion or orotracheal intubation…

The most common used therapies to obtain pain control and proper sedation in the emergency are morphine and its derivatives. Morphine use is widespread for pain control and its usage is becoming standardized [1]. The most regularly utilized sedatives include: the mixture oxygen-nitrous oxide (Kalinox®) which is the most commonly used for the pediatric age group and sometimes for adult procedures [2,3,4], and the midazolam [5]. The ketamine use which was reduced for several year is emerging recently specially in pediatric age group [6,7]. In the adults, the combination of morphine or fentanyl to midazolam is most common [8,9].

Since the 1990's, propofol use has been increasing [10]. Several publications compared the above-mentioned products alone or in combination for conscious sedation prior to procedures [11-14]. Propofol has been introduced for the use in the emergency department in North America. There are publications about its recommended use [18,19]. In one of the studies, in 74% of cases, the same physician is responsible of the conscious sedation and the procedure itself, in 20% of cases there were two. [20]

Propofol 1% is an intra venous sedative and hypnotic with amnesic properties. It belongs to the class of diidopropylphenols, which is different from the barbiturates or benzodiazepines. It is available in a lipophilic emulsion in an ampoule of 200mg per 20ml. Its onset of action is short (30seconds), its duration of action is brief (5-10minutes). The time to wake up is usually fast (4minutes) and confortable [21-23]. In addition it has anti emetic properties. No aspiration has been reported during its use in the emergency [24]. Its common use for conscious sedation in emergency starts with an intravenous bolus of 1mg/kg followed

if needed by lower doses till obtaining the necessary sedation effect [15,16]. For orotracheal intubation, the initial loading dose is usually 2 to 2.5mg/kg [19]. Its effect is dose dependent and predictable. Its clearance is fast by liver metabolism and volume distribution. Because of its pharmacodynamics, the redosing lasts longer than the initial dose. Its side effects include mainly hypotension and respiratory depression.
When comparing Fentanyl +Propofol versus Ketamine+ midazolam in the pediatric emergency room, it has shown that for the same efficacy, recovery was significantly faster in the propofol group (20min versus 54minutes) and that using average dose of propofol of 4.55mg/kg [25]. In children, the doses are higher than the adults but the pediatric age group has less risk factor for non-tolerating it. Its pharmacokinetics and its easy handling make it a perfect drug to be used in the emergency room. Despite its qualifications and its documented usefulness since many years and in many settings by physicians non anesthesiologists, propofol is not a well known drug by emergency physicians in France [25,26]. So it is logical to assess and evaluate its use in an emergency hospital in France.

OBJECTIVES

Evaluate the efficacy and tolerance of propofol in an adult emergency room.

METHODS

It's a prospective study from January 1st, 2007 till December 31st, 2008 in an adult emergency department in a Parisian suburb. To all the patients we were going to give propofol we noted: age, sex, weight, past medical history, vital signs, indication for sedation, and the propofol dose used, side effects, add-on therapies. Risk factors were defined as all that could increase the risk for adverse reactions: previous history of cardiovascular disease, pulmonary disease, liver disease, obesity… All patients were monitored via EKG monitoring; SpO2 via pulse oxymeter and blood pressure via sphygmomanometer was measured every minute. This monitoring was followed up until the patient woke up. Patient was kept in the procedure room under cardiac monitoring until 30 minutes after the last dose of propofol was given. Side effects include, drop in blood pressure and in SpO2, bradypnea or respiratory pause. Major Side effects included: urgent intubation, inhalation, shock requiring more 1000ml of crystalloids or cardiac arrest. Two emergency physicians and one registered nursed specialized in emergency medicine were required: one physician with the RN were responsible of administering the propofol, of the general observation and monitoring for the side effects, the second physician was responsible in doing the procedure for which the propofol was indicated. All patients were infused with an ante-cubital 500ml of D5W. The loading propofol dose was of 1mg/kg. Both physicians decided the following doses that were given in boluses. The physician who was performing the procedure decided whether the propofol dose was enough or no. The other physician was responsible of the dose and the frequency of boluses. The decision of using the propofol for conscious sedation was left for both physicians. No obligation for its use, it can be used as first line or in case the other alternatives (combination of nitrous oxide and oxygen or midazolam) failed. All patients must receive analgesics prior to procedure as per emergency protocol.

RESULTS

During the two years the study was conducted, the emergency department received a total of 60366 above 15 years of age. 50 patients received propofol for conscious sedation. Four files contained missing information therefore weren't included in the study. **Table1** includes the overall results of the 46 patients (30 men, 16 women). The average age, weight, total dose of propofol and dose per kg are included in the **table 2**. 20 patients (43.4%) had increased risk factor (cardiac disease, respiratory problem…) 44 patients (95.6%) received analgesics (class I, II or III).
The indications for conscious sedation were: shoulder dislocation (19, 4 of which were posterior), hip prosthesis dislocation (15), ankle dislocation (5), elbow dislocation (4), toe dislocation (1), mandibular dislocation (1), lumbar puncture (1). In 100% of cases, the painful procedure was successful. Six patients (13%) had hypoventilation requiring ventilation with an ambu-bag (<5minutes). Six patients (13%) had a transient hypotension that resolved spontaneously in less than 5 minutes. 100% of patients were fully awake and stable at minute 30. No major side effects were noted. None of the patients vomited or had an unexpected side effect.

DISCUSSION

Our prospective study over two years showed that utilization of propofol for deep but brief sedation in the emergency department is very efficacious and very well tolerated for the adult population of all age group with no co-morbidities. All painful procedures for which propofol was indication were performed successfully. No major side effect and no unexpected outcome occurred.
The observed side effects are comparable, in frequency and quality, to those described in the literature [17, 27]. However, our study comprises elderly patients aged between 91 and 94 years maybe the eldest ever published. Extremes that were previously found were 69 years [27], and 78 years [16]. Moreover, some of our patients were suffering from co-morbidities that were rarely mentioned in previous publications (the percentage of patients rated 1 as per ASA score (free of all pathology) is at 62 % according to Miner and Danahy [16].
It seems that we are opening the first series of propofol use in the emergency medicine in France. Propofol use is well defined in the emergency room in the United States, it wasn't practical to conduct new comparative studies with other therapies nor pharmacokinetic studies, both of which were already done. On the other hand, as the medical environment is not comparable between east and west of the Atlantic, we think it's useful to evaluate the propofol use in the in-hospital emergency medicine in France. The results are very conclusive.
Nevertheless, the study presented many bias. First, numerous patients received other products then the propofol for the same indications during the study period. The choice of using the propofol was left to the physicians to decide however most were used to use other type of treatments. This bias didn't prevent us from studying propofol's effect in those patients who received it. Second, the study was conducted in a single center although our emergency department was similar to other departments in France, however we can't know if the results can be extrapolated to other centers. Since propofol is easily handled and the side effects were predictable, the results are most probably reproducible if the practice was widespread. However one must not forgot that

Table 1 : Data of the studied population

	Age	Diagnosis	Weight Kg	Dose mg	Dose mg/kg	Hypotension	Fluid replacement	Hypoventilation	Ventilation with BVM
1	94	Hip dislocation, Prosthesis	50	100	2	0	0	0	0
2	45	Toe dislocation	110	370	3,3	0	0	0	0
3	72	Hip dislocation, Prosthesis	50	100	2	0	0	Yes	5 min
4	49	Shoulder ant dislocation	50	80	1,6	0	0	0	0
5	77	Shoulder post dislocation	66	140	2,12	0	0	Yes	5 min
6	34	Ankle fracture dislocation	80	180	2,25	0	0	0	0
7	91	Hip dislocation, Prosthesis	48	90	1,875	0	0	Yes	2 min
8	78	Hip dislocation, Prosthesis	76	100	1,3	0	0	0	0
9	59	Shoulder ant dislocation	82	110	1,34	0	0	0	0
10	34	Ankle fracture dislocation	66	130	2	0	0	0	0
11	47	Shoulder ant dislocation	79	180	2,25	0	0	Yes	0
12	35	Shoulder post dislocation	78	200	2,5	Yes	0	0	0
13	40	Shoulder post dislocation	65	200	3	0	0	0	0
14	19	Shoulder ant dislocation	70	200	2,85	0	0	0	0
15	74	Shoulder ant dislocation	80	50	0,625	Yes	0	Yes	1 min
16	26	Shoulder ant dislocation	80	80	1	0	0	0	0
17	84	Hip dislocation, Prosthesis	75	150	2	Yes	0	0	0
18	33	Shoulder fracture dislocation	102	200	2	0	0	0	0
19	85	Hip dislocation, Prosthesis	75	90	1,2	Yes	0	Yes	5 min
20	42	Shoulder fracture dislocation	75	40	0,53	0	0	0	0
21	41	Shoulder ant dislocation	70	80	1,14	0	0	0	0
22	75	Hip dislocation, Prosthesis	60	60	1	0	0	0	0
23	19	Shoulder ant dislocation	76	130	2	0	0	0	0
24	70	Ankle fracture dislocation	70	120	1,71	0	0	0	0
25	24	Shoulder post dislocation	73	150	2	0	0	0	0
26	54	Mandible dislocation	54	130	2,4	0	0	0	0
27	55	Hip dislocation, Prosthesis	73	90	1,23	Yes	0	0	0
28	73	Hip dislocation, Prosthesis	80	120	1,5	0	0	0	0
29	47	Lumbar Punction	85	300	3,5	0	0	0	0
30	78	Hip dislocation, Prosthesis	60	120	2	0	0	0	0
31	55	Shoulder ant dislocation	70	70	1	0	0	0	0
32	23	Shoulder ant dislocation	80	200	2,5	0	0	0	0
33	38	Ankle fracture dislocation	80	80	1	0	0	0	0
34	61	Ankle fracture dislocation	60	120	2	0	0	0	0
35	78	Hip dislocation, Prosthesis	60	90	1,5	Yes	0	Yes	0
36	64	Elbow dislocation	70	70	1	0	0	0	0
37	23	Elbow dislocation	70	70	1	0	0	0	0
38	65	Hip dislocation,Prosthesis	80	80	1	0	0	0	0
39	45	Hip dislocation, Prosthesis	95	100	1,05	0	0	0	0
40	82	Shoulder ant dislocation	65	30	0,5	0	0	0	0
41	28	Shoulder ant dislocation	61	60	0,98	0	0	0	0
42	82	Shoulder ant dislocation	65	70	1,07	0	0	0	0
43	33	Elbow dislocation	73	70	0,95	0	0	0	0
44	45	Hip dislocation, Prosthesis	95	80	0,8	0	0	0	0
45	36	Elbow Fracture dislocation	70	150	2,1	0	0	Yes	0
46	49	Hip dislocation, Prosthesis	96	200	2,1	0	0	Yes	0

Table 2: Average of age, weight, total dose of propofol and dose / kg				
	Age	Weight kg	Total dose mg	Dose mg/kg
Average	53,5	72,8	122	1,67
Standard deviation	21,6	13,4	66,3	0,73
Extremes	19-94	48-110	30-370	0,5-3,5

propofol is a very potent hypnotic sedative. Emergency physicians must follow a specific protocol about its use and monitoring prior to its use. One must question the feasibility and safety of propofol use by non-anesthesiologists. This issue was questioned in the states when propofol was first introduced in the practice of emergency physicians, and the answer was obvious [12,28,29]. Several publications have showed its efficacy and safety when used by emergency physicians [14,15, 16,17,19,20,25,27,28]. The adverse effects are predictable and dose dependent. They are of two types: hemodynamics and respiratory. In both cases, they can be handled by a well-formed emergency physician. The handling of the adverse effects is so simple that the short half-life of propofol and its reversibility is even simpler with spontaneous resolution of its side effects. Measuring of the expired CO2, even if it is safer is not mandatory [30,31,32,33]. Lots of questions remained unanswered, whether supplemental oxygen is beneficial or not. [34]. Oxygen supplement via nasal prongs can mask a hypoventilation that is detected with a rise of expired CO2. And shouldn't we monitor the respiratory rate and the chest rise and lower the threshold to active ventilation with ambu-bag for few minutes. And is it better not supplement oxygen because a drop in SpO2 is a faster indicative of hypoventilation. In other hands, pre oxygenation and a higher SpO2 are better factors for systemic tolerance to respiratory pauses and hypotension [28, 32, 34]. Despite all this, our protocol didn't oblige the use of oxygen supplement. Administration of nasal oxygen could take place before the conscious sedation procedure or in the course of it in case of desaturation without bradypnea. We have only mentioned the cases that required ventilation by BVM. A study needs to be done to answer the question of oxygen supplement during conscious sedation. We didn't determine whether the patients had an empty stomach or not, for several reasons. First the conscious sedation is indicated for procedures that don't require delay (one cannot postpone reduction of a dislocated ankle fracture). Second, no publication on conscious sedation in the emergency room has shown any complication related to having a non-fasting stomach. Only one clinical case since its use at Emergency rooms indicates an inhalation but the patient had not eaten for five hours [35]. A pediatric series shows absence of any difference in terms of vomiting and respiratory complications amongst patients whether they had an empty stomach or not [36]. The depth and duration of sedation seem to be a reason for inhalation more than the digestive state [37]. Recommendations over fasting before CSP at emergency that were published are based on the depth and duration of the sedation that is envisaged [38]. However, they remain theoretical and subject to criticism [39]. Our series consist of unselected patients who reach the emergency room to which conscious sedation was mandatory without any delay. All patients met recommendations for fasting for CSP because they did not require a prolonged sedation [38]. None of the patients vomits or inhales.

CONCLUSION

Propofol is an effective drug to be used for conscious sedation for acute and common situations in the emergency room. Widely used in the states, it wasn't a well know drug to be used in the emergency room in France. Our series has shown that in the near future its use will also become widespreadin the emergency situations in France as it is in the United States.

What was known?
Propofol is a sedative and a hypnotic molecule used mainly in ICU and anesthesia
It is widely used in the trans-Atlantic in the emergency room because of its efficacy and it is easily handled.

What this article add:
Propofol is an efficacious drug for conscious sedation before painful procedures in the emergency room.
A qualified emergency physician can use it and can handle any of its undesirable side effects.
Propofol use in the emergency room as a conscious sedation drug before any painful procedure will start to increase in France, as it is being done in the Unites States.

REFERENCES

1. Trinh Duc A, Santin A, Sureau C, Actualisation 2007 de la troisième conférence de consensus de médecine d'urgence de la société francophone des urgences médicales d'avril 1993 : le traitement médicamenteux de la douleur de l'adulte dans un service d'accueil et d'urgences. Douleur 2008; 9: 248-278.
2. Bardeau A, Lecointre C, Pommereau R, Demonts JM. Utilisation du protoxyde d'azote comme seul agent analgésique dans la petite chirurgie de l'enfant ; cahier d'anesthesiologie 1981 ; 29 : 433-442.
3. Pellat JM, Hadaj H, Kaddour A, Long JA, Payen JF, Jacquot C, Aliben JP. Meopa dans le traitement de la douleur. Douleur 2004, 5: 275-281.
4. Otteni JC, Collin F, Fournier S. Protoxyde d'azote ? Conférence d'actualisation 39e congrès national d'anesthésie et de réanimation. 1997; Elsevier, Paris et SFAR.
5. Davis PJ, Tome JA, McGowan FX, et al. Preanesthetic medication with intranasal midazolam for brief pediatric surgical procedures. Anesthesiology 1995;82: 2–5.
6. Green SM, Nakamura R, Johnson NE. Ketamine sedation for pediatric procedures: part 1, a prospective series. Ann Emerg Med 1990;19: 1024–1032.
7. Green SM, Johnson NE. Ketamine sedation for pediatric procedures: part 2, review and implications. Ann Emerg Med 1990;19: 1033–46.
8. Adnet F, Lapostole F. Sédation et anesthésie en médecine d'urgence. In Carli P, Riou B, Télion C, editors. Urgences médico chirurgicales de l'adulte. Rueil-Malmaison Arnette 2004.p. 1397-1402.
9. Kennedy RM, Porter FL, Miller JP, Jaffe DM. Comparison of fentanyl/midazolam with ketamine/midazolam for pediatric orthopedic emergencies. Pediatrics 1998;102: 956-963.
10. Swanson ER, Seaberg DC, Mathias S. The use of propofol for sedation in the emergency department. Acad Emerg Med. 1996; 3:234-238.
11. Taylor DMD, O'Brien D, Ritchie P, et al. Propofol versus midazolam/fentanyl for reduction of anterior shoulder dislocation. Acad Emerg Med.2005; 12: 13-19.
12. Pepperman ML, Macrae D. Comparison of propofol and other sedative use in pediatric intensive care in the United Kingdom. Ped Anesth 1997; 7: 143-153.
13. Kennedy R, Mc Allister J. Midazolam with ketamine : who benefits ? Ann Emerg Med 2000; 35: 297-299.
14. Willman EV, Andolfatto G. A prospective evaluation of ketofol (Ketamine/propofol combination) for procedural sedation and analgesia in the emergency department. Ann Emerg Med. 2007; 49: 23-30.
15. Godambe SA, Eliot V, Matheny D. Comparison of propofol/fentanyl versus ketamine/midazolam for brief orthopedic procedural sedation in a pediatric emergency department. Pediatrics. 2003; 112: 116-123.
16. Miner JR, Danahy M, MochA, et al. Randomized clinical trial of etomidate versus propofol for procedural sedation in the emergency department. Ann Emerg Med. 2007 ;49:15-22.
17. Symington L, Thakore S. A review of the use of propofol for procedural sedation in the emergency department. Emerg Med J. 2006;23:89-93
18. Godwin SA, Caro DA, Wolf SJ, Jagoda AS, Charles R, Marett BE, Moore J. Clinical policy: Procedural Sedation and Analgesia in the Emergency Department. Ann Emerg Med 2005; 45: 177-196.
19. Miner JR, Burton JH. Clinical practice advisory Emergency Department procedural sedation with propofol. Ann Emerg. Med 2007; 50 (2):182-187.
20. Sacchetti A, Stander E, Ferguson N, Maniar G, Valko P. Pediatric Procedural sedation in the community Emergency Department: Results from the ProSCED registry. Pediatr Emerg Care 2007; 23: 218-222.
21. Astra Zeneca, Diprivan, fiche Vidal 2009.
22. Shafer A, Doze VA, Shafer SL. Pharmacokinetics and pharmacodynamics of propofol infusions during general anesthesia. Anesthesiology 1988; 69: 348-356.
23. Shafer SL. Advances in propofol pharmacokinetics and pharmacodynamics. J Clin Anesth 1993; 5: 14S-21S.
24. Martin TM, Nicolson SC, Bargas MS. Propofol anesthesia reduces emesis and airway obstruction in pediatric outpatients. Anesth Analg 1993; 76: 144-148.
25. Rodrigo MR, Jonsson E. Conscious sedation with propofol. Br Dent J 1989;166: 75-80
26. Vargo JJ, Zuccaro Jr G, Dumot JA, Shermock KM, Morrow JB, Conwell DL, Trolli PA, Maurer WG. Gastroenterologist-administrated propofol versus meperidine and midazolam for advanced upper endoscopy:a prospective, randomized trial. Gastroenterology 2002;123:8-16
27. Frazee BW, Park RS, Lowery D, Baire M. Propofol for deep procedural sedation in the emergency department. Am. J Emerg Med. 2005; 23: 190-195.
28. Bassett KE, Anderson JL, Pribble CG. Propofol for procedural sedations in children in the Emergency Department. Ann Emerg Med 2003; 42: 773-782.
29. Green SM, Krauss B. Barriers to propofol use in emergency medicine. Ann Emerg Med. 2008; 52: 392-398.
30. Miner JR, Heegaard W, Plummer D. End-tidal carbon dioxide monitoring during procedural sedation. Acad Emerg Med 2002;9: 275-280.
31. Burton JH, Harrah JD, Germann CA. Does end-tidal carbon dioxide monitoring detect respiratory events prior to current sedation monitoring practices ? Acad Emerg Med 2006;13:500-504.
32. Anderson JL, Junkins E, Pribble C, et al. Capnography and depth of sedation during propofol sedation in children . Ann Emerg Med. 2007; 49: 9-14.
33. Green SM. Research advances in procedural sedation and analgesia. Ann Emerg Med 2007; 49: 31-36.
34. Deitch K, Chudnofsky CR, Dominici. The utility of supplemental oxygen during emergency department procedural sedation and analgesia

with midazolam and fentanyl: a randomized, controlled trial. Ann Emerg Med. 2007 ;49:1-8.
35. Cheung KW, Watson ML, Field S, Campbell SG. Aspiration pneumonitis requiring intubation after procedural sedation and analgesia: a case report. Ann Emerg Med. 2007, 49:462-464
36. Agrawal D, Manzi SF, Gupta R, Krauss B. Procedural fasting state and adverse events in children undergoing procedural sedation and analgesia in a pediatric emergency department. Ann Emerg Med 2003; 42:647-650.
37. Green SM, Krauss B. Pulmonary aspiration risk during emergency department procedural sedation – an examination of the role of fasting and sedation depth. Acad Emerg Med 2002; 9:35-42.
38. Green SM, Roback MG, Miner JR, Burton JH, Krauss B. Fasting and emergency department procedural sedation and analgesia: a consensus-based clinical practice advisory. Ann Emerg Med 2007; 49: 454-461.
39. Paris PM, Yealy DM. A procedural sedation and analgesia fasting consensus advisory: one small step for emergency medicine, one giant challenge remaining. Ann Emerg Med 2007; 49: 465-467.

MED EMERGENCY/URGENCE

Revue Méditerranéenne de Médecine d'Urgence

Mediterranean Journal of Emergency Medicine

Because you deserve the best...

More than a journal, Med Emergency a quarterly publication, is one of the first forums in the Mediterranean and Arab countries where emergency professionals share their experiences and expertise across the region and the whole world. High standards whilst reader friendly.

NEW HEALTH CONCEPT

For information:
info@newhealthconcept.net - www.newhealthconcept.net

FIRE SMOKE INHALATION
MECHANISMS OF TOXICITY AND RECOMMENDATIONS FOR MANAGEMENT.
Intoxication par inhalation de fumées d'incendie
Mécanismes de toxicité et recommandations de prise en charge

MEGARBANE B. LEFORT H. Fire smoke inhalation: mechanisms of toxicity and recommendations for management. Med Emergency, MJEM 2013; 14: 21-30
Keywords: Smoke inhalation; intoxication/poisoning; carbon monoxide; cyanide; antidote; hydroxocobalamine; acute respiratory distress syndrome

ABSTRACT

Smoke inhalation causes systemic and mucosal toxicity due to the asphyxiant and irritant properties of toxic gases. It represents the first cause of death at the fire scene and after hospital admission. Carbon monoxide and cyanide are the main gases produced during combustion in fires: they are responsible for a syndrome of oxygen deprivation. In smoke inhalation victims, loss of consciousness may result from either carbon monoxide or cyanide inhalation, although differentiating the exact role of each of them remains quite impossible. The occurrence of hypotension, abnormal respiratory pattern and/or significant lactic acidosis (with plasma lactate concentration ≥10 mmol/l) is consistent with smoke inhalation induced-cyanide poisoning. Irritant gases contained in smoke are responsible for the ocular and respiratory mucosal injuries. Dysphonia and bronchial ronchi are predictive of delayed lung injury possibly resulting in acute respiratory failure. In smoke inhalation victims, supportive treatment is the cornerstone, based on oxygen administration and aiming at treating respiratory failure. If consciousness impairment persists despite oxygen (100% FiO_2), cyanide intoxication should be suspected. According to the recommendations of the European Society of Emergency Medicine, hydroxocobalamin should be early administered as first-line antidote on the scene. Its efficiency has been well-recognized and its safety well-assessed. After hospital transfer, hyperbaric oxygen should be discussed according to the severity of features attributed to carbon monoxide poisoning. In the presence of irritant gas-related lung injuries, treatment of acute respiratory distress syndrome is based on the usual critical cares. However, final outcome of fire smoke-poisoned survivors remains critical, with possible significant cognitive sequellae.

RÉSUMÉ: L'inhalation de fumées d'incendie est responsable d'une toxicité systémique et muqueuse liée respectivement à la présence de gaz asphyxiants et irritants. Il s'agit de la cause principale de décès sur le site et dans les suites d'un incendie. Le monoxyde de carbone et le cyanure sont les principaux gaz asphyxiants produits lors d'un feu d'habitation : ils sont responsables d'un syndrome de privation en oxygène. Chez une victime d'inhalation de fumées, un trouble de conscience évoque une telle intoxication, sans pouvoir pour autant discriminer entre ces deux gaz toxiques. Par contre, la présence d'une hypotension, d'une anomalie de la ventilation et/ou d'une acidose lactique importante (supérieure ou égale à 10 mmol/L) rend fortement probable une intoxication cyanhydrique associée. L'intoxication par les multiples gaz irritants présents dans les fumées est à l'origine de lésions muqueuses oculaires et/ou respiratoires. La dysphonie et les râles bronchiques à l'auscultation doivent mettre en garde contre le risque de survenue retardée d'une bronchopneumonie avec insuffisance respiratoire aiguë. Le traitement symptomatique est la pierre angulaire de la prise en charge de toute victime d'inhalation de fumées d'incendie. Il inclut oxygénation et traitement de la défaillance respiratoire. Si le trouble de conscience persiste malgré une oxygénation avec une FiO_2 de 100%, une intoxication cyanhydrique doit être suspectée. Selon les recommandations de la Société Européenne de Médecine d'Urgence, l'hydroxocobalamine est alors l'antidote de choix et doit être administré dès la prise en charge pré-hospitalière sur le site de l'incendie. Son efficacité est désormais reconnue et sa bonne tolérance bien documentée. Par la suite, une oxygénothérapie hyperbare doit être discutée en fonction de la gravité des manifestations cliniques attribuées au monoxyde de carbone. En cas de lésions pulmonaires par les gaz irritants, le traitement du syndrome de détresse respiratoire aigue fait appel aux mesures habituelles de réanimation. Le pronostic final d'un patient survivant après une intoxication par fumées d'incendie reste réservé, en raison de possibles séquelles, notamment cognitives.

Mots-clés : Fumées d'incendie ; intoxication ; monoxyde de carbone ; cyanure ; antidote ; hydroxocobalamine ; syndrome de détresse respiratoire aigue

Authors title and affiliation:
Correspondant author :
Professeur Bruno Mégarbane
Medical and Toxicological ICU ,Lariboisière hospital,
INSERM U705, Université Paris-Diderot, Paris, France
bruno-megarbane@wanadoo.fr

Dr Hugues Lefort: Emergency Medical Department, Fire Brigade – Paris.

Article history / info:
Category: Continuous education
Received: Jan 17, 2013
Original in French: published online

Conflict of interest statement: no conflict of interest to declare

INTRODUCTION

Residential fires cause the vast majority of victims whereas warehouse fires cause often simple material losses (1). In fact, fires are the cause of smoke poisoning in addition to the well-known risks of thermal burns and defenestration. These are the leading cause of death, victims being generally found in the fire floor or in the one above. More than 5000 fire deaths are reported in the United States each year, of which 80% are related to smoke inhalation (2). In France, the Departmental Fire and Assistance Services reported, in 2006, 334012 interventions for fires, causing 11533 victims and 341 deaths (3). The annual incidence of poisoning by fire smokes is estimated at 20-40 per 100000 inhabitants in urban areas and the annual mortality 0.5-2 per 100000 inhabitants (4). However, despite all efforts of prevention, these figures have been sadly unchanged for the past 50 years. Residential fires often originate early morning, when people are deeply sleeping; and are closely correlated with vulnerable socio-economic conditions, smoking cigarettes and alcohol consumption by the victims themselves (5, 6).

Poisoning by inhalation of fire smokes combines, to varying degrees, a systemic neurological and cardiac involvement, due to anoxic gases and respiratory and ocular mucosal lesions, due to irritant gases found in smokes. Rescuers, firefighters and emergency physicians must be fully familiar with the management principles of these poisonings, including the diagnostic approach and methods of antidotes administration, because of the vital risks to the victims. The purpose of this overview is to present the latest international recommendations related to the subject.

I- MECHANISMS OF FIRE SMOKE TOXICITY

More than one hundred active ingredients with multiple toxicities are found in the fumes. The thermal degradation of materials produces heat, smoke and toxic gases; and combustion decreases the partial pressure of oxygen in the residential fire. Experimental studies conducted in the combustion chamber have revealed two types of materials thermal degradation: pyrolysis, namely the chemical decomposition of molecules under heat effect leading to flameless gas emission; and combustion corresponding to oxidation with heat and flames. Generated products depend on the nature of the initial fuel, the reached temperature and the richness of oxygen in the atmosphere.

During a fire in a confined space, reduction in fraction of inspired oxygen (FiO_2) can occur in 1-2 minutes from 21% to 5.5%, with a parallel increase in the concentrations of CO and CO_2, respectively at 5% and 10% (7). The central respiratory depression and neurological disorders appear at FiO_2<17%, while at FiO_2<10%, life becomes impossible.

Toxic gases produced during the thermal degradation of materials act either by cellular asphyxia and depression of the central nervous system, or by respiratory tract irritation **(Table 1)**. In experimental models, high concentrations of these toxics caused death. However, lower concentrations are disabling, decelerating the leak and increasing the exposure time, and therefore the resulting morbidity and mortality. Incapacitating and irritating phenomena appear earlier than asphyxial phenomena, their effects being not only additive, but sometimes synergistic. The main toxic fumes in a fire are:

• **Carbon monoxide (CO):** It is constantly produced in fire due to incomplete combustion. The absorption of CO increases during hyperventilation due to the effort to escape the fire. CO attaches to hemoglobin and then limits oxygen transfer to tissues **(Figure 1)**. A value of 40% of carboxyhemoglobin is incapacitating and a value of about 60% is deadly.

• **Carbon dioxide (CO_2):** It is produced in large volumes during a fire. Even if CO_2 is non-toxic by itself, low concentrations are sufficient to result in hyperventilation, facilitating the absorption of other toxic gases. For $FiCO_2$ at 2%, ventilation minute increases by 50%, while it is doubled for $FiCO_2$ at 5% and multiplied by 10 for $FiCO_2$ at 10%. CO_2 also causes respiratory acidosis, thus increasing the cerebral distribution of certain poisons, such as cyanide (CN) (8). The exact mechanism of these changes in tissue distribution is not unique, but corresponds to the increase in cerebral blood flow and to probable changes in the permeability of the blood-brain barrier.

• **Hydrogen cyanide (HCN):** During a residential fire, the combustion of many natural polymers (such as silk or wool) and synthetic polymers (such as polyurethane, polyamide, polyacrylonitrile, and polystyrene) containing nitrogen, generates CN. The nature of the burning material determines the amount of generated CN. Thus, in an experimental combustion chamber, it is possible to obtain about 120, 200, 400 and 1500 ppm of HCN from 1g of foam rubber, wool, polyurethane or polyacrylonitrile, respectively (9,10). At the cellular level, CN binds to the mitochondrial cytochrome oxidase and blocks ATP production by the respiratory chain **(Figure 1)**. CN can kill a human within minutes **(Figure 2)**. The toxicity of HCN measured in monkeys depends on concentration in inspired air and duration of exposure (11). As with CO_2, low concentrations of HCN in the inspired air (up to 80 ppm) lead to hyperventilation, which increases its own absorption and that of other toxic gases. The incapacitation is 20 times stronger than with CO. Exposure to 60 ppm of HCN for 30 minutes causes central nervous system depression, increased ventilation, but is free of cardiovascular effects. Depression becomes severe at 80-150 ppm HCN concentrations. At 196 ppm of HCN, the animal becomes unconscious in 2 minutes, but quickly awakens.

• **Soot:** They are microparticulate aerosols made of heavy hydrocarbons, polycyclic compounds of nitrogen and carbon. They are placed in the respiratory tract according to their size,

forming an adherent film on the bronchial epithelium. Soots are irritating and adsorbed on the surface, and thus can irritate mucous membranes with hypersecretion and scaling, which can cause bronchiolar obstruction. They are also the source of heat transfer, more than gases, therefore representing an important factor in burning both thermal and chemical airways.

• **Water vapor:** They lead to thermal damage at the bronchial tree level, because of their penetration depth and the amount of delivered heat.

• **Aldehydes:** The combustion of carbon chains generates many aldehydes, such as acrolein, formaldehyde, butyraldehyde and acetaldehyde. The acrolein and formaldehyde have a clear pulmonary toxicity, respectively 50 and 5 times as hydrochloric acid.

• **Derivatives of nitrogen:** Nitrogen oxides (NO and NO_2) and ammonia are released by polymers and /or nitrogen additives. Isocyanates are produced by the depolymerisation of polyurethanes. Amines are produced by the hydrolysis of isocyanates or volatilized from certain polymers (e.g.: epoxides, polyurethanes), which are the customary auxiliaries. Nitrogen peroxide reacts with hemoglobin to lead to methemoglobinemia.

• **Anhydrides:** Sulfur dioxide is released by the combustion of natural polyamides (wool, silk, leather), while the acid anhydrides are resulting from certain polyesters or phthalates plasticizers.

• **Mineral acids** (hydrochloric, hydrofluoric, hydrobromic acids) carbon oxyhalides (phosgene ($COCl_2$): thermal degradation of materials containing chlorine (PVC, polymers fluorochlorohydrocarbons) produce hydrochloric acid. Various compounds are produced from Teflons®, depending on temperature and mode of combustion: hydrogen fluoride, carbonyl fluoride, tetrafluoroethylene, hexafluoropropylene, perfluoroisobutylene and hexafluoroethane. These compounds have a significant pulmonary toxicity and, in some cases, additional systemic toxicity.

• **Other gas with systemic toxicity:** In addition to highly irritating sulphur dioxide, other sulfur compounds are found, such as hydrogen sulphide (H_2S). A concentration of about 500 ppm causes coma and acute pulmonary edema. Flame retardants of plastics decrease burns risk but increase toxic risk, particularly convulsions by production of new compounds.

II – DIAGNOSTIC APPROACH

Smoke inhalation is the cause of two different toxic syndromes that may be present at varying degrees: syndrome of cellular deprivation of oxygen due to asphyxiating gases and syndrome of poisoning by toxic gases (12,13). For rescuers, it is essential to identify victims among the exposed people based on a simple clinical approach. The knowledge of cyanide toxidrome allows the administration of the antidote only to patients who need them. Thus, the presence of soot in the upper airways (nose, mouth and sputum) is a sensitive but nonspecific sign of smoke inhalation and therefore of poisoning from the two most dangerous gases, CO and CN. The absence of soot has an excellent negative predictive value.

II – 1 - Syndrome of cellular deprivation of oxygen

Anoxia is expressed by neurological, metabolic, and cardiovascular diseases **(Table II)**. The spectrum of neurological involvement may be limited to headaches, dizziness, weakness, loss of consciousness or reach psychiatric disorders (agitation or confusion), coma, convulsions, and focal neurological deficit. Neurological manifestations can be associated with intoxication by CO, CN, or both. The decline in FiO_2 is also accompanied by the lack of physical co-ordination, depression of the central nervous system, and decrease in muscle strength. The initial loss of consciousness is always a sign of a significant systemic toxicity by asphyxiating gases. It also predicts the inhalation risk and respiratory complications. Central neurological disorders are constant in the case of cyanide poisoning.
Collapse, shock or cardiac arrest is caused by exposure to poison gases, rarely involving CO alone, except for massive exposure (14). The combination of neurological disorder and hypotension should evoke poisoning by CN. The presence of "abnormal breathing", whether polypnea, wide ventilation, hypopnea or apnea, is also highly suggestive of cyanide poisoning.

For a fire victim without extended skin burns, lactacidemia is an excellent biological marker of cyanide poisoning. A concentration ≥ 10 μmol/L is a sensitive and specific indicator of intoxication

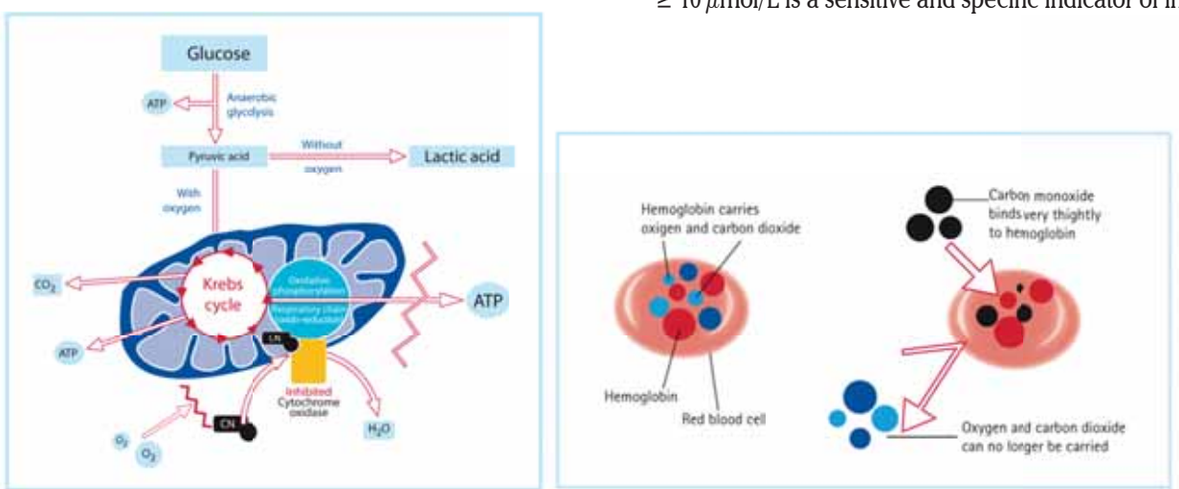


Figure 1 - Mechanisms of toxicity of the two asphyxiating gases present in the fire smokes: Carbon monoxide binds to hemoglobin to give carboxyhemoglobin and thus reduces oxygen transport to the tissues. Cyanide inhibits mitochondrial cytochrome oxidase and blocks the oxidative phosphorylation responsible for ATP production: it causes anaerobic glycolysis and transformation of pyruvate to lactate.

defined by a CN concentration ≥ 40 μmol/L (15). Lactic acidosis only related to CO poisoning is rarely too severe (14). The

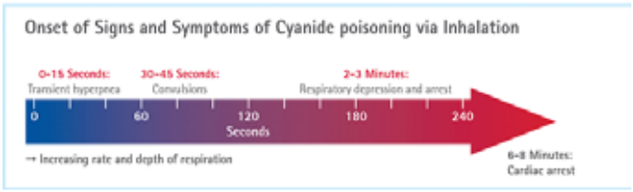


Figure 2 - Cyanide toxicity following inhalation is dependent on exposure time

interpretation of lactate levels must also take into account various factors in practice, such as extended burns, hypoxia, shock, associated trauma, presence of other toxics (ethanol) or use of adrenergic drugs (15,16). CN poisoning should be suspected when lactic acidosis persists after oxygenation and correcting blood volume (17).

Carboxyhaemoglobin and blood CN measurements should be ideally performed on a sample obtained at the fire scene before any treatment (oxygen, antidotes). There is a correlation between CO concentration and severity of poisoning. For fire victims, there is also a significant correlation even low between blood levels of CN and CO, however, making unreliable the prediction of CN concentration in blood from that of CO (18).

It is important to recognize cyanide poisoning, because of the need to administer a specific treatment. The following presentations are suspecting such poisoning:

- Cardiac arrest: Approximately 75% of these patients have a blood concentration of CN ≥ 40 μmol/L.
- Coma and respiratory arrest: CO does not change respiratory frequency while the CN is a cause of sudden apnea.
- An initial loss of consciousness accompanied by dyspnea. Even if a bronchopulmonary bulk may cause dyspnea, lactic acidosis should be suspected, due to CN.

The formal confirmation of the diagnosis is then obtained secondarily by measuring blood CN: 40 μmol/L is considered the threshold for toxicity and 100 μmol/L threshold for lethality.

II – 2 - Syndrome of irritant gases-related toxicity

Mucosal lesions by gas released at the initial stage of the thermal degradation of materials in fire are formed in hours or few days (12,19). Eye irritation is manifested by conjunctivitis and corneal ulceration. It raises concerns for associated acute respiratory distress. Lesions of the tracheo-bronchial tree are manifested by acute respiratory failure that may exist immediately, independently from consciousness disorder. In the vast majority of cases, respiratory failure is still delayed a few hours from exposure. Dysphonia or auscultation abnormalities, such as rhonchi (snoring rhonchi) or sibilants (sharp hissing rhonchi) are evident in more than half of the victims. The presence of rhonchi is predictive of the occurrence of bronchopulmonary co-infection; usually associated with prolonged stay in the intensive care unit; in contrast, sibilants may be transitional and be cleared under bronchodilators (20).

Several types of injuries can co-exist in the respiratory tract, contributing to hypoxemia: laryngeal edema, bronchospasm, bronchial congestion by carbonaceous material, atelectasis, pulmonary edema of delayed onset… Tissue hypoxia is worsened by CO and/or CN poisoning. Cochineal red coloration of the skin in case of high carboxyhemoglobinemia hides any cyanosis. In addition, conventional pulse oximetry, unable to distinguish carboxyhemoglobin from oxyhemoglobin, can generate falsely reassuring SpO_2.

Fire smokes cause chemical bronchial pneumonia and more rarely acute respiratory distress syndrome (ARDS). However, pulmonary infection by community germs (staphylococci, streptococci, anaerobic bacteria) is common during the first

Table I- Main gases and particles in fire smokes

Compounds causing toxicity by cell anoxia
Carbon monoxide (CO)
Hydrogen cyanide (HCN)
Carbon dioxide (CO_2)
Nitrous monoxide (NO)
Anhydrous: sulphur andrid, hydrogen sulphide
Compounds causing toxicity by mucosal irritation
Soot (polycyclic microparticulate compound containing nitrogen and carbon)
Burning water vapor
Aldehydes: acrolein, formaldehyde, butyraldehyde et acetaldehyde
Nitrogen derivatives: nitrous oxide and ammonia, isocyanates and amines
Mineral acids: hydrochloric acid, hydrofluoric and hydrobromic
Carbon oxyhalides: phosgene

Table II- Differences in clinical presentation between victims of carbon monoxide and cyanide poisoning victims

Clinical presentation related to carbon monoxide poisoning
Neurological manifestations
Normal breathing (unless inhalation following a consciousness disorder)
Absence of hemodynamic failure
Low elevation of plasma lactate levels (~ 3 mmol/l)
Post-interval neurological syndrome
Anoxic sequelae
Death
Clinical presentation related to cyanide poisoning
Neurological manifestations
Normal breathing: polypnea, hyperpnea, hypopnea or apnea
Circulatory failure: arterial hypotension, collapsus, shock, cardiac arrest
Significant elevation of plasma lactate levels (≥10 mmol/l)
Anoxic sequelae
Death

few days, with high incidence of aspiration pneumonia, especially in case of coma. This is also a significant condition explaining the need to prolong mechanical ventilation. If chest X-ray is part of the admission record, its prognostic value and specificity of abnormalities remain low. It can be completely normal, even though further development will be unfavorable. Poorly defined and disseminated alveolar-interstitial condensations are the most frequently observed abnormalities. Although abnormal, the images (bronchial thickening, pulmonary edema) do not allow to orient the differential diagnosis between cardiogenic pulmonary edema and lung injury, to support bacterial infection, or to provide adequate prognosis. In addition, hypoxia is not correlated with the extent of X-ray abnormalities. The presence of soot in the nasal or oropharyngeal cavity cannot predict the distal lung damage, but is associated with prolonged mechanical ventilation (21). The systematic implementation of bronchial fibroscopy has been proposed for diagnostic, prognostic, and therapeutic purposes. Some teams offer such a strategy to immediately confirm exposure to fumes and classify lesions. One of the simplest classifications of ENT and tracheo-bronchial injuries is completed in three stages: stage 1 (edema, hyperemia, and hypersecretion), stage 2 (mucous bullous detachment, superficial mucosal ulcers, and exudates) and stage 3 (deep mucosal ulcerations and necrosis). For non-burnt patients, even if bronchial injuries may precede the appearance of arterial blood gases or radiological anomalies, it seems difficult to assign a predictive value. In addition, the appearance of the mucosa may be falsely reassuring by the paleness in patients with collapse. Conversely, in case of burnt patients who have inhaled toxic gases, fiberoptic endoscopy may facilitate intubation in the presence of severe injuries in upper airways, allow bronchial clearance removing mucous debris and soot secretions difficult to mobilize, and predict the risk of death from ARDS (22,23). Pro-inflammatory profile of cytokines measured in plasma or bronchoalveolar lavage fluid in these patients reflects the severity of the lesions of broncho-pulmonary inhalation and is closely correlated with final prognosis (23,24). However, a strong initial hypo-immune response to heat stress appears to be associated with a fatal outcome (25).

III – MEDICAL MANAGEMENT

The main goal when treating a smoke inhalation victim is to ensure satisfactory oxygenation (26,27). After having secured airways, oxygen is delivered to the patient as soon as the pre-hospital stage and, if necessary, tracheal intubation is performed in the presence of respiratory or neurological failure. Finding stridor should draw attention to the risk of rapidly progressing obstruction of the airways. In practice, about 50% of inhalation victims suffering from burns should be intubated. Tracheal intubation should be early in case of dysphonia and dyspnea, even though it is not recommended as prophylaxis. Any delay and/or secondary accidental extubation may lead to death. In case of massive laryngeal edema, a tracheotomy may be necessary immediately.

The treatment of acute respiratory failure due to ARDS usually caused by irritating gas-related bronchial and alveolar injuries is based on the principle of protective ventilation to minimize the risk of barotrauma maintaining a plateau pressure <30 cmH_20. Less conventional techniques of ventilation or oxygenation (high frequency ventilation, percussive ventilation, and extracorporeal membrane oxygenation) have been proposed in refractory cases; however, no controlled studies have been performed in humans in the setting of smoke inhalation, even though hopes to reduce mortality really exist (28).

Curiously, an experimental model seems to suggest a less favorable evolution with Airway Pressure Release Ventilation (APRV) than with conventional ventilation (29). Administration of inhaled nitric oxide has not been specifically evaluated in this indication. It should be noted that fumes are very rich in nitrous monoxide, while its role is not precisely known among fire victims (30).

Effectiveness of ß2-agonists by inhalation route has not been specifically evaluated; however, they be immediately administered to treat bronchospasm and improve ventilatory mechanics (31). Inhaled epinephrine is often used in practice: interestingly, a recent experimental study seems to show an interest in reducing hyperemia, mucosal edema, and deleterious bronchial reactivity after smoke inhalation-related acute lung injury (32). Administration of inhaled antioxidants like N-acetylcysteine or inhaled anticoagulants like heparin is widely practiced (31). Additionally, like γ -tocopherol, several other therapies have been proposed to reduce the damage of ARDS on experimental studies basis (33). Innovative therapies are currently being tested **(Table III)**. Conversely, the use of corticosteroids has not proven effective neither in animal models nor in clinical studies (34). Their administration in burnt victims with inhalation injuries increases even the risk of infection and mortality. However, their prescription can be discussed case by case when bronchospasm refractory to conventional therapy will complicate lesions inhalation. Prescribing prophylactic antibiotics can be harmful. The antibiotic therapy is indicated only for documented infections and will be guided by the results of microbiological samples.

III -1-Treatment of carbon monoxide poisoning associated with smoke inhalation

A fire victim shall receive isobaric oxygen upon discovery (26,27). There is no randomized controlled trial evaluating the value of hyperbaric oxygenation (HBO) on the final outcome of smoke inhalation victims. Thus, although some authors report a possible interest in prophylactic HBO on the level of progression of smoke inhalation-related pulmonary inflammatory injuries (35), the decision to use it should depend only on the suspicion of associated CO poisoning (36). Moreover, HBO does not affect blood CN concentrations, and therefore the need to use a specific treatment (37). Regarding the consequences of CO poisoning, current data show that victims who exhibited no neurological manifestation, even though minor, and who are stable from a hemodynamic point of view, have a very low risk of developing subsequent neurologic sequelae. These patients can be treated with isobaric oxygen therapy. In contrast, in the presence of consciousness disorders, HBO treatment is preferable, if immediately available. Pregnant women, even asymptomatic, should benefit, to prevent fetal hypoxia. Children should also benefit, even if the data regarding the fate of children poisoned by CO fumes are limited (38). There is no consensus on the minimum rate of COHb that imposes an HBOT treatment. Two pitfalls should be avoided in clinical practice: on the one hand, ignorance of clinical signs at the fire scene or upon admission to the hospital, leading to the abstention of hyperbaric therapy, and on the other, in case of HBO unavailability, a worsening of the clinical situation caused by the transfer of an unstable patient because of associated injuries (burns, trauma).

III-2-Treatment of cyanide poisoning associated to smoke inhalation

Many antidotes are available to treat cyanide poisoning (12,25,27,39). Their mechanism of action are well known, but no clinical study has compared their effectiveness. Methemoglobinizing agents (sodium nitrite, amyl nitrite and 4-dimethylaminophenol) are effective, with the strict condition of inducing 20-30% methemoglobinemia. They are hence totally not recommended in a fire context due to their related reduced blood capacity to carry oxygen and vasodilatation that sometimes brutally occurs. Thus, experimentally, these agents have been shown to increase mortality in animals treated for poisoning by mixed CO and CN (40). Sodium thiosulfate increases the speed of CN physiological transformation into thiocyanate by rhodanese of Lang also called hepatic thiosulfate sulfurtransferase: it is effective and well tolerated, but its action is too slow compared to the hyperacute time-course of fire poisoning victims.

EDTA dicobaltique is very effective experimentally, but its bad hemodynamic tolerance and side-effects (vomiting, urticaria, anaphylactoid reactions, and ventricular arrhythmia) are limiting factors. Hydroxocobalamin or vitamin B12 is a large molecule containing a cobalt atom **(Figure 3)**. It acts rapidly by neutralizing the CN without compromising tissue oxygenation (12,39,41). Due to its high affinity for CN, it is able to redistribute it from its target (mitochondrial cytochrome oxidase) into the plasma compartment to form cyanocobalamin, a stable and non-toxic molecule, in a mole-to-mole combination. Hydroxocobalamin features a remarkable tolerance that has been demonstrated not only in patients with suspected CN poisoning by ingestion but also among fire victims having inhaled fumes and being or not intoxicated by CN (42,43). Even in the absence of randomized clinical trials, its effectiveness is now recognized to treat cyanide poisoning related to fire smoke inhalation (41). Moreover, its efficacy and excellent tolerability in children or pregnant women have been assessed in several published clinical cases (44,45). But in the absence of more significant data, its current use should be limited to cases where the benefits go beyond the expected risks. Based on these studies, the European Society for Emergency Medicine (46) and the Australian Resuscitation Council (47) have recommended the use of hydroxocobalamin as first-line antidote at the fire scene itself, in any patient with suggestive features of cyanide poisoning before further confirmation or exclusion based on toxicological analusis. **4A and 4B figures** show the European guidelines for the pre- and intra-hospital management of fire smoke inhalation victims. During a fire, cyanide poisoning is highly probable in the presence of soot in the upper airways and neurological disorders (loss of consciousness particularly) with one of the following three signs: cardiovascular collapse, polypnoea or bradypnea and/or plasma lactate concentration ≥ 10 mmol/l **(Table IV)**. To clarify pre-hospital management **(Figure 4A)**, European recommendations have focused on the persistence of consciousness disorders despite oxygenation with 100% FiO_2 for few minutes, a presentation highly suggesting cyanide poisoning. In these patients and due to its safety, administration of hydroxocobalamin is fully recommended (46). For adults, the initial dose is 5 g and 70 mg/kg for children, without exceeding a maximum of 5 g. Intravenous infusion is mandatory **(Figure 3)**. Treatment effectiveness is evaluated by the improvement in hemodynamic status with catecholamine weaning and lactic acidosis correction. Depending on the severity of poisoning and clinical response, a second dose may be infused in adults (5 g) as in children (without exceeding a maximum of 5 g). This is recommended in case of initial cardiac arrest, persistent shock or absence of fast lactate normalization. After administration of hydroxocobalamin, it is possible to confirm the diagnosis of CN poisoning by measuring the amount of cyanocobalamin excreted in the urine during the first 3 days (48,49). Hydroxocobalamin side-effects are minimal: reversible pink color of the skin, mucous membranes, and urine, reversible facial edema, as well as a transient and usually asymptomatic increase in blood pressure (41). Note, however, the possibility of interference with some laboratory tests like carboxyhemoglobin measurement (50), as well as alarms of some extracorporeal renal replacement devices, which must be recalibrated (51-53). Sodium thiosulfate is recommended in the hospital in case of persistent hyperlactatemia due to cyanide poisoning despite the administration of 10 g of hydroxocobalamin (46). However, in case of simultaneous infusion of sodium thiosulfate and hydroxocobalamin, two separate venous lines should be used because these two molecules are chemically incompatible (47).

Table III – Pharmacological agents and oxygenation devices under investigation for the treatment of acute respiratory distress syndrome (ARDS) resulting from irritant gas inhalation in fire smoke.

Innovative pharmacologic agents
NO synthase inhibitor:
Antioxydants: γ-tocopherol, 21-aminosteroid
Endothelin-I receptor antagonists of (tezosentan)
P-selectin antagonists
Nebulisation of deferoxamine and starch complexes
Nebulisation of amphoteric chelating agents
Optimization of tissue oxygenation
High frequency percussive ventilation
Airway pressure release ventilation
Diffusive volumetric ventilation
Extracorporeal membrane oxygenation (ECMO)
Arteriovenous CO_2 removal devices

IV- COMPLICATIONS AND SEQUELAE

Hospital mortality remains high (30-50%), when extended skin burns (≥ 10% body surface area) exist. Among non-burnt victims, mortality is lower (<10%). Smoke inhalation is associated with either ARDS or with irreversible neurological anoxic injuries. Mortality of fire victims found in cardiac arrest exceeds 80%. The few victims who survive may then suffer from chronic post-anoxic encephalopathy or extremely incapacitating neurological sequelae.

Barotraumatic injuries of mechanical ventilation and hospital-acquired pulmonary infections are the cause of early respiratory

sequelae. Later, other respiratory sequelae may occur: non-specific bronchial hyperreactivity (including the reactive airways dysfunction syndrome), bronchiolitis obliterans, and bronchiectasis (54). Despite very short exposure times to CO, smoke inhalation may represent a cause of post-interval syndrome whose frequency of occurrence has not been established and which may result in potentially serious manifestations including abnormal movements, cortical blindness, and akinetic mutism. Cyanide poisoning may also leave central nervous system sequelae in approximately 20% of survivors (55). Interpretation of brain imaging then requires special expertise, due to similarities and overlapping between CO- and CN-related brain injuries (56). Smoke inhalation may finally lead to irreversible cognitive or emotional disturbances, causing disruption of social and professional life. It is therefore a typical example of poisoning-related chronic disease, which may sometimes be excessively disabling.

Table IV – Indications and methods of hydroxocobalamin administration

Indications
1. Soot around the mouth, nose and/or pharyngeal and/or sputum
2. Neurological disorders (including loss of consciousness)
3. One of the following signs: respiratory abnormalities (bradypnea or polypnea), hypotension, shock, cardiac arrest or lactic acidosis (plasma lactate concentration ≥ 10 mmol/l)
Methods of administration
Reconstitute the 5 g vial with 200 ml of 0.9% NaCl
Turn the bottle upside down several times without stirring for 1 minute
Connect the infusion set provided in the kit
Administer the drug by IV infusion during 15 min

CONCLUSIONS

Fire smokes are responsible for pulmonary and systemic toxicity resulting in the majority of immediate and delayed deaths. CO and CN are the two main cell-asphyxiating and poisonous gases, with potential synergistic toxicities. Oxygenation, including by the route of intubation and mechanical ventilation should always be prompt. In the presence of signs suggestive of cyanide poisoning, an efficient antidote should be immediately administered on the fire scene. Because of its safety and effectiveness, both clearly assessed on relatively large cohorts of patients, hydroxocobalamin is considered to date as the first-line anti-cyanide antidote. Finally, smoke inhalation remains a major cause not only of acute life-threatening organ failures, but also of chronic diseases altering the final functional outcome by possible respiratory and neurological sequelae.

Editor's note
We would like to thank the authors for this comprehensive approach of fire smoke inhalation: its mechanisms and its management.

Aknowledgement
Dr Laurent Domanski,
Prof Jean-Pierre Tourtier,
Emergency Medical Department
Fire Brigade of Paris – France

Photos
Used with the kind attention of the Fire brigade-Paris (BSPP), France

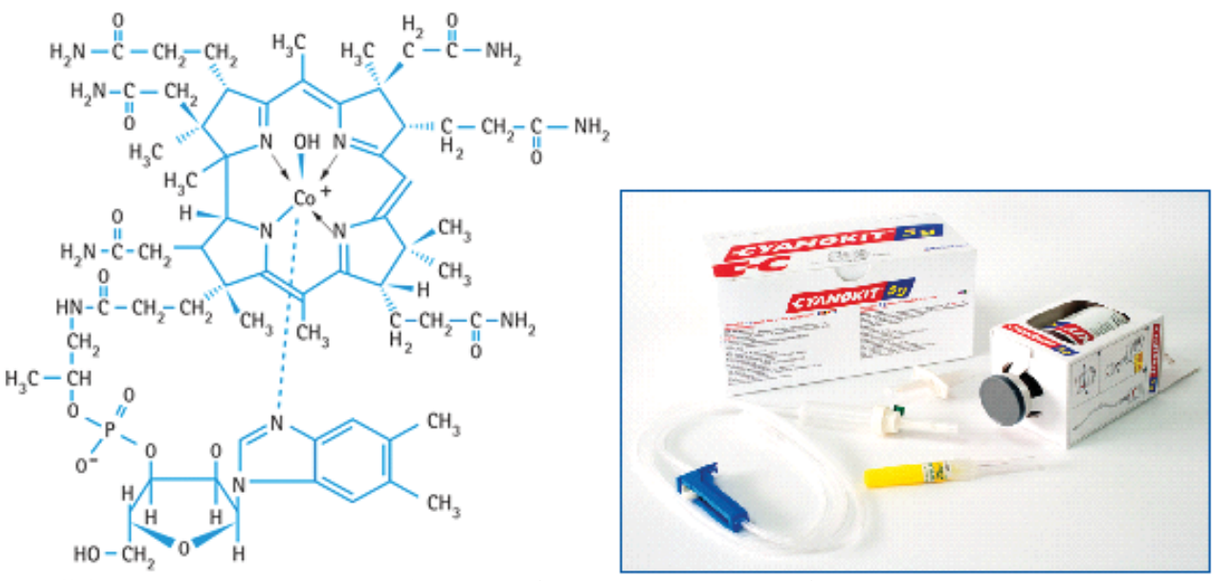


Figure 3 - Hydroxocobalamin: chemical structure and presentation of the treatment together with its infusion set

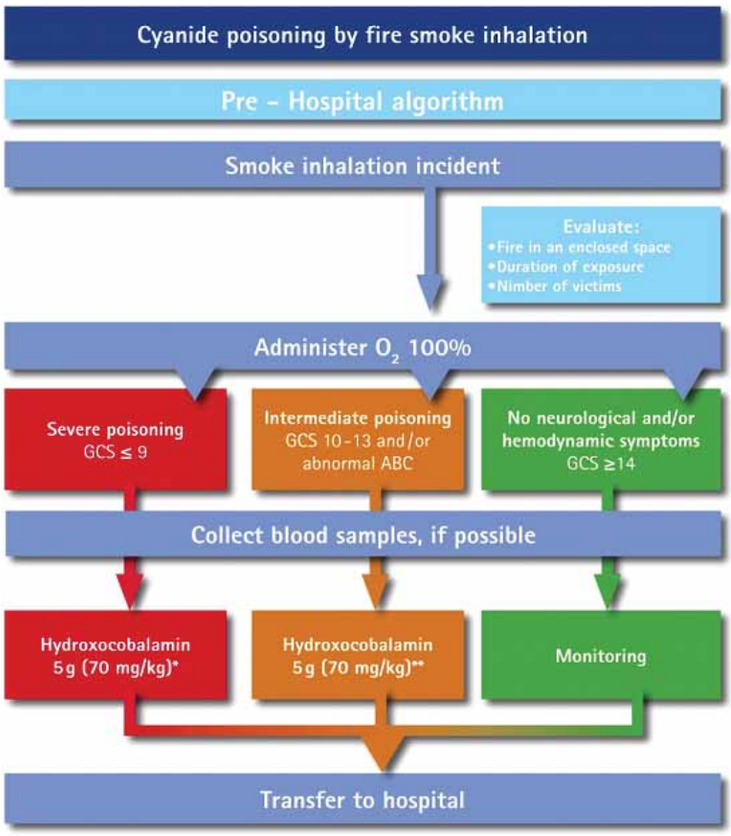


Figure 4A - The European recommendations for the pre-hospital management of fire smoke inhalation victims [adapted from Anseeuw et al. (46)]

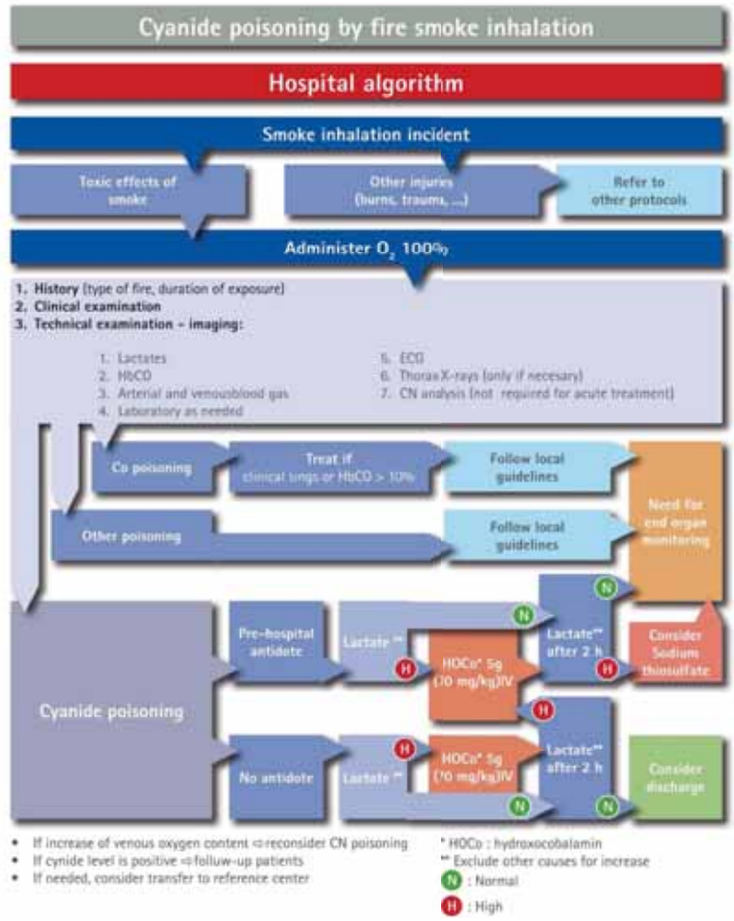


Figure 4B - The European guidelines for hospital care of fire smoke inhalation victims [adapted from Anseeuw et al. (46)]

REFERENCES

1- McGwin G Jr, Chapman V, Rousculp M, Robinson J, Fine P. The epidemiology of fire-related deaths in Alabama, 1992-1997. J Burn Care Rehabil 2000; 21: 75-8.
2- Birky MM, Clarke FB. Inhalation of toxic products from fires. Bull N Y Acad Med 1981; 57: 997-1013.
3- French Ministry of the Interior, Overseas and Territorial Collectivities, statistics of fire and rescue departments. Edition 2007. Directorate of Civil Security and Defence.
4- Diguiseppi C, Edwards P, Godward C, Roberts I, Wade A. urban residential fire and flame injuries: a population based study. Inj Prev 2000; 6: 250-4.
5- Davis CS, Esposito TJ, Palladino-Davis AG, Rychlik K, Schermer CR, Gamelli RL, Kovacs EJ. Implications of alcohol intoxication at the time of burn and smoke inhalation injury: an epidemiologic and clinical analysis. J Burn Care Res 2013; 34:120-6.
6- Rajpura A. The epidemiology of burns and smoke inhalation in secondary care: a population- based study covering Lancashire and South Cumbria. Burns 2002; 28: 121-30.
7- Garnier R, Chataigner D, Efthymiou ML. Toxicité des produits de dégradation thermique des principaux polymères. Données expérimentales. Réan Urg 1990; ii: 411-26.
8- Djerad A, Monier C, Houzé P, Borron SW, Lefauconnier JM, Baud FJ. Effects of respiratory acidosis and alkalosis on the distribution of cyanide into the brain. Toxicol Sci 2001; 61: 273-82.
9- Bertol E, Mari F, Orzalesi G, Volpato I. Combustion products from various kinds of fibers: toxicological hazards from smoke exposure. Forens Sci Int. 1983; 22: 111-6.
10- Alarie Y. The toxicity of smoke from polymeric materials during thermal decomposition. Ann Rev Pharmacol Toxicol 1985; 25: 325-47.
11- Purser DA, Grimshaw P, Berrill KR. Intoxication by cyanide in fires: a study in monkeys using polyacrylonitrile. Arch Environ Health 1984; 39: 394-400.
12- Mégarbane B, Delahaye A, Goldgran-Tolédano D, Baud FJ. Antidotal treatment of cyanide poisoning. J Chin Med Assoc 2003; 66:193-203.
13- Huzar TF, George T, Cross JM. Carbon monoxide and cyanide toxicity: etiology, pathophysiology and treatment in inhalation injury. Expert Rev Respir Med 2013; 7:159-70.
14- Benaissa ML, Mégarbane B, Borron SW, Baud FJ. Is elevated plasma lactate a useful marker in the evaluation of pure carbon monoxide poisoning? Intensive Care Med 2003; 29:1372-5.
15- Baud FJ, Barriot P, Toffis V, Riou B, Vicaut E, Lecarpentier Y, Bourdon R, Astier A, Bismuth C. Elevated blood cyanide concentrations in victims of smoke inhalation. N Engl J Med 1991; 325: 1761-6.
16- Baud FJ, Borron SW, Mégarbane B, Trout H, Lapostolle F, Vicaut E, Debray M, Bismuth C. Value of lactic acidosis in the assessment of the severity of acute cyanide poisoning. Crit Care Med 2002; 30:2044-50.
17- Barillo DJ, Goode R, Esch V. Cyanide poisoning in victims of fire : analysis of 364 cases and review of the literature. J Burn Care Rehab 1994; 15: 46-57.
18- Grabowska T, Skowronek R, Nowicka J, Sybirska H. Prevalence of hydrogen cyanide and carboxyhaemoglobin in victims of smoke inhalation during enclosed-space fires: a combined toxicological risk. Clin Toxicol (Phila) 2012; 50: 759-63.
19- Demling RH. Smoke inhalation lung injury: an update. Eplasty 2008; 8:e27.
20- Hantson Ph, Butera R, Clemessy JL, Michel A, Baud FJ. Early complications and value of initial clinical and paraclinical complications in victims of smoke inhalation without burns. Chest 1997 ; 111 : 671-5.
21- Ikonomidis C, Lang F, Radu A, Berger MM. Standardizing the diagnosis of inhalation injury using a descriptive score based on mucosal injury criteria. Burns 2012; 38: 513-9.
22- Masanes MJ, Legendre C, Lioret N, Maillard D, Saizy R, Lebeau B. Fiberoptic bronchoscopy for the early diagnosis of subglottal inhalation injury : comparative value in the assessment of prognosis. J Trauma 1994 ; 36 : 59-67.
23- Albright JM, Davis CS, Bird MD, Ramirez L, Kim H, Burnham EL, Gamelli RL, Kovacs EJ. The acute pulmonary inflammatory response to the graded severity of smoke inhalation injury. Crit Care Med 2012; 40: 1113-21.
24- Davis CS, Janus SE, Mosier MJ, Carter SR, Gibbs JT, Ramirez L, Gamelli RL, Kovacs EJ. Inhalation Injury Severity and Systemic Immune Perturbations in Burned Adults. Ann Surg 2012 (in press).
25- Davis CS, Albright JM, Carter SR, Ramirez L, Kim H, Gamelli RL, Kovacs EJ. Early pulmonary immune hyporesponsiveness is associated with mortality after burn and smoke inhalation injury. J Burn Care Res 2012; 33: 26-35.
26- O'Brien DJ, Walsh DW, Terriff CM, Hall AH. Empiric management of cyanide toxicity associated with smoke inhalation. Prehosp Disaster Med 2011; 26: 374-82.
27- Lawson-Smith P, Jansen EC, Hyldegaard O. Cyanide intoxication as part of smoke inhalation--a review on diagnosis and treatment from the emergency perspective. Scand J Trauma Resusc Emerg Med 2011; 19:14.
28- Asmussen S, Maybauer DM, Fraser JF, Jennings K, George S, Keiralla A, Maybauer MO. Extracorporeal membrane oxygenation in burn and smoke inhalation injury. Burns 2013; 39: 429-35.
29- Batchinsky AI, Burkett SE, Zanders TB, Chung KK, Regn DD, Jordan BS, Necsoiu C, Nguyen R, Hanson MA, Morris MJ, Cancio LC. Comparison of airway pressure release ventilation to conventional mechanical ventilation in the early management of smoke inhalation injury in swine. Crit Care Med 2011; 39: 2314-21.
30- Soejima K, Traber LD, Schmalstieg FC et al. Role of nitric oxide in vascular permeability after combined burns and smoke inhalation injury. Am J Respir Crit Care Med 2001; 163: 745-52.

31- Toon MH, Maybauer MO, Greenwood JE, Maybauer DM, Fraser JF. Management of acute smoke inhalation injury. Crit Care Resusc 2010;12: 53-61.
32- Lange M, Hamahata A, Traber DL, Cox RA, Kulp GA, Nakano Y, Traber LD, Herndon DN, Enkhbaatar P. Preclinical evaluation of epinephrine nebulization to reduce airway hyperemia and improve oxygenation after smoke inhalation injury. Crit Care Med 2011; 39:718-24.
33- Yamamoto Y, Enkhbaatar P, Sousse LE, Sakurai H, Rehberg SW, Asmussen S, Kraft ER, Wright CL, Bartha E, Cox RA, Hawkins HK, Traber LD, Traber MG, Szabo C, Herndon DN, Traber DL. Nebulization with γ-tocopherol ameliorates acute lung injury after burn and smoke inhalation in the ovine model. Shock 2012; 37: 408-14.
34- Nieman GF, Clark WR, Hakim T. Methylprednisone does not protect the lung from inhalation injury. Burns 1991 ; 17 : 384-90.
35- Thom SR, Mendiguren I, Fisher D. Smoke inhalation-induced alveolar lung injury is inhibited by hyperbaric oxygen. Undersea Hyperb Med 2001; 28: 175-9.
36- Hart GB, Strauss MB, Lennon PA, Whiteraft DD. Treatment of smoke inhalation by hyperbaric oxygen. J Emerg Med 1985; 3: 211-5.
37- Lawson-Smith P, Jansen EC, Hilsted L, Hyldegaard O. Effect of hyperbaric oxygen therapy on whole blood cyanide concentrations in carbon monoxide intoxicated patients from fire accidents. Scand J Trauma Resusc Emerg Med 2010; 18:32.
38- Chou KJ, Fisher JL, Silver EJ. Characteristics and outcome of children with carbon monoxide poisoning with and without smoke exposure referred for hyperbaric oxygen therapy. Pediatr Emerg Care 2000; 16: 151-5.
39- Borron SW, Baud FJ. Antidotes for acute cyanide poisoning. Curr Pharm Biotechnol 2012; 13: 1940-8.
40- Norris JC, Moore SJ, Hume AS. Synergistic lethality induced by the combination of carbon monoxide and cyanide. Toxicology 1986 ; 40 : 121-9.
41- Thompson JP, Marrs TC. Hydroxocobalamin in cyanide poisoning. Clin Toxicol (Phila) 2012; 50:875-85.
42- Borron SW, Baud FJ, Barriot P, Imbert M, Bismuth C. Prospective study of hydroxocobalamin for acute cyanide poisoning in smoke inhalation. Ann Emerg Med 2007; 49: 794-801.
43- Borron SW, Baud FJ, Mégarbane B, Bismuth C. Hydroxocobalamin for severe acute cyanide poisoning by ingestion or inhalation. Am J Emerg Med 2007; 25: 551-8.
44- Roderique EJ, Gebre-Giorgis AA, Stewart DH, Feldman MJ, Pozez AL. Smoke inhalation injury in a pregnant patient: a literature review of the evidence and current best practices in the setting of a classic case. J Burn Care Res. 2012 Sep-Oct;33(5):624-33.
45- Breton D, Jouvet P, de BJ, Delacourt C, Hubert P. [Toxicity of fire smoke. Apropos of 2 pediatric cases] . Arch Fr Pediatr 1993; 50: 43-45 .
46- Anseeuw K, Delvau N, Burillo-Putze G, De Iaco F, Geldner G, Holmström P, Lambert Y, Sabbe M. Cyanide poisoning by fire smoke inhalation: a European expert consensus. Eur J Emerg Med 2013; 20: 2-9.
47- Reade MC, Davies SR, Morley PT, Dennett J, Jacobs IC; Australian Resuscitation Council. Review article: management of cyanide poisoning. Emerg Med Australas. 2012 Jun;24(3):225-38.
48- Houeto P, Hoffman JR, Imbert M, Levillain P, Baud FJ. Relation of blood cyanide to plasma cyanocobalamin concentration after a fixed dose of hydroxocobalamin in cyanide poisoning. Lancet 1995 ; 346 : 605-8.
49- Schwertner HA, Valtier S, Bebarta VS. Liquid chromatographic mass spectrometric (LC/MS/MS) determination of plasma hydroxocobalamin and cyanocobalamin concentrations after hydroxocobalamin antidote treatment for cyanide poisoning. J Chromatogr B Analyt Technol Biomed Life Sci. 2012; 905:10-6.
50- Livshits Z, Lugassy DM, Shawn LK, Hoffman RS. Falsely low carboxyhemoglobin level after hydroxocobalamin therapy. N Engl J Med 2012; 367: 1270-1
51- Sutter M, Tereshchenko N, Rafii R, Daubert GP. Hemodialysis complications of hydroxocobalamin: a case report. J Med Toxicol 2010; 6: 165-7.
52- Abdelmalek J, Thornton S, Nizar J, Schneir A, Sanchez AP. Successful use of continuous renal replacement therapy after hydroxocobalamin administration. Dial. Transplant 2011; 40: 415-17.
53- Sutter ME, Clarke ME, Cobb J, Daubert GP, Rathore VS, Aston LS, Poppenga RH, Ford JB, Owen KP, Albertson TE. Blood leak alarm interference by hydoxocobalamin is hemodialysis machine dependent. Clin Toxicol (Phila) 2012; 50: 892-5.
54- Hsu TH, Kou YR. Airway hyperresponsiveness to bronchoconstrictor challenge after wood smoke exposure in guinea pigs. Life Sci 2001; 68: 2945-56.
55- Alarie Y. Toxicity of fire smoke. Crit Rev Toxicol 2002; 32: 259-89.
56- Baud F, Boukobza M, Borron SW. Cyanide: an unreported cause of neurological complications following smoke inhalation. BMJ Case Rep 2011; 2011.

TEST YOUR KNOWLEDGE: HOW TO MANAGE A SMOKE INHALATION VICTIM?

Que faire chez une victime d'inhalation de fumées d'incendie?

MEGARBANE B. How to manage a smoke inhalation victim? Med Emergency, MJEM 2013; 14: 31-34
Keywords: Smoke inhalation; cyanide; carbon monoxide; oxygen; hydroxocobalamin.

ABSTRACT

Smoke inhalation is responsible for systemic toxicity mainly related to carbon monoxide and cyanide as well as mucosal injuries of the respiratory tract due to irritant gases. Loss of consciousness as well as coma suggest asphyxic gas inhalation, although distinguishing between carbon monoxide and cyanide is quite impossible. In contrast, occurrence of apnea, cardiac failure, and/or major lactic acidosis (>10 mmol/l) highly suggest smoke inhalation-associated cyanide poisoning. Supportive care is the cornerstone of management of smoke inhalation victims and consists in adequate oxygenation and treatment of acute respiratory failure. When cyanide poisoning is suspected, hydroxocobalamin (Cyanokit®) is the recommended first-line antidote that was proved to be efficient and safe.

RÉSUMÉ: L'inhalation de fumées d'incendie est responsable d'une toxicité systémique liée principalement au monoxyde de carbone et au cyanure ainsi que de lésions muqueuses de l'arbre respiratoire dues aux gaz irritants. Une perte de connaissance ou un coma évoquent un gaz asphyxiant sans pouvoir discriminer le monoxyde de carbone du cyanure. Par contre, l'apparition d'une apnée, d'une défaillance hémodynamique et/ou d'une acidose lactique majeure (>10 mmol/l) font suspecter une intoxication cyanhydrique associée. Le traitement symptomatique est l'élément fondamental de la prise en charge et consiste à assurer une oxygénation efficace et traiter la défaillance respiratoire aiguë. En cas de suspicion d'intoxication cyanhydrique, l'hydroxocobalamine (Cyanokit®) est l'antidote de première ligne, efficace et sans danger.

Mots-clés : Inhalation de fumées ; cyanure ; monoxyde de carbone ; oxygène ; hydroxocobalamine.

CASE REPORT

A 55-year old man is discovered in cardiopulmonary arrest by the fireman brigade behind the door of his apartment in fire. He is rapidly extracted by the first aid responders outside to the building hall. At the arrival of the Emergency Medicine Services, the patient is in a hypotonic, hyporeflexic and areactive coma with a Glasgow coma scale of 3, without focal neurological symptoms, intermediate light reactivity of pupils. His vital signs are as follows: Blood pressure 82/58 mmHg, heart rate 88/min respiratory rate 5/min with agonic gasping. There are traces of soot on his face, in his noose and in the oral cavity as well as superficial burns of his two palms. He is intubated in a rapid sequence based on a combination of etomidate and suxamethonium and ventilated with 100% FiO_2. Few minutes later, his SpO_2 is around 91% and ABGs made with a portable machine show the followings: pH of 6.85, PaO_2 of 150 mmHg, $PaCO_2$ of 65 mmHg, bicarbonates of 3 mmol/l, and SaO_2 of 98%. His plasma lactate concentration is 12.5 mmol/l. The patient is immediately transferred to the ICU for further management.

BSPP/BCOM/Pascal Burner©

QUESTIONS

Question 1- To which toxic gazes the patient could have been exposed?
A- Carbone monoxide (CO)
B- Carbone dioxide
C- Hydrogen cyanide (HCN)
D- Steam
E- Mustard gas

Question 2- Among the following affirmations about fires, which one is correct?
A- Fire casualties have been significantly decreasing during the last decade because of preventive measures.
B- The main causes of death in fire are due to the burns' consequences.
C- The toxicity of fire smoke is limited to carbone monoxide.
D- Smokes expose to the risk of upper airway irritation.
E- Soots cannot reach the bronchi because of the important weight of the particles.

Question 3- Among the following propositions on fire smoke inhalation, which ones are correct?
A- In a person discovered on a fire scene, the absence of soot traces on the face and the ENT region make fire smoke inhalation less probable.
B- All victims of fire smoke inhalation have skin burns.
C- A moderate hypotension associated with polypnea doesn't indicate a vital risk.
D- Plasma lactate concentration rarely increases following fire smoke inhalation.
E- There is no risk of sequelae if a smoke fire intoxicated patient survives.

Question 4- Among the following findings regarding the ABGs interpretation, which ones were present in our patient?
A- Metabolic acidosis of lactic origin.
B- Mixed acidosis
C- Hyperventilation to compensate acidosis
D- Alveolar hypoventilation
E- Severe Hypoxemia

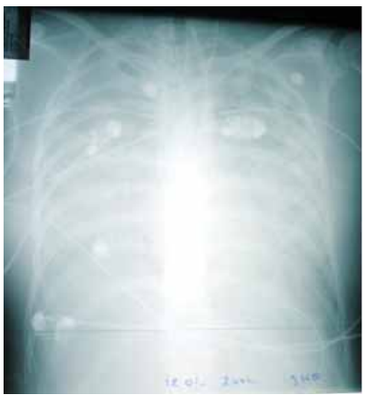
Question 5- Among the following statements regarding the biological tests to be done in case of fire smoke inhalation, which ones are wrong?
A- SpO_2 is a faithful reflect of SaO_2.
B- Carboxyhemoglobin (COHb) measured two hours after the patient's transfer to the ICU remain interpretable identically as if it was done on the fire scene.
C- Initial increase in plasma lactate concentration is explained by mitochondrial dysfunction due to cyanide.
D- Measurement of blood cyanide concentration is essential before giving antidote.
E- There is an excellent correlation between the level of carboxyhemoglobin and the rise in blood cyanide concentration.

Question 6- Among the following measures, which ones are not adequate to treat a fire smoke inhalation victim?
A- Oxygen therapy with a BVM
B- Intravenous administration of steroids
C- Hyperbaric oxygen therapy
D- Administration of a methemoglobin agent (4-dimethylaminophenol)
E- Infusion of hydroxocobalamin (Cyanokit®)

Question 7- Among the following statements regarding the modality and administration risks of treatment with hydroxocobalamin (Cyanokit®) in a fire smoke inhalation victim, which ones are correct?
A- The recommended dose is 5 g in adults and 70 mg/kg in children.
B- This dose should be repeated in case of cardiac arrest.
C- Hydroxocobalamin administration should be made by intravenous flash route.
D- Hydroxocobalamin administration is associated with pink teguments coloration.
E- Hydroxocobalamin administration leads for transitory hypotension.

EVOLUTION

Due to the suspicion of associated cyanide intoxication, the patient benefited from hydroxocobalamin administration on the scene in parallel to the supportive treatments. He recovered a normal blood pressure without catecholamine. He also presented signs of waking up. Nevertheless, due to an extensive pneumonia responsible for acute respiratory distress syndrome (ARDS) due to smoke-related injuries, he was sedated and kept intubated for 10 days to allow the healing of pulmonary lesions. Because of associated intoxication by carbon monoxide (COHb measured at 21% upon management), hyperbaric oxygen therapy (2,5 ATA for 1h) was performed a few hours after ICU admission as soon as his cardiovascular situation improved. Antibiotics were included in his treatment and adapted to bacteria observed on the culture of his distal pulmonary swabs. The final outcome was favorable with extubation at day 10, ICU discharge at day 15 and recovery at home.



ARDS

ANSWERS / SOLUTIONS

Question 1 – A, B, C, D

In case of fire, several toxic gases emanate during the thermal degradation of materials [1] and act, whether by cellular asphyxia mainly leading to central nervous system depression (carbon monoxide, cyanide and hydrogen sulphide), or by irritation of respiratory tract mucosa (soot, aldehydes, anhydrous substances, and mineral acids). Carbon monoxide is constantly produced in a fire, resulting from the incomplete combustion of materials containing carbon (wood, oil products) in the absence of oxygen. Hydrogen cyanide, also called hydrocyanic acid, is produced from several materials containing nitrogen, whether natural (example: silk, wool) or synthetic (example: polyurethane, polyamide, polyacrylonitrile). Carbon dioxide (CO_2) is also produced in large quantities in a fire. Although it is not toxic by itself, its indirect effects

shall not be underestimated. Therefore, low concentrations of CO_2 increase the respiratory frequency and tidal volume, facilitating the absorption of other toxic gases. Water vapor represents an important reservoir, inducing severe thermal lesions of the respiratory tract, in relation to the deepness of its penetration and the quantity of given heat. Mustard gas is a cytotoxic chemical compound and a blistering agent used as chemical weapon during the World War I, inflicting to the enemy chemical burns in the eyes, the skin, and the mucous membranes. It is not present in fire smokes.

Question 2 – D

The incidence of intoxications by fire smokes does not decrease, despite all the means of prevention. In the United States, it amounts to around 20-40 cases for 100 000 inhabitants per year in urban zones, with a mortality rate of 0.5-2 for 100 000 inhabitants per year, rather constant during the past 50 years. Around 80% of the cases of death during a fire are related to toxic smoke inhalation [1]. Fires are responsible for thermal burns, traumatisms by defenestration, and poisonings by smoke inhalation. Clinical features include eye, respiratory and mucous irritation due to the irritating gases present in the smokes, as well as systemic neurological, metabolic, respiratory and cardiovascular impairments, secondary to cellular anoxia by asphyxiating gases. Soots are also micropraticulate aerosols of heavy hydrocarbons and of carbon and nitrogenous polycyclic compounds. They are deposited in the respiratory tract according to their granulometry and constitute an adhesive film to the bronchial epithelium. These particles are loaded with irritants, absorbed at their surface, and can induce mucous caustic lesions, with hypersecretion and desquamation, threatening to provoke bronchiolar obstructions. Finally, soots generates significant thermal transfer, which is more marked than for gases, thus representing an important burning factor for airways, whether thermal or chemical.

Question 3 - A

The first sign supporting fire smoke inhalation is the presence of soot in the upper airways (nose, mouth and expectoration) [1,2]. The absence of soot has an excellent negative predictive value. Conversely, skin burns are not constant in fire victims. The hand/face localization characterizes the patient who has tried to protect himself from flames attacks. The circulatory collapse or cardiac arrest results from exposure to asphyxiating gases, rarely involving only carbon monoxide, except in case of massive exposure. Dyspnea may result from metabolic acidosis due to cyanide poisoning, even if an alternative respiratory cause can be suspected like pulmonary edema or aspiration. Hypotension and polypnoea are the warning symptoms of cyanide poisoning with vital risks. Hyperlactatemia, which is common in victims of smoke inhalation, is mostly directly related to the cellular toxicity of cyanide which blocks the oxidative phosphorylation of mitochondria. However, its interpretation must take into account various factors, like extensive burns, hypoxia, hypotension, associated trauma, presence of other toxic substances, and the use of adrenergic drugs.

In case of non-burnt victims, mortality is about 10% [1,2] and linked either to the initial irreversible anoxic neurological pain or to the respiratory lesions in relation to irritating gases. Mortality rate of fire victims suffering from cardiac arrest exceeds 80%. At a later stage, other respiratory sequelae may appear as the Reactive Airways Dysfunction Syndrome, obliterative bronchiolitis or bronchiectasis.

Question 4 – A,B,D,E

Blood gas analysis in our patient reveals a mixed acidosis with a metabolic part from lactic origin (with a probable anion gap, given the major lactatemia) and a respiratory part related to alveolar hypoventilation. Severe hypoxemia is also present with a PaO_2/FiO_2 ratio of about 150 mmHg.

Hypoxemia is quasi-constant upon ICU admission of smoke inhalation victims. Possible causes are numerous and include: laryngeal obstruction, bronchial obstruction by carbonaceous or necrotic material, bronchospasm, atelectasis, delayed onset pulmonary edema, pulmonary superinfection, etc. Chemical bronchopneumonia as in our patient can cause ARDS, requiring a chest radiography which does not exclude the diagnosis

even if subnormal in comparison to admission. Apparition of diffuse alveolar opacities is delayed in comparison with clinical presentation.

Question 5 – A,B,D,E

SpO_2 obtained using a traditional pulse oximeter is based on an optical measurement with two wavelengths only. It can be falsely increased in comparison with SaO_2 measured by CO-oximetry using spectrophotometry. First-generation pulse oximeters do not distinguish between carboxyhemoglobin (COHb) and oxyhemoglobin (HbO_2), because light absorption is very similar for both molecules on the selected wavelengths. Thus, for a COHb level at 20% and HbO_2 at 75% measured using CO-oximetry, SpO_2 is at 95%.

Measurement of carboxyhemoglobin and blood cyanide concentration should be performed based on a sample obtained at the fire scene, preferably before any antidote administration. Since cyanide poisoning is life-threatening, it is clear that the administration of specific treatments (oxygen and hydroxocobalamin) must be done before any results of blood cyanide and guided only by the presence of a cyanide toxidrome. COHb level should be interpreted according to the smoking status of the subject (N <5% for non-smokers and <10% for smokers), the period elapsed since the cessation of exposure to carbon monoxide, and the amount of oxygen (FiO_2 and duration of administration) received prior to the measurement. Therefore, its value at the time of exposure should be determined, based on the COHb value measured upon ICU admission, taking into account time and oxygen amount. For this extrapolation, we

use COHb half-life which is ~300 min in air and ~60 min under normobaric oxygen. Then, based on the theoretical value of COHb calculated immediately following exposure, we can find a correlation between the blood levels of carbon monoxide and the severity of poisoning.
Lactate production is mainly related to mitochondrial oxidative dephosphorylation due to the attachment of cyanide on cytochrome oxidase. The lactacidemia is directly correlated with the concentration of cyanide in fire victims without extended burns. At admission, a plasma lactate concentration ≥ 10 mmol/L is a sensitive and specific indicator of intoxication, defined by a blood cyanide concentration ≥ 40 mmol/L.
There is a significant, but low, correlation between blood levels of cyanide and carbon monoxide, making it nevertheless unreliable in predicting the blood concentration of cyanide based on that of carbon monoxide. Thus, fire smoke-related deaths are due to carbon monoxide alone, some due to cyanide alone and others because of their combination, with probably an additional synergy between these two gases. Please note that few cases of death can't be explained by either carbon monoxide or cyanide alone: they involve other toxic substances in the smoke, but the exact mechanism of toxicity is not established.

Question 6 – B,D

The major treatment of smoke inhalation victims is oxygen [1-4]. It is an antidote of the two main toxic gases, carbon monoxide and cyanide, allowing reversing tissue hypoxia. Decision to use hyperbaric oxygen therapy depends on the severity of associated carbon monoxide poisoning. As for our patient, hyperbaric oxygen therapy is preferable if available immediately in the presence of consciousness disorders and an elevated COHb level.
Treatment of cyanide poisoning due to smoke inhalation relies on hydroxocobalamin as first-line antidote based on to the latest European and Australian recommendations [3,4]. Methemoglobin agents (nitrites, 4-dimethylaminophenol) could theoretically be effective in reducing cyanide toxicity, but induced methemoglobin should reach 20 to 30% to be effective. These molecules are hence not recommended in the context of smoke inhalation [1-4], since they decrease proportionately the oxygen-carrying capacity and can also cause vasodilation which can sometimes be brutal.

Question 7 – A,B,D

Hydroxocobalamin is the first-line treatment of cyanide poisoning due to smoke inhalation, according to the latest international recommendations [1,2]. Initial dose is 5 g for adults and 70 mg/kg for children suffering from neurological, respiratory (polypnea or bradypnea), and/or circulatory disorders. The bottle of 5 g should be diluted in 200 ml of 0.9% NaCl, upturned several times without shaking for 1 min, connected to the infusion set provided in the kit then administered within 15 min. An additional dose should be infused immediately for patients who had cardiac arrest or persistent cardiovascular collapse: extra 5 g for adults and identical to the first dose of 70 mg/kg for children without exceeding 5 g overall. The effectiveness of this antidote can be assessed by the hemodynamic status improvement after cessation of catecholamines and correction of lactic acidosis. Hydroxocobalamin is not a substitute for oxygen, but since its effectiveness depends on the rapidity of administration, it must be infused at the fire scene. This treatment is well tolerated, but induces a reversible pinkish color of teguments, mucous membranes, urine as well as other body fluids. A transient increase, usually not revealing blood pressure, has been reported. Due to its excellent tolerance, hydroxocobalamin can be administered in case of suspected cyanide poisoning before any definitive confirmation, which is secondarily obtained, whether by measuring the blood cyanide concentration in a sample taken prior to administration of antidote or by the measurement, during the first 3 days, of the total cyanocobalamin level in urine, a stable and atoxic byproduct resulting from mole-to-mole cyanide neutralization by hydroxocobalamin.


J1 J7
Pinkish color of urine

REFERENCES

1- Mégarbane B, Delahaye A, Goldgran-Tolédano D, Baud FJ. Antidotal treatment of cyanide poisoning. J Chin Med Assoc 2003;66:193-203.
2- Borron SW, Baud FJ. Antidotes for acute cyanide poisoning. Curr Pharm Biotechnol. 2012;13:1940-8.
3- Anseeuw K, Delvau N, Burillo-Putze G, De Iaco F, Geldner G, Holmström P, Lambert Y, Sabbe M. Cyanide poisoning by fire smoke inhalation: a European expert consensus. Eur J Emerg Med 2013;20:2-9.
4- Reade MC, Davies SR, Morley PT, Dennett J, Jacobs IC; Australian Resuscitation Council. Review article: management of cyanide poisoning. Emerg Med Australas 2012;24:225-38.

SÉDATION ET ANESTHÉSIE DU PATIENT EN CHOC HÉMORRAGIQUE

Sedation and anesthesia in hemorrhagic shock patient

DABAN J-L, DONAT N, DEBIEN B. Sédation et anesthésie du patient en choc hémorragique. Med Emergency, MJEM 2013; 14: 35-42.
Mots clés : Sédation, anesthésie, état de choc, intubation à séquence rapide
Key words: sedation, anesthesia, shock, rapid sequence intubation.

ABSTRACT

Anesthesia of a patient in a state of hemorrhagic stock is a real challenge to the Emergency room physician, the intensivist or the anesthesiologist. On a hemodynamic level, the suppression of the physiological response to hypovolemia by anesthetic agents aggravates hypotension. On the respiratory level the urgent intubation of a patient in shock with a non-empty stomach is in itself a risky procedure (failure to intubate, aspiration….). After taking into consideration the risk/ benefit, the time and place of induction (pre-hospital or in-hospital, in the emergency room or in the operation room), the anesthesia must comply with the safety principles: patient assessment (context, pathology, predictive criteria for difficult intubation), pre-oxygenation, monitoring, surveillance and maintaining anesthesia. Safety of use and the choice of anesthetic agents result from their pharmacological knowledge. Lower volume of distribution, cardiac output, and protein binding will imply a reduction in dose and titration of anesthetics for the same efficacy. Rapid sequence intubation of any patient in shock is made of a combination ketamine - succinylcholine (or etomidate - succinylcholine). Maintaining anesthesia is made of midazolam - sufentanil or ketamine - sufentanil.

RÉSUMÉ: L'anesthésie du patient en état de choc hémorragique est un véritable défi pour l'urgentiste ou l'anesthésiste-réanimateur.Au plan hémodynamique, la suppression des mécanismes physiologiques compensateurs de l'hypovolémie par les agents anesthésiques aggrave l'hypotension.Au plan respiratoire, l'intubation en urgence d'un patient choqué à l'estomac plein est une procédure à risques (échec d'intubation, inhalation…).Après l'analyse du rapport bénéfice/risque, le choix du lieu ou du moment de l'induction (préhospitalière ou intrahospitalière, aux urgences ou au bloc), l'anesthésie doit respecter ses principes fondamentaux de sécurité : évaluation du patient (terrain, pathologie, critères prédictifs d'intubation difficile), préoxygénation, monitorage, surveillance et entretien de l'anesthésie.De la connaissance de la pharmacologie des agents anesthésiques découle leur sécurité d'emploi et le choix des produits.La diminution du volume de distribution, du débit cardiaque, la baisse de la fixation protéique impose une réduction des doses et la titration des agents anesthésiques pour une même efficacité.L'induction à séquence rapide du patient choqué « tout venant » associe kétamine - succinylcholine (ou étomidate – succinylcholine).L'entretien de l'anesthésie repose sur l'association midazolam - sufentanil ou kétamine - sufentanil.

Authors' affiliation:

Correspondant author :
Professor Bruno Debien
Anesthesiologist - Intensivist
Intensive Care Unit
American Hospital of Paris
63 Bd Victor Hugo - BP 109
92202 Neuilly sur Seine - France

Nicolas Donat, MD.
Jean-Louis DABAN, MD.
Intensive Care Unit
Military Teaching Hospital Percy
Clamart - France

Article history / info:

Category: Continuous Education
Received: June 2010 (UP)
Revised: Feb. 20, 2013

Conflict of interest statement:

No conflict of interest to declare


Urgence Pratique

INTRODUCTION

Les traumatismes sont la principale cause de décès des sujets jeunes de moins de 40 ans, et l'hémorragie en est, avec le traumatisme crânien grave, la principale étiologie(1). L'anesthésie d'un patient en état de choc hémorragique est un véritable défi pour l'anesthésiste-réanimateur ou le médecin urgentiste. Elle associe trois composantes : la narcose (avec des hypnotiques), l'analgésie (avec des morphiniques), et la myorelaxation (avec des curares).

INDICATIONS DE L'ANESTHÉSIE AU COURS DU CHOC HÉMORRAGIQUE

En premier lieu, la sédation ou l'anesthésie permet de réaliser une analgésie optimale du blessé pour les gestes de désincarcération, d'alignement de membres ou de dégagement difficile. L'anesthésie peut aussi être indiquée par la nécessité de contrôler la ventilation chez un patient présentant une insuffisance respiratoire aiguë ou un traumatisme crânien grave. Elle permet, enfin et surtout, la réalisation du geste d'hémostase chirurgicale ou de radiologie interventionnelle à l'hôpital.

EFFETS DE L'ANESTHÉSIE SUR LE CHOC

Effets négatifs

L'anesthésie du patient en choc hémorragique a de nombreuses conséquences physiologiques par modification des mécanismes compensateurs de l'hypovolémie destinés à maintenir la perfusion tissulaire (vasoconstriction périphérique et redistribution régionale vasculaire par réponse sympathique adrénergique) [2-5].
Les modifications physiologiques sont variables dans leur nature et dans leur intensité selon le type d'agent anesthésique employé, mais ils sont presque tous responsables d'une vasodilatation périphérique. De nombreux agents présentent en outre une action inotrope négative, facteur supplémentaire de diminution de la perfusion tissulaire et du transport de l'oxygène [3, 6].
Par ailleurs, il existe également des interactions hémodynamiques liées à la ventilation mécanique nécessaire au cours d'une anesthésie générale. La ventilation mécanique est une ventilation en pression positive responsable d'une élévation des pressions intrathoraciques diminuant le retour veineux. Dans le cas particulier de l'épanchement péricardique, cette élévation des pressions intra thoraciques est encore plus délétère car elle se surajoute à l'élévation de la pression intra péricardique et peut conduire à l'arrêt cardiaque.

Effets positifs

L'anesthésie peut permettre d'améliorer la tolérance du choc hémorragique par plusieurs mécanismes distincts. Le premier résulte du blocage du stimulus douloureux et de sa réponse neuro-humorale. Il a été démontré que la présence de lésions tissulaires et/ou la stimulation des fibres nociceptives amplifie la réponse physiopathologique lors d'une spoliation sanguine et potentialise un état de choc [7, 8]. Le deuxième mécanisme est la diminution de 10 à 15 % de la consommation d'oxygène de l'organisme (VO_2) par l'anesthésie alors que cette consommation est, au contraire, augmentée en cas de douleur, de polypnée ou d'anxiété. Or le transport artériel d'oxygène est diminué en cas d'hémorragie par la baisse conjointe du débit cardiaque et du taux d'hémoglobine **(figure 1)**. Dans cette optique, toute intervention thérapeutique permettant d'améliorer l'équilibre entre les apports et les besoins est bénéfique. Il faut toutefois faire attention à ne pas diminuer davantage le débit cardiaque (par les effets adverses de l'anesthésie) qu'on ne diminue les besoins (en endormant le patient) [2, 9, 10].

$TaO2 = CaO2 \times IC$

$CaO2 = SaO2 \times Hb \times 1,34 + 0,031 \times PaO2$

IC : index cardiaque ; Hb : taux d'hémoglobine

PaO_2 : pression artérielle en oxygène ; CaO_2 : contenu artériel en oxygène

SaO_2 : saturation artérielle en oxygène ; TaO_2 : transport artériel en oxygèn

Figure 1: d'après Marino PL. The ICU Book, Williams & Wilkins, 2nd ed. 1977.

EFFETS DU CHOC SUR L'ANESTHÉSIE

Les études sont basées essentiellement sur des modèles expérimentaux animaux de choc contrôlé ou d'hémorragie modérée chez un animal anesthésié, dont les résultats sont extrapolés à l'homme (11,12). La pharmacocinétique étudie le devenir d'un principe actif d'un médicament dans l'organisme (absorption, distribution, métabolisme et élimination). La pharmacodynamie s'intéresse aux effets du médicament après qu'il ait atteint son site d'action (récepteur, enzyme...).
Dans le choc hémorragique, la principale modification pharmacocinétique est une majoration de l'effet des agents anesthésiques par différents mécanismes :
la diminution du volume sanguin augmente de facto la concentration sanguine de l'agent administré par diminution du volume de distribution ;
la diminution du débit cardiaque s'accompagne d'une diminution de la dilution de l'agent anesthésique et donc d'une augmentation de la concentration apparente ;
la diminution de l'albuminémie, liée à la spoliation sanguine et à la dilution, augmente la fraction libre du médicament (forme pharmacologiquement active) et donc la fraction diffusible ;
enfin, la vasoconstriction sympathique préserve la circulation cérébrale, ce qui majore encore l'effet des anesthésiques.

PRODUITS DE L'ANESTHÉSIE

Les Hypnotiques

De nombreux agents hypnotiques, aux propriétés pharmacologiques différentes, sont disponibles à l'hôpital.

Thiopental sodique

Le thiopental sodique fait partie des agents les plus anciens. Son délai d'action est de 30 secondes à 1 minute, sa durée d'action de 5 à 10 minutes environ. Il est dépresseur respiratoire, dépresseur

cardiovasculaire : vasodilatation périphérique par inhibition du système sympathique et diminution du débit cardiaque par effet inotrope négatif [9, 13-16]. Les effets cardiovasculaires du thiopental sont dépendants de la dose et de la vitesse d'injection. La dose d'induction habituelle est de 5-7 mg • kg-1, elle est fortement réduite chez le patient en état de choc. En raison d'un phénomène d'accumulation, il n'est pas adapté à l'entretien de l'anesthésie. Les études pharmacologiques anciennes ne suggèrent pas de modification pharmacodynamique au cours de l'état de choc [3, 17, 18].

Propofol
Le propofol présente un profil d'action cardiovasculaire similaire. Il réalise une inhibition du système sympathique avec vasoplégie ainsi qu'un effet inotrope moins marqué que le thiopental. Le délai d'action est de 30 secondes à 1 minute, la durée d'action de 5 à 10 minutes environ. Les études pharmacologiques mettent en évidence une diminution de la clairance plasmatique du produit, une diminution du volume de distribution, mais également une possible augmentation de sensibilité de l'organe cible en situation de choc indépendamment de son taux plasmatique [19]. Ainsi, la dose d'induction, habituellement de 2,5 mg • kg-1, doit être réduite de 50 à 60 % en appliquant le principe de titration [19-24].

Étomidate
L'étomidate est actuellement l'hypnotique de choix en préhospitalier pour l'induction anesthésique des patients en état de choc. Le délai d'action est de 30 secondes, la dose d'induction de 0,3 mg • kg-1, la durée d'action de 4 à 6 minutes environ. Son retentissement hémodynamique est réduit : effet inotrope négligeable, pas de vasodilatation périphérique ni de modification du baroréflexe. Dans le choc hémorragique, les modifications pharmacodynamiques et pharmacocinétiques sont modérées (diminution de la clairance, du volume de distribution et élévation de la fraction libre). Il est cependant recommandé de réduire la dose d'induction à 0,2 mg • kg-1 [25, 26].

Chlorhydrate de kétamine
Le chlorhydrate de kétamine possède des effets spécifiques. Il est responsable d'un effet direct inotrope négatif et vasodilatateur, et d'un effet sympathomimétique indirect avec comme traduction une augmentation de la fréquence cardiaque, du débit cardiaque, de la pression artérielle et des résistances vasculaires pulmonaires. Au cours d'un état de choc, la réaction sympathique est limitée par un effet seuil, et l'effet direct dépresseur myocardique s'exprime. La kétamine présente aussi des effets sur la circulation cérébrale : elle est responsable d'une élévation de la pression intracrânienne, du débit sanguin cérébral, et de la consommation d'oxygène cérébrale, qui l'a longtemps contre-indiquée en cas de traumatisme crânien [16]. Les études pharmacologiques mettent en évidence la nécessité de réduire de moitié de la dose d'induction chez les patients en état de choc (1,5 mg • kg-1). Le délai d'action est de 30 secondes à 1 minute, la durée d'action de 5 à 15 minutes [6, 17, 27, 28].

Midazolam
Le midazolam (Hypnovel®) est utilisé pour la sédation ou l'anesthésie du patient en choc hémorragique. Il est responsable d'une vasodilatation périphérique avec baisse des résistances périphériques, de la pression artérielle et du débit cardiaque. Il modifie également le baroréflexe avec risque de bradycardie en situation d'hypovolémie. Sa pharmacocinétique est modifiée par l'hypovolémie, nécessitant une réduction des doses administrées. Le délai d'action est de 2 à 3 minutes, la durée d'action de 10 à 20 minutes [29, 30].

Hydroxybutyrate de sodium
L'hydroxybutyrate de sodium (Gamma-OH®) est responsable d'une vasoconstriction et d'une tachycardie avec élévation modérée du débit cardiaque et de la pression artérielle. Malheureusement, cet agent anesthésique peu utilisé est également peu étudié dans la littérature. Il semble que les variations modérées de la volémie ne modifient pas son volume de distribution ni sa clairance. Le délai d'action est de 4 à 10 minutes, la dose d'induction de 50 à 70 mg • kg-1, la durée d'action de 60 à 90 minutes[31].

Les Analgésiques
Les agents utilisables appartiennent à la classe des morphinomimétiques. Leurs effets cardio-vasculaires sont réduits chez le patient normovolémique. Il s'agit essentiellement d'une bradycardie par hypertonie vagale, réversible sous atropine. Ils sont par ailleurs dépresseurs respiratoires et responsables d'une rigidité musculaire thoracique dépendante de la dose et de la vitesse d'injection. Parmi les différents morphinomimétiques disponibles, il n'existe pas de différence en termes de tolérance hémodynamique, et seule la morphine peut présenter un effet vasodilatateur par histaminolibération. Les morphinomimétiques sont tous sympatholytiques; ils suppriment donc les mécanismes compensateurs du choc, avec risque d'hypotension sévère chez le patient hypovolémique.

Morphine
Le chlorhydrate (ou sulfate) de morphine est l'agent de base pour l'analgésie du patient traumatisé. Son emploi repose sur le principe de titration. Il ne s'envisage que chez le patient conscient, et n'est pas adapté à un usage d'agent anesthésique. Ses paramètres pharmacologiques sont modifiés chez le patient en état de choc hémorragique résultant en une élévation des taux sériques à dose identique [32,33].

Fentanyl
Le fentanyl (Fentanyl®) a un délai d'action de 30 secondes et une durée d'action de 20 à 30 minutes. Du fait de son ancienneté, ses propriétés pharmacologiques en cas de choc hémorragique sont mieux connues. Les volumes des compartiments centraux et périphériques sont réduits ainsi que la clairance plasmatique. Les doses d'induction et d'entretien de l'anesthésie doivent donc être réduites et obéir au principe de titration[34].

Sufentanil
Le sufentanil (Sufenta®, Sufentanil®) possède un délai d'action de 2 minutes ; sa durée d'action est de 50 à 70 minutes. Les données de la littérature sont pauvres concernant les modifications pharmacologiques induites par le choc hémorragique. Sa pharmacologie est assimilée à celle du fentanyl dont il est dérivé (réduction des doses et titration).

Rémifentanil
Le rémifentanil (Ultiva®) est un morphinique de durée d'action ultra-courte. Son délai d'action est de 90 secondes, sa durée d'action de 10 minutes. Il a été démontré l'absence de modifications pharmacologiques dans l'état de choc hémorragique [35]. Son mode d'administration (voie intraveineuse continue) est inadapté

à son utilisation préhospitalière ou aux urgences.

Alfentanil
L'alfentanil (Rapifen®) est un morphinique d'action courte, son délai d'action est de 20 secondes, sa durée d'action de 7 à 15 minutes. En dépit de cette durée d'action courte, l'alfentanil présente une clairance d'élimination faible, ce qui conduit à un effet d'accumulation lors des réinjections.

Les Curares
La myorelaxation fait appel à deux familles de curares : les curares dépolarisants dont le seul représentant est la succinylcholine (ou suxaméthonium), et les curares non-dépolarisants. Les curares, quelle que soit leur classe, ne présentent pas d'effets hémodynamiques intrinsèques, mais peuvent être responsables d'une diminution du retour veineux par baisse de la pression intra-abdominale après relâchement musculaire de la paroi.

Succinylcholine
La succinylcholine (Célocurine®) est un curare d'action rapide (environ 1 minute). Sa durée d'action est de 10 minutes et sa posologie de 1 mg • kg-1. Il bloque la transmission neuromusculaire en maintenant une dépolarisation permanente de la membrane postsynaptique, empêchant ainsi la formation de nouveaux potentiels d'action. On décrit une phase initiale de fasciculations en rapport avec la dépolarisation initiale (durée de 30 secondes à une minute), puis une seconde phase de paralysie musculaire flasque affectant tous les muscles striés d'action volontaire liée à l'inexcitabilité de la plaque motrice. L'état de choc hémorragique ne semble pas modifier ses caractéristiques pharmacologiques.

Atracurium
L'atracurium (Tracrium®) et son énantiomère en cis, le cisatracurium (Nimbex®) sont les plus utilisés au bloc opératoire. Il existe peu d'études sur leur pharmacologie au cours de l'état de choc hémorragique. Il a été évoqué un possible effet cardiovasculaire hypotensif lors d'administration prolongée par le biais d'un métabolite, la laudanosine [36]. Pour l'atracurium, le délai d'action est de 2-3 minutes, la dose d'induction de 0,5 mg • kg-1, la durée d'action de 20 à 40 minutes. Pour le cisatracurium, le délai d'action est de 3 à 4 minutes, la dose d'induction de 0,2 mg • kg-1, la durée d'action de 45 minutes environ.

Vécuronium
Le vécuronium (Norcuron®) a l'avantage de se présenter sous forme de lyophilisat pouvant être conservé à température ambiante, à la différence des autres curares non dépolarisants. Son délai d'action est de 2 à 3 minutes, la dose d'induction de 0,15 mg • kg-1, la durée d'action de 20 à 30 minutes.

Rocuronium
Le rocuronium (Esméron®) a pour particularité un délai d'action court (1 minute). C'est dans cette optique qu'il est proposé par certains comme une alternative à la succinylcholine dans le protocole d'intubation à séquence rapide, à la dose de 1 mg • kg-1. Sa durée d'action est de 30 à 40 minutes. Il n'existe pas de données dans la littérature sur d'éventuelles modifications pharmacologiques liées à l'état de choc hémorragique [37-41].

Mivacurium
Le mivacurium (Mivacron®), curare non dépolarisant de durée d'action courte (10-20 minutes), et le pancuronium (Pavulon®), curare non dépolarisant d'action longue (60 minutes) n'ont pas leur place dans l'anesthésie du patient en état de choc hémorragique.
Compte tenu des lacunes concernant la pharmacologie des curares, il est nécessaire de monitorer systématiquement la curarisation, sans réduire a priori les doses administrées chez les patients en état de choc hémodynamique.

STRATÉGIE DE PRISE EN CHARGE

Évaluation préanesthésique
La réalisation de l'anesthésie en urgence d'un patient en état de choc hémorragique ne saurait être comparable à l'anesthésie réglée du patient au bloc opératoire. Cependant, les règles essentielles sont communes, indispensables à la sécurité du patient, et ne peuvent être ignorées. L'anesthésie obéit à une démarche intellectuelle réfléchie et non pas à l'application aveugle d'un protocole unique. Elle s'appuie sur une évaluation du rapport bénéfice/risque en fonction de l'indication, du terrain, du traumatisme, et de la mise en évidence de critères prédictifs d'intubation difficile.

Évaluation du terrain
L'évaluation du terrain recherche, par l'interrogatoire, des allergies (notamment à la succinylcholine), un traitement anticoagulant (pouvant majorer du saignement), la prise de bêtabloquants (masquant la tachycardie malgré l'hypovolémie) ou d'antihypertenseurs (aggravant l'hypotension). L'existence d'une cardiopathie (ischémique, valvulaire ou rythmique) ou d'antécédents respiratoires (asthme ou bronchopathie chronique obstructive) modifie peu la prise en charge en urgence du patient.

Examen clinique
L'examen clinique met en évidence les signes cliniques du choc hémorragique : tachycardie (sauf traitement par bêtabloquants ou hypovolémie profonde brutale), hypotension, pincement de la pression artérielle différentielle, soif, pâleur cutanéo-muqueuse, marbrures, allongement du temps de recoloration cutané, angoisse, agitation [42]. L'importance du choc peut être évaluée sur le retentissement clinique **(tableau I)**.

Intubation difficile
On recherche les critères prédictifs d'intubation difficile: traumatisme de la face ou du rachis cervical, score de Mallampati, ouverture de bouche, distance thyro-mentonnière, obésité...
En parallèle, la mise en condition du blessé est complétée : oxygénothérapie, pose de deux voies veineuses périphériques. Simultanément, deux prélèvements sanguins sont réalisés: une goutte de sang pour détermination de l'hématocrite ou du taux d'hémoglobine par micro méthode et un tube pour groupage sanguin et recherche d'anticorps irréguliers avant le remplissage vasculaire. En effet, le saignement et l'hémodilution

Estimation du volume des pertes sanguines

Basée sur les données de l'examen clinique, de la fréquence cardiaque, de la pression artérielle, de la conscience et de la diurèse.

Stade	Signes cliniques	Perte sanguine estimée
I	FC < 100 bpm, PA conservée	Inférieure à 750 mL
II	100 < FC < 120 bpm, hypotension, oligurie, anxiété	Entre 750 et 1 500 mL
III	120 < FC < 140 bpm, hypotension, oligurie, confusion, anxiété	Entre 1 500 et 2 000 mL
IV	FC > 140 bpm, hypotension, anurie, somnolence	Supérieure à 2 000 mL

Tableau I: d'après Committee on Trauma. Advanced Trauma Life Support ® Student Course Manual. Chicago : American College of Surgeons ; 2012. p. 69.

peuvent perturber voire rendre impossible ultérieurement la détermination du groupe.

Choix de la technique anesthésique

Anesthésie périmédullaire

Les techniques d'anesthésie périmédullaire peuvent être d'emblée écartées chez le patient en état de choc du fait de leur retentissement hémodynamique par blocage sympathique.

Anesthésie locorégionale

Les techniques d'anesthésie locorégionale des membres peuvent trouver une place dans le cadre limité de l'analgésie, même associées à une anesthésie générale. C'est le cas du bloc iliofascial, réalisable en préhospitalier [43].

Sédation

La sédation n'a pas sa place dans la prise en charge des patients à l'estomac plein, que sont tous les traumatisés graves, car elle expose au risque d'inhalation. D'autre part, l'usage de sédatifs est rendue difficile par les modifications pharmacocinétiques avec un retentissement neurologique, hémodynamique ou respiratoire imprévisible.

Anesthésie générale

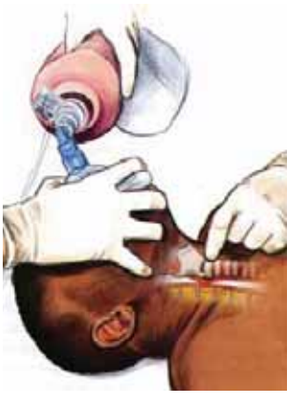
L'anesthésie générale est donc bien souvent la seule technique utilisable chez le patient en état de choc hémorragique. Cette anesthésie est dite « balancée », faisant appel aux trois composantes évoquées plus haut (narcose, analgésie, myorésolution). Les agents anesthésiques se potentialisent, permettant de réduire leurs doses et de diminuer leurs effets hémodynamiques.

Choix des produits

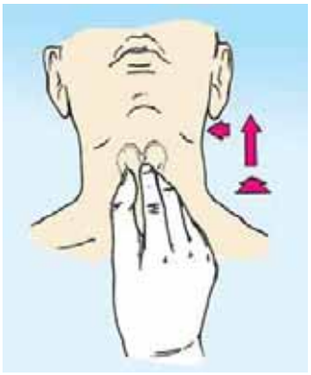
Il repose sur deux critères : la rapidité d'action et un retentissement hémodynamique réduit. Les agents à long délai d'action tels que l'hydroxybutyrate de sodium et les benzodiazépines sont à exclure. Le thiopental et le propofol ne sont pas adaptés du fait de leur important retentissement hémodynamique. Le choix de l'hypnotique doit donc se faire entre l'étomidate et la kétamine. L'étomidate a pour avantage d'être bien « installé » dans la culture et les protocoles préhospitaliers. La principale limitation quant à son utilisation est le freinage de l'axe corticotrope même dans le cas d'une injection unique [44]. En traumatologie, son utilisation a été associée à une augmentation de la durée de ventilation et de la durée de séjour en réanimation [45]. L'étude KETASED a comparé l'hypnomidate et la kétamine pour l'induction à séquence rapide en urgence. Elle a mis en évidence une insuffisance surrénalienne plus fréquente dans le groupe Etomidate vs. Kétamine mais pas de différence de mortalité, de défaillance d'organes ou de durée d'hospitalisation [46].Les auteurs concluent que la kétamine est un médicament sûr, efficace et qu'il constitue une alternative intéressante. Le retentissement potentiel de la kétamine sur l'hémodynamique intracérébrale a longtemps limité son utilisation en cas d'association de traumatisme crânien. En fait, deux méta-analyses récentes ont remis en cause cet effet délétère tant comme agent d'induction qu'en sédation [47,48]. La possible utilisation délictueuse de la kétamine par certains toxicomanes nécessite un stockage et une utilisation comparable à celle des stupéfiants. Le choix du curare est simple, il s'agit de la succinylcholine pour sa rapidité d'action et sa réversibilité. Une alternative par rocuronium est envisageable s'il existe des contre-indications formelles (allergie, hyperkaliémie, para- ou tétraplégie et brûlures graves de plus de 48 heures) [49].

Induction de l'anesthésie

L'induction de l'anesthésie générale doit être débutée une fois l'hypovolémie corrigée ou, tout au moins, sa correction entamée. Tout patient en état de choc hémorragique est considéré comme ayant l'estomac plein, quel que soit le délai de jeûne. On réalise donc une induction à séquence rapide pour limiter les risques d'inhalation de liquide gastrique. Ce protocole d'induction est alors en contradiction avec le principe de titration qui devrait prévaloir compte tenu de l'instabilité hémodynamique. En pratique, la posologie de l'hypnotique d'induction est estimée, a priori, d'autant plus réduite que le patient est instable mais le produit est injecté en quelques secondes par voie intraveineuse directe. L'induction de l'anesthésie débute après une préoxygénation par masque à haute concentration ou masque étanche. Le patient est monitoré, perfusé, une canule d'aspiration à portée de main. La correction de l'hypovolémie doit être débutée. Si elles sont nécessaires, les catécholamines sont à débuter avant l'induction. La procédure est expliquée au patient, et un aide applique une pression cricoïdienne (manœuvre de Sellick). Cette technique est réalisée avant la phase d'induction, avec une pression d'environ 1 kg, puis dès l'induction la pression est augmentée à 3 kg. En pratique, cette pression équivaut à la force nécessaire pour déplacer le piston d'une seringue obturée de 50 à 33 mL. Cette pression doit être maintenue jusqu'à vérification de la bonne position de la sonde d'intubation. Pour améliorer les conditions d'intubation, nous recommandons d'installer le patient en position amendée de Jackson, de préparer un mandrin rigide dans la sonde d'intubation, et de compléter, si besoin, la manœuvre de Sellick par une manœuvre BURP (backward, upward, rigthward pressure) [50]. On procède à



Manœuvre de Sellick



Manœuvre de BURP

NDLR : Décrite par une équipe d'anesthésistes canadiens, la manœuvre de BURP permet d'effacer de l'axe trachéal les incisives supérieures et de diminuer la gêne occasionnée par la base de la langue.
Le laryngoscope ne pouvant complètement écarter la langue, l'orifice trachéal n'est pas toujours strictement médian. Le mouvement que doit réaliser votre aide consiste en une triple pression postéro-céphalique droite à exercer sur le cartilage thyroïde. La pression (Pressure) s'exerce sur le plan postérieur (Backwards), vers la tête du patient (Upwards), et la droite de son cou (Rightwards). Elle permet de réorienter correctement l'ouverture trachéale.

l'injection successive de l'hypnotique et immédiatement après du myorelaxant, par exemple étomidate (0,2 mg • kg-1) puis succinylcholine (1 mg • kg-1). L'exposition débute 30 secondes à 1 minute après la fin de l'injection. La vérification de la bonne position de la sonde d'intubation se fait sur l'auscultation, et sur la constatation de trois cycles respiratoires successifs au capnographe. Une fois l'intubation réalisée et vérifiée, l'entretien de l'anesthésie doit être débuté.

Entretien de l'anesthésie

L'entretien de l'anesthésie repose également sur l'association d'agents hypnotiques et d'analgésiques. La curarisation continue n'est pas indispensable mais peut être entretenue en préhospitalier en cas de difficultés ventilatoires. En outre, l'administration d'un curare peut permettre, par potentialisation, de diminuer la dose des autres produits anesthésiques, permettant ainsi de réduire leur retentissement hémodynamique [51]. Les critères pharmacocinétiques et pharmacodynamiques de choix des agents d'entretien de l'anesthésie diffèrent de celui des agents d'induction. La caractéristique pharmacologique principale recherchée est l'absence d'accumulation. Ainsi, l'étomidate n'est pas un agent d'entretien de l'anesthésie car il expose au risque d'accumulation et d'insuffisance surrénalienne. Le thiopental présente le même risque d'accumulation, le rendant impropre à l'entretien de l'anesthésie. Le propofol ne présente pas de risque d'accumulation mais doit être réservé à l'anesthésie du patient dont l'hémorragie est contrôlée et compensée du fait du fort retentissement hémodynamique dont il est responsable. Finalement, le midazolam présente des caractéristiques pharmacologiques intéressantes dans le cadre de l'entretien de l'anesthésie du patient en état de choc hémorragique : sa cinétique est stable, l'effet d'accumulation est modéré pour des durées d'administration de quelques heures, sa tolérance hémodynamique est satisfaisante. L'entretien est réalisé en perfusion continue au pousse seringue électrique, à posologie réduite, de 30 à 100 μg • kg^{-1} • h^{-1}. La kétamine possède les critères pharmacologiques requis pour l'entretien de l'anesthésie. L'entretien se fait au pousse seringue électrique à la dose de 0,1 à 0,4 mg • kg^{-1} • h^{-1}, au tiers des doses classiquement proposées. L'hydroxybutyrate de sodium présente également des caractéristiques pharmacocinétiques et pharmacodynamiques intéressantes pour l'entretien de l'anesthésie : demi-vie longue, stabilité hémodynamique. La dose d'entretien est de 25 à 35 mg • kg^{-1} • h^{-1}. Les critères de choix de l'agent analgésique d'entretien sont identiques à ceux de l'hypnotique. Ainsi, les agents de choix sont le fentanyl ou le sufentanil, au pouvoir analgésique respectivement 100 et 1 000 fois supérieur à celui de la morphine. En outre, le sufentanil ne présente pas d'effet d'accumulation pour une période d'utilisation de moins de 8 heures. Comme nous l'avons vu, l'alfentanil et le rémifentanil n'ont pas leur place dans l'entretien de l'anesthésie du fait de leur cinétique. Les morphinominétiques sont administrés en injection discontinue à faible posologie (par exemple : sufentanil en bolus de 5 μg ou fentanyl 50 μg. Les doses mentionnées sont indicatives; l'entretien de l'anesthésie doit être adapté à l'objectif de sédation (score de Ramsay), à la variabilité inter-individuelle, et à la tolérance hémodynamique du patient. La réalisation de gestes invasifs, tels que la pose d'un drain thoracique ou l'alignement d'un membre fracturé, justifie l'approfondissement de l'anesthésie par le biais de sa composante analgésique.

CONCLUSION

La réalisation de l'anesthésie du patient en état de choc hémorragique est une anesthésie à risque : risque d'inhalation chez un sujet à l'estomac plein, risque d'intubation orotrachéale difficile imprévue, mais surtout risque d'aggravation de l'instabilité hémodynamique chez un patient hypovolémique. Sa réalisation nécessite la connaissance des mécanismes physiopathologiques du choc hémorragique, de la pharmacologie des produits de l'anesthésie et une évaluation attentive du rapport bénéfice/risque.

REFERENCES

1. Sauaia A, Moore FA, Moore EE, et al. Epidemiology of trauma deaths: a reassessment. J Trauma 1995; 38: 185-93.
2. Shafer SL. Shock values. Anesthesiology 2004; 101: 567-8.
3. Zimpfer M, Manders WT, Barger AC, et al. Pentobarbital alters compensatory neural and humoral mechanisms in response to hemorrhage. Am J Physiol 1982; 243: H713-21.
4. Zimpfer M, Sit SP, Vatner SF. Effects of anesthesia on the canine carotid chemoreceptor reflex. Circ Res 1981; 48: 400-6.
5. Vatner SF, Braunwald E. Cardiovascular control mechanisms in the conscious state. N Engl J Med 1975; 293: 970-6.
6. Weiskopf RB, Bogetz MS, Roizen MF, et al. Cardiovascular and metabolic sequelae of inducing anesthesia with ketamine or thiopental in hypovolemic swine. Anesthesiology 1984; 60: 214-9.
7. Rady MY. Possible mechanisms for the interaction of peripheral somatic nerve stimulation, tissue injury, and hemorrhage in the pathophysiology of traumatic shock. Anesth Analg 1994; 78: 761-5.
8. Rady MY, Kirkman E, Cranley J, et al. Comparison of the effects of skeletal muscle injury and somatic afferent nerve stimulation on the response to hemorrhage in anesthetized pigs. J Trauma 1993; 35: 756-61.
9. Samii K. Anesthésie Réanimation Chirurgicale, Première partie : bases scientifiques. Paris : Flammarion ; 2005.
10. Baele P. Transport de l'oxygène dans le sang - Notions de transport du CO2 et des ions hydrogènes. In : Dalens B, editor. Traité d'anesthésie génerale. Paris : Arnette ; 2003.
11. Wiggers HC, Ingraham RC. Hemorrhagic shock: definition and criteria for its diagnosis. J Clin Invest 1946; 25: 30-6.
12. Asehnoune K, Pinaud M. Actualité sur le choc hémorragique. Réanimation 2008 ; 17 : 311-7.
13. Van der linden P, De Hert S. Anesthésie du patient en état de choc hémorragique. 2000, JEPU. Accessible : http://www.jepu.fr
14. Lenfant F, Anesthésie du patient en état de choc hémorragique. JEPU, 2004. Accessible : http://www.jepu.fr
15. Santelli D, Ortega D, Martin C. Anesthésie du patient en état de choc. In : Dalens B, Editor. Traité d'anesthésie générale. Paris : Arnette ; 2002.
16. Mion G. Kétamine. Paris : Arnette ; 2003.
17. Gustafsson U, Sjöberg F, Lewis DH, et al. Influence of pentobarbital, propofol and ketamine on skeletal muscle capillary perfusion during hemorrhage: a comparative study in the rabbit. Int J Microcirc Clin Exp 1995; 15: 163-9.
18. Vatner S.F. Effects of anesthesia on cardiovascular control mechanisms. Environ Health Perspect 1978; 26: 193-206.
19. De Paepe P, Belpaire FM, Rosseel MT, et al. Influence of hypovolemia on the pharmacokinetics and the electroencephalographic effect of propofol in the rat. Anesthesiology 2000; 93: 1482-90.
20. Adachi YU, Watanabe K, Higuchi H, et al. The determinants of propofol induction of anesthesia dose. Anesth Analg 2001; 92: 656-61.
21. Johnson KB, Egan TD, Kern SE, et al. Influence of hemorrhagic shock followed by crystalloid resuscitation on propofol: a pharmacokinetic and pharmacodynamic analysis. Anesthesiology 2004; 101: 647-59.
22. Johnson KB, Egan TD, Layman J, et al. The influence of hemorrhagic shock on propofol: a pharmacokinetic and pharmacodynamic analysis. Anesthesiology 2003; 99: 409-20.
23. Kazama T, Kurita T, Morita K, et al. Influence of hemorrhage on propofol pseudo-steady state concentration. Anesthesiology 2002; 97: 1156-61.
24. Kurita T, Kazama T, Morita K, et al. Influence of fluid infusion associated with high-volume blood loss on plasma propofol concentrations. Anesthesiology 2004; 100: 871-8.
25. De Paepe P, Belpaire FM, Van Hoey G, et al. Influence of hypovolemia on the pharmacokinetics and the electroencephalographic effect of etomidate in the rat. J Pharmacol Exp Ther 1999; 290: 1048-53.
26. Johnson KB, Egan TD, Layman J, et al. The influence of hemorrhagic shock on etomidate: a pharmacokinetic and pharmacodynamic analysis. Anesth Analg 2003; 96: 1360-8.
27. Longnecker DE, Sturgill BC. Influence of anesthetic agent on survival following hemorrhage. Anesthesiology 1976; 45: 516-21.
28. Weiskopf RB, Bogetz MS. Haemorrhage decreases the anaesthetic requirement for ketamine and thiopentone in the pig. Br J Anaesth 1985; 57 : 1022-5.
29. Adams P, Gelman S, Reves JG, et al. Midazolam pharmacodynamics and pharmacokinetics during acute hypovolemia. Anesthesiology 1985; 63 : 140-6.
30. Klockowski PM, Levy G. Kinetics of drug action in disease states. XXV. Effect of experimental hypovolemia on the pharmacodynamics and pharmacokinetics of desmethyldiazepam. J Pharmacol Exp Ther 1988; 245 : 508-12.
31. Van Sassenbroeck DK, De Paepe P, Belpaire FM, et al. Influence of hypovolemia on the pharmacokinetics and electroencephalographic effect of gamma-hydroxybutyrate in the rat. Anesthesiology 2002 ; 97 : 1218-26.
32. De Paepe P, Belpaire FM, Rosseel MT, et al. The influence of hemorrhagic shock on the pharmacokinetics and the analgesic effect of morphine in the rat. Fundam Clin Pharmacol 1998; 12: 624-30.
33. Isoyama T, Anaka J, Sato T, et al. Effects of naloxone and morphine in hemorrhagic shock. Circ Shock 1982; 9 : 375-82.
34. Egan TD, Kuramkote S, Gong G, et al. Fentanyl pharmacokinetics in hemorrhagic shock: a porcine model. Anesthesiology 1999; 91: 156-66.
35. Johnson KB, Kern SE, Hamber EA, et al. Influence of hemorrhagic shock on remifentanil: a pharmacokinetic and pharmacodynamic analysis. Anesthesiology 2001; 94: 322-32.
36. Fodale V, Santamaria LB. Laudanosine, an atracurium and cisatracurium metabolite. Eur J Anaesthesiol 2002; 19: 466-73.
37. Chamorro C, Romera MA, Valdivia M. Rocuronium in emergent intubation. Anesth Analg 2006; 103: 253-4.
38. Karcioglu O, Arnold J, Topacoglu H, et al. Succinylcholine or rocuronium? A meta-analysis of the effects on intubation conditions. Int J Clin Pract 2006; 60: 1638-46.

39. Lysakowski C, Suppan L, Czarnetzki C, et al. Impact of the intubation model on the efficacy of rocuronium during rapid sequence intubation: systematic review of randomized trials. Acta Anaesthesiol Scand 2007; 51: 848-57.
40. Perry JJ, Lee JS, Sillberg VA, et al. Rocuronium versus succinylcholine for rapid sequence induction intubation. Cochrane Database Syst Rev 2008 (2): CD002788.
41. Sluga M, Ummenhofer W, Studer W, et al. Rocuronium versus succinylcholine for rapid sequence induction of anesthesia and endotracheal intubation: a prospective, randomized trial in emergent cases. Anesth Analg 2005; 101: 1356-61.
42. Barriot P, Riou B. Hemorrhagic shock with paradoxical bradycardia. Intensive Care Med 1987; 13: 203-7.
43. Société française d'anesthésie et de réanimation. Conférence d'experts 2002. Pratique des anesthésies locales et locorégionales par des médecins non spécialisés en anesthésie-réanimation, dans le cadre des urgences. 2002. Accessible: http://sfar.org/t/spip.php? article203
44. Vinclair M, Broux C, Faure P. Duration of adrenal inhibition following a single dose of etomidate in critically ill patients. Intensive Care Med 2008; 34: 714-9.
45. Hildreth AN, Mejia VA, Maxwell RA, Smith PW, Dart BW, Barker DE. Adrenal suppression following a single dose of etomidate for rapid sequence induction: a prospective randomized study. J Trauma 2008; 65: 573–79.
46. Jabre P, Combes X, Lapostolle F, Dhaouadi M, Ricard-Hibon A, Vivien B et al. Etomidate versus ketamine for rapid sequence intubation in acutely ill patients: a multicentre randomised controlled trial. Lancet. 2009 Jul 25; 374(9686):293-300.
47. Hughes S. Towards evidence based emergency medicine: best BETs from the Manchester Royal Infirmary. BET 3: is ketamine a viable induction agent for the trauma patient with potential brain injury. Emerg Med J 2011; 28:1076-7
48. Roberts DJ, Hall RI, Kramer AH, Robertson HL, Gallagher CN, Zygun DA. Sedation for critically ill adults with severe traumatic brain injury: a systematic review of randomized controlled trials. Crit Care Med. 2011 Dec; 39(12): 2780-2
49. Martyn JA, Richtsfeld M. Succinylcholine-induced hyperkalemia in acquired pathologic states: etiologic factors and molecular mechanisms. Anesthesiology 2006; 104: 158-69.
50. Knill RL. Difficult laryngoscopy made easy with a «BURP». Can J Anaesth 1993; 40: 279-82.
51. Ekman A, Stalberg E, Sundman E, et al. The effect of neuromuscular block and noxious stimulation on hypnosis monitoring during sevoflurane anesthesia. Anesth Analg 2007; 105: 688-95

EM upcoming conferences

First European Congress on Paediatric Resuscitation and Emergency Medicine
May 2-3, 2013. Ghent, Belgium

14th European Congress of Trauma and Emergency Surgery (ECTES)
May 4-7, 2013. Lyon - France

2d Global Network Conference of Emergency Medicine
First Emirates Society of Emergency Medicine (ESEM) Confernce.
May 2-6, 2013. Dubai – UAE

Global Health and Emergency Care: A Research Agenda
May 15, 2013. Atlanta, Georgia, USA

VII Congresso Argentino de Medicina de Emergencias
May 23-24, 2013. Buenos Aires, Argentina

18th World Congress on Disaster and Emergency Medicine
May 28-31, 2013. Manchester, United Kingdom

16th Annual Management of Humanitarian Emergencies: Focus on Children, Women and Families
June 3-7, 2013. Cleveland, OH

7th Congress of the French Society for Emergency Medicine (SFMU)
June 5-7, 2013. Paris - France

International Congress of Pediatrics
August 24-29, 2013. Melbourne, Australia
Hosted by: International Pediatric Association

Developing EM 2013
September, 2013. Havana, Cuba

VIIth Mediterranean Emergency Medicine Congress (MEMC 2013)
September 7-11, 2013. Marseilles, France

7th Asian Conference on Emergency Medicine (ACEM 2013)
October 23-25, 2013. Tokyo, Japan

Emergency Medicine Society of South Africa 2013 (EMSSA 2013)
November 5-7, 2013. Cape Town, South Africa

IMAGING IN ACUTE PANCREATITIS

NADER Lucie. Imaging in acute pancreatitis. Med Emergency, MJEM 2013; 14: 43-45.
Key words: Acute pancreatitis, CT severity index, Complications, MRI indications

ABSTRACT

Acute pancreatitis may vary from a mild disease to a life threatening disease. The diagnosis of acute pancreatitis is generally based on clinical and laboratory findings; however, CT is the imaging of choice in confirming the diagnosis, staging the disease and detecting complications. Based on CT findings, Balthazar and al established a CT severity index (CTSI) for acute pancreatitis. Acute pancreatitis is therefore graded between A and E. MRI can also have an important role in staging the severity of acute pancreatitis especially in patient who cannot undergo contrast enhanced CT and may be superior to CT for the characterization of peripancreatic collections.

Authors' affiliation:
NADER Lucie, MD, MBA, MHM
Chief of Imaging Department
Nawfal Medical Center – Byblos, Lebanon
Email: lucienader@hotmail.com

Article history / info:
Category: continuous education
Received: Jan, 13 2013
Revised: Jan 30, 2013
Accepted: Feb14, 2013

Conflict of interest statement:
No conflict of interest to declare

INTRODUCTION

Acute Pancreatitis could vary from a mild disease to a life-threatening disease. It is the 1992 Atlanta International Symposium on Acute Pancreatitis that has classified this entity into mild acute pancreatitis and severe acute pancreatitis. 80% of cases of acute pancreatitis are very mild; however 20% may run serious clinical course with pancreatic necrosis and multisystem organ failure. Etiologies of acute pancreatitis are mainly alcohol abuse and gallstones. Post-ERCP acute pancreatitis has been also described, but it is usually a mild course disease.

CLINICAL ISSUES

Severe acute pancreatitis runs a biphasic course [1]. During the first 1-2 weeks there is a pro-inflammatory response that leads to a systemic inflammatory response syndrome. It is a sterile response. If the disease is severe it will lead to multiple organ failure. After the first 1-2 weeks there is a transition to an anti-inflammatory response during which the patient is at risk for developing infection of necrotic tissue and fluid collections. The sepsis may lead to severe complications and death.

IMAGING OF ACUTE PANCREATITIS

Ultrasound in acute pancreatitis
Abdominal ultrasound could be indicated early in the acute phase of pancreatitis, to help evaluate for the presence of gallbladder and/or common bile duct stones. But it should be kept in mind that the visualization of the pancreas is often impaired because of overlying bowel gas. Abnormal US findings are seen in 33% to 90% of patients with acute pancreatitis mainly as a diffusely enlarged and hypoechoic gland consistent with interstitial edema [2].

CT evaluation of acute pancreatitis
CT scanner is the imaging of choice in diagnosing and staging acute pancreatitis. However, within the first 72 hours, there is no additional value in performing a CT, as it could be misleading in staging the pancreatitis, it may underestimate the severity of the disease and shows a normal, homogeneously enhancing pancreas. The diagnosis should therefore be made on clinical and biological findings.
Based on CT findings, Balthazar and al established a CT severity index (CTSI) for acute pancreatitis. This CTSI assigns points related to the grade of acute pancreatitis by analyzing non enhanced and enhanced CT scanner (required for identifying and staging pancreatic necrosis) [3].

Therefore acute pancreatitis could be evaluated as follow:
1-Interstitial pancreatitis
It is a self-limiting disease with recovery occurring in 80% of patients. The patients have Balthazar A to C. There is a normal enhancement of the entire pancreas, sometimes associated to mild fatty infiltration [4].

CT severity index				
		Necrosis		
GT Grade	Points	Percentage	Additional points	Severity index
A	0	0	0	0
B	1	0	0	1
C	2	>30	2	4
D	3	30-50	4	7
E	4	>50	6	10
CT Grade points are added to points assigned for percentage of necrosis				

Balthazar, RSNA 2002

2-Exudative pancreatitis

It is an intermediate form of pancreatitis without pancreatic necrosis with an intermediate clinical course. This is also called extrapancreatic necrosis. The patients have Balthazar grade D or E. There is a normal enhancement of the entire pancreas associated to extensive peripancreatic collections. It consists of necrosis of peripancreatic fat that it is difficult to identify on CT.

3-Necrotizing pancreatitis

It occurs in 20% of the patients with acute pancreatitis. It is characterized by a high incidence of local complications and a high mortality rate. There are 2 or more fluid collections with more than 50% of the pancreas not showing enhancement. Detection of pancreatic necrosis is important because most life-threatening complications occur in patients with pancreatic necrosis [5].

Necrosis could become infected and this usually occurs in the second or the third week. This is the most severe complication in acute pancreatitis and the most common cause of death in acute pancreatitis. Air bubbles are only seen in 20% of cases with infected necrosis.

4-Peripancreatic collections

These collections may develop early in acute pancreatitis. They do not have wall or capsule. They are the result of the release of activated pancreatic enzymes which also causes necrosis of the surrounding tissues. This explains why a lot of these collections contain solid debris. 50% of these collections show spontaneous regression, the other 50% either remain stable or increase.

They may remain sterile or develop infection.

It is important to note that CT cannot differentiate between fluid and debris in peripancreatic collections and MRI could be the best alternative. It also cannot differentiate between sterile and infected collections as air is only present in 20% of infected cases.

MRI in acute pancreatitis

MR imaging is an excellent alternative to CT scan helping in evaluating patients who cannot receive iodinated contrast material due to allergic reactions or renal insufficiency [6]. Gadolinium-enhanced T1-weighted gradient-echo MR sequences can show pancreatic necrosis as non enhanced areas within the pancreas. T2- weighted sequences can identify collections, pseudocysts, as well as hemorrhage. MR could be considered as an alternative modality that can be used for staging acute pancreatitis or sometimes better characterizing equivocal CT abnormalities specially when it comes to differentiate between fluid filled collections and debris filled collections [7].

CONCLUSION

Clinical and laboratory evaluation are the first objective assessment of the severity of acute pancreatitis. After 72 hours, non enhanced and contrast enhanced CT scan is the imaging modality of choice for diagnosing and staging the severity of acute pancreatitis, it shows pancreatic necrosis, and depicts local complications [8]. MRI is used as an alternative modality when CT scan could not be performed and as a more sensitive technique in differentiating fluid filled collections from debris filled collections.

REFERENCES

1- WERNER J. et al. Management of acute pancreatitis: from surgery to interventional intensive care. Gut 2005; 54: 426-36.

2- JEFFREY RB. Sonography in acute pancreatitis. Radiol Clin North Am 1989; 27: 5–17.

3- BALTHAZAR E. Acute pancreatitis: Assessment of severity with clinical and CT evaluation. Radiology 2002; 223: 603-613.

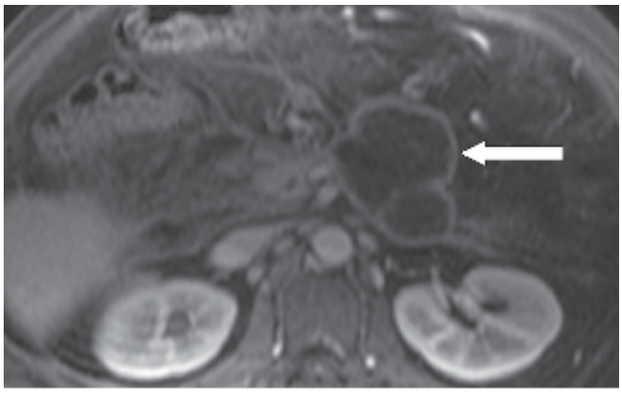
4- LENHART K., BALTHAZAR E. MDCT of acute mild (nonnecrotizing) pancreatitis: abdominal complications and fate of fluid collections. AJR 2008; 190: 643-649.

5- WHITCOMB. Acute pancreatitis. N. Engl. J. Med. 2006; 354(20): 2142-2150.

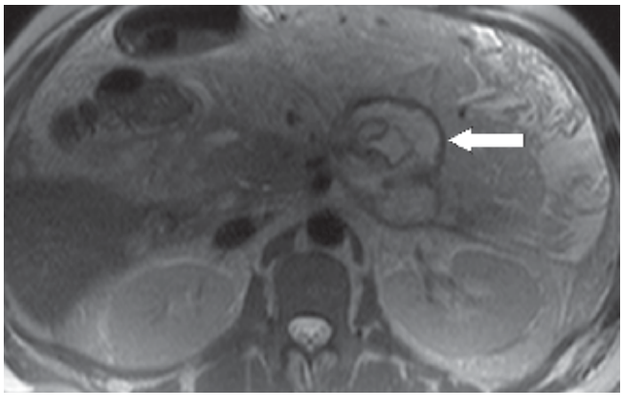
6- MORGAN DE, BARON TH, SMITH JK, ROBBIN ML, KENNY PJ. Pancreatic fluid collections prior to intervention: evaluation with MR imaging compared with CT and US. Radiology 1997; 203: 773–778.

7- REINHOLD C. Acute pancreatitis: interobserver agreement and correlation of CT and MR cholangiopancreatography with outcome. Radiology 1999; 211: 727–735.

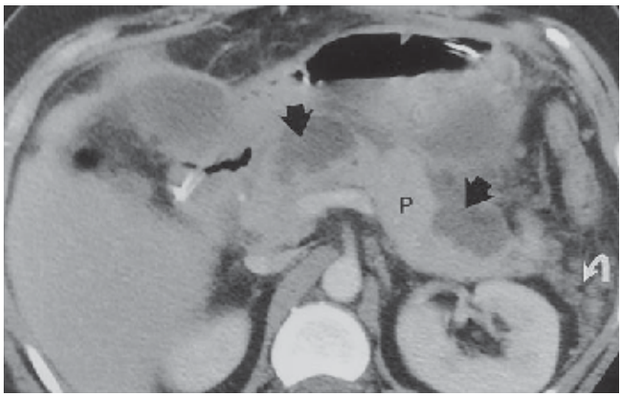
8- DARIO CASAS J. et al. Prognostic value of CT in the early assessment of patients with acute pancreatitis. AJR 2004; 182: 569-574.



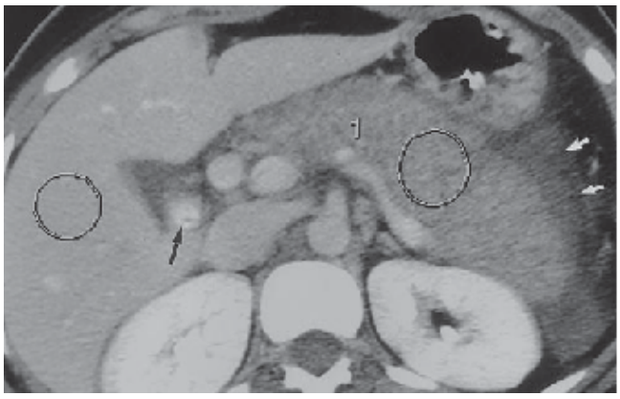
MRI in acute pancreatitis:
An axial enhanced T1-weighted fat-suppressed gradient-echo image obtained during arterial phase shows peripheral enhancement of a pseudocyst.



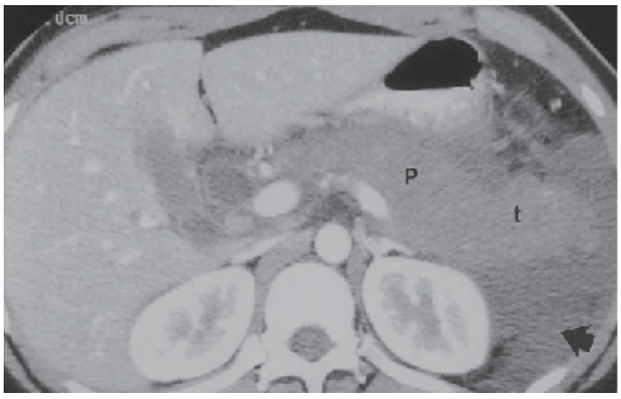
MRI in acute pancreatitis:
Axial T2-weighted HASTE image shows septations and debris inside a pseudocyst



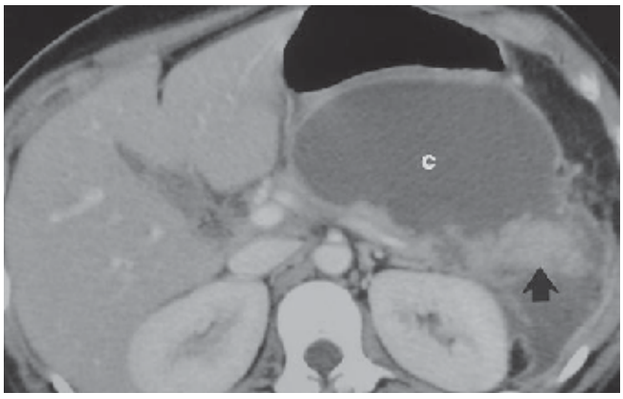
Contrast enhanced CT scan in acute pancreatitis:
There are two zones (straight arrows) of liquefied pancreatic necrosis in the neck and tail of the gland. There are residual nodular areas adjacent to the tail of the pancreas, consistent with fat necrosis (curved arrow).



Contrast enhanced CT scan in acute pancreatitis:
Large, edematous, homogeneously attenuating pancreas with peripancreatic inflammatory changes.



Contrast enhanced CT scan in acute pancreatitis:
Initial early transverse CT scan reveals an enlarged low-attenuating pancreas (P) with pancreatic ischemia and necrosis. There is a large fluid collection (arrow) around the pancreatic body and tail (t).



Contrast enhanced CT scan in acute pancreatitis:
There is a fluid collection associated with liquified necrosis of most of the body of the pancreas, with the development of a pseudocyst (c). The tail of the pancreas (arrow) is enhancing normally.

10th Pan Arab Congress of ANESTHESIA

Intensive Care and Pain Management

Pan Arab Congress of Anaesthesia
Intensive Care & Pain Management

SCIENTIFIC SESSIONS

Risk Evaluation & Management
Airway Management, Adult & Pediatric
Ambulatory Anesthesia
The Morbidly Obese Patient
Acute & Chronic Pain Management
Regional Anesthesia
Ultrasound In Anesthesia & ICU
Neuro-Anesthesia & Critical Care
Cardio-Thoracic Anesthesia
Obstetric Anesthesia & Analgesia
Pediatric Anesthesia
Intensive Care Medicine
Emergency & Resuscitation
Trauma,Transfusion & Hemostasis
Nutrition In The ICU
Anesthesia For Organ Transplantation
Pharmacology
Research & Evidence Based Practice
Education
Ethics
Patient Safety & Quality Improvement

PBLD SESSIONS, WORKSHOPS:

Difficult Airway Management
Simulation
Regional Anesthesia, Cadaveric Dissection
Tee, US In The ICU
Thoracic Anesthesia
Mechanical Ventilation

12 - 15, September 2013
Hilton Habtoor Grand Hotel
Beirut - Lebanon
www.panarabanesthesia2013.org

European Society of Anaesthesiology ESA

Infomed
INTERNATIONAL FOR EVENTS

Abi Rached Center, 3rd Floor, Jisr El Bacha
Tel: + 961 1 510881/2/3 , Fax: + 961 1 482116
P.O. Box: 90 -361 - Lebanon
Email: infomed@infomedweb.com
www.infomedweb.com

Med Emergency, MJEM

The Mediterranean Journal of Emergency Medicine

The Journal publishes articles in English and/or French pertaining to Emergency Medicine from its scientific aspect (research, case studies, clinical articles, orientation and practical conduct), administrative (Management and organization of Emergency Medicine), medical-legal and social aspects. It also accepts articles that deal with prevention of emergencies. Although it focuses more on practical issues of emergency medicine, the Journal accepts theoretical, methodological and analytical articles. It is also interested in communications, letters, commentaries and critiques of issues related to emergency. Priority is given to articles that pertain to the practice of emergency medicine specifically in the Mediterranean and MENA region. Some editions will be consecrated to specific subjects such as accidents, catastrophes, cardiac arrest and first aid. We would also welcome any announcements of events (national and international) related to emergency medicine such as workshops, conferences, courses and new books and publications.

Authors can submit their original articles and the accompanying references to the editor: New Health Concept B.P. 90.815 Jdeideh-Lebanon or via email. The article should be accompanied by a letter by the author/s that clearly states that joint authors of the article are aware of the application to publish and have agreed to allow free accessing of texts by New Health Concept Edition publication. Please create a separate file (indicating the name of the author) for all the photographs, tables and graphs you would like to be included in the article and send them to the following address: mjem@newhealthconcept.net All submissions will undergo a preliminary evaluation and an ethical revision by the editorial board to determine whether it will be allowed to appear in the journal. Articles that pass this preliminary evaluation will also be anonymously reviewed by two members of a scientific committee. Once the article has been approved for publication, a biography of 10 lines should be developed.

Manuscript Preparation

Articles are to be submitted in a typewritten format. Paragraphs are double spaced. Font size should be 12. The submitting author should send his contact details with the article such as telephone number or an email address. The original text of the article should be sent without illustrations in its original format (e.g. Microsoft Word). Pages should be numbered. Titles and subtitles of equal importance should be marked identically. Abbreviations should be explained when first encountered in the text. The articles should not exceed 2500 words or not more than 10 pages.

Abstracts and Key Words: Each article should include an abstract In English (and in French for French articles) no longer than 300 words. Keywords (not more than 6 words) and the title of the article should also be presented in both languages.

Text: The author needs to respect the following formatting procedures when submitting the article:

- On the front page- the author's name, affiliations, complete mailing address, telephone number and email address. The names and the affiliations of collaborators should be clearly indicated. Please ensure that this information is only presented on the front page and does not appear on the other pages of the article.
- Bibliographic References need to appear in order of appearance in the text. They must be identified in the text by Arabic numbers in brackets. There should be about 10-30 references. They must conform to presentation norms applied in the scientific editing world (E.g. APA).
- Photographs, figures, graphs and tables: these should be sent in separate files and need to be numbered and marked with the author's name and commentary. They need to be numbered in chronological ordered when they are to be referred to in the text. The term "graph/table/figure/photo number x" should be used in order to avoid confusion with bibliographical references.
- End notes should be listed separately at the end of the text and not at the end of each page.

PS: It's strongly recommended to add photography of the author who can also allow us to communicate his E-mail address.

ADENDUM

Conflict-of-Interest Statement* Conflict of interest exists when an author (or the author's institution), reviewer, or editor has financial or personal relationships that inappropriately influence (bias) his or her actions (such relationships are also known as dual commitments, competing interests, or competing loyalties). These relationships vary from those with negligible potential to those with great potential to influence judgment, and not all relationships represent true conflict of interest. The potential for conflict of interest can exist whether or not an individual believes that the relationship affects his or her scientific judgment. Financial relationships (such as employment, consultancies, stock ownership, honoraria, paid expert testimony) are the most easily identifiable conflicts of interest and the most likely to undermine the credibility of the journal, the authors, and of science itself. However, conflicts can occur for other reasons, such as personal relationships, academic competition, and intellectual passion.

Statement of Informed Consent* Patients have a right to privacy that should not be infringed without informed consent. Identifying information, including patients' names, initials, or hospital numbers, should not be published in written descriptions, photographs, and pedigrees unless the information is essential for scientific purposes and the patient (or parent or guardian) gives written informed consent for publication. Informed consent for this purpose requires that a patient who is identifiable be shown the manuscript to be published. Authors should identify Individuals who provide writing assistance and disclose the funding source for this assistance. Identifying details should be omitted if they are not essential. Complete anonymity is difficult to achieve, however, and informed consent should be obtained if there is any doubt. For example, masking the eye region in photographs of patients is inadequate protection of anonymity. If identifying characteristics are altered to protect anonymity, such as in genetic pedigrees, authors should provide assurance that alterations do not distort scientific meaning and editors should so note.

Statement of Human and Animal Rights* When reporting experiments on human subjects, authors should indicate whether the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000 (5). If doubt exists whether the research was conducted in accordance with the Helsinki Declaration, the authors must explain the rationale for their approach, and demonstrate that the institutional review body explicitly approved the doubtful aspects of the study. When reporting experiments on animals, authors should be asked to indicate whether the institutional and national guide for the care and use of laboratory animals was followed.

**International Committee of Medical Journal Editors ("Uniform Requirements for Manuscripts Submitted to Biomedical Journals") -- February 2006*

MED EMERGENCY/URGENCE
Revue Méditerranéenne de Médecine d'Urgence
Mediterranean Journal of Emergency Medicine

MEMBERSHIP	4 ISSUES/ YEAR ($USD)	8 ISSUES/2 YEARS ($USD)
Individual	❑ 80	❑ 140
Student	❑ 60	❑ 100
Institution	❑ 100	❑ 180
Outside Lebanon*	❑ Add +20%	❑ Add +20%

* +$10 USD to send outside Lebanon

Kindly fill and return to: MED EMERGENCY Publications
P.O. Box 90.815, Jdeideh- Lebanon, Tel: +961-1-888921; Fax: +961-1-888922

Name : . . . . . .
Surname : . . . . . .
. . . . . .
Address : . . . . . .
. . . . . .
P.O. Box: : . . . . . .City : . . . . . .
Country : . . . . . Email : . . . . . .

Telephone: ----------

Profession: ---------- Affiliation: ----------

❑ Bank Check (Cheque Bancaire)
Please send to: MED EMERGENCY PUBLICATIONS - New Health Concept, Samra Center, Block C 4th floor Fanar, Jdeidet El Metn P.O. Box 90.815.

DIRECTOR OF PUBLICATION
Dr. Nagi SOUAIBY

EDITORIAL BOARD
Jean Claude DESLANDES (France)
Karim FARAH (Lebanon)
Maria Paula GOMEZ (Spain)
Chokri HAMOUDA (Tunisia)
Abdo KHOURY (France)
Jean Yves LE COZ (France)
Daryl MACIAS (USA)
Steve PHOTIOU (Italy)
Jean-Cyrille PITTELOUD (Switzerland)
Alissar RADY (WHO)

COVER PICTURES
BSPP
BURP maneuver
Pinkish Urine
CT abdomen

PRINTING AND LAYOUT
MELKI PRINT INTERNATIONAL S.A.L.
UNILEB BLDG 1ST FLOOR
MAR ANTONIOS STR.
JDEIDEH, LEBANON
TELEFAX: +961-1-888545

Quarterly Journal
ISSN No 2222-9442
Printed in Lebanon

PHYSIO CONTROL

TrueCPR™ COACHING DEVICE

Better outcomes demand exceptional CPR

Respond with TrueCPR from Physio-Control

Today's responsive emergency team is always looking to elevate the level of care they deliver, and they rely on evidence and data to get there. The only CPR coaching device on the market that accurately measures depth, TrueCPR™ Coaching Device is designed to optimize manual CPR performance and quality through true depth measurement and more accurate feedback on depth, rate, recoil and pauses.

Get ready for a more responsive approach to CPR.

Physio-Control Lebanon Sales Offshore s.a.l.
D: +961 4 718 414 | M: +961 3 631 222 | F: +961 4 718 415
sami.jabbour@physio-control.com

www.physio-control.com

Chemical Threats

Rapid cyanide detoxification[1,2]

- Antidotes for all forms of Cyanide poisoning[3]
- Binds directly to cyanide ion[1,2]
- New 5 g single vial for easier reconstitution and administration*
- Smaller packsize for easier storage*

Medical or Commercial queries : please email at cyanide@merckgroup.com NATO code : 6505 14 570 4045

[1] Toffis V. Importance de l'intoxication cyanhydrique au cours de l'inhalation de fumées d'incendie. Intérêt de l'action antidotique de l'hydroxocobalamine. DEA de Toxicologie Fondamentale et Appliquée, Créteil 1989 **[2]** Houeto P. Relation of blood cyanide to plasma cyanocobalamin concentration after a fixed dose of hydroxocobalamin in cyanide poisoning The Lancet, Volume 346, Issue 8975, Pages 605-608. **[3]** A. Dueñas-Laita, G. Burillo Putze Bases et al. del manejo clínico de la intoxicación por humo de incendios, Medicina Intensiva 2010, 34-9; 609-619. **[4]** Guidotti T. Acute cyanide poisoning in prehospital care: new challenges, new tools, for intervention. Prehosp Disaster Med. 2005;21(2):s40-s48. **[5]** la revue des SAMU, Médecine d'urgence , Tomme XXXII, N4, June 2010, 263-267.

* When compared to the previous 2 vial presentation

CYANOKIT 5 g powder for solution for infusion. PHARMACEUTICAL FORM: Dark red crystalline *powder for solution for infusion (IV):* 1 vial (containing 5 g of hydroxocobalamin) + 1 sterile transfer device + 1 sterile intravenous infusion set + 1 sterile short catheter for administration to children. **COMPOSITION*:** After reconstitution with 200 ml of diluent, each ml of the reconstituted solution contains 25 mg of hydroxocobalamin. **INDICATIONS:** Treatment of known or suspected cyanide poisoning in all age ranges. Cyanokit is to be administered together with appropriate decontamination and supportive measures. **POSOLOGY AND METHOD OF ADMINISTRATION*: Initial dose:** *Adults:* 5 g. *Paediatric population:* 70 mg/kg body weight not exceeding 5 g.

Body weight in kg	5	10	20	30	40	50	60
Initial dosage in g in ml	 0.35 14	 0.70 28	 1.40 56	 2.10 84	 2.80 112	 3.50 140	 4.20 168

Subsequent dose: Depending upon the severity of the poisoning and the clinical response, a second dose may be administered. *Adults:* 5 g. *Paediatric population:* 70 mg/kg body weight not exceeding 5 g. **Maximum dose:** *Adults:* 10 g. *Paediatric population:* 140 mg/kg not exceeding 10 g. **Renal and hepatic impairment:** Cyanokit is administered as emergency therapy in an acute, life-threatening situation only and no dose adjustment is required in these patients. **Method of administration:** Initial dose of Cyanokit is administered as an intravenous infusion over 15 minutes. The rate of intravenous infusion for the second dose ranges from 15 minutes (for patients extremely unstable) to 2 hours based on patient condition. **CONTRAINDICATIONS:** None. **SPECIAL WARNINGS AND PRECAUTIONS FOR USE*: Treatment of cyanide poisoning must include immediate attention to airway patency, adequacy of oxygenation and hydration, cardiovascular support, and management of seizures. Treatment decisions must be made on the basis of clinical history and/or signs and symptoms of cyanide intoxication.** Smoke inhalation: Before Cyanokit is administered, it is recommended to check affected persons for the presence of exposure to fire smoke in an enclosed area, soot present around mouth, nose and/or oropharynx, altered mental status. Hypotension and/or a plasma lactate concentration ≥ 10 mmol/l are highly suggestive of cyanide poisoning. In the presence of the above signs, treatment with Cyanokit must not be delayed to obtain a plasma lactate concentration. Known hypersensitivity to hydroxocobalamin or vitamin B_{12} must be taken into benefit-risk consideration before administration of Cyanokit. Transient, generally asymptomatic, increase in blood pressure may occur with a maximal increase toward the end of infusion. Effects on blood cyanide assay: Draw the blood sample before initiation of treatment with Cyanokit. Interference with burn assessment due to red colouration of the skin: skin lesions, oedema, and pain are highly suggestive of burns. Interference with laboratory tests because of hydroxocobalamin's deep red colour: Caution is required when reporting and interpreting laboratory results. Interference with haemodialysis: Hydroxocobalamin may cause haemodialysis machines to shut down due to an erroneous detection of a 'blood leak'. This should be considered before haemodialysis is initiated in patients treated with hydroxocobalamin. Use with other cyanide antidotes: has not been established; they must not be administered concurrently in the same intravenous line. **INTERACTION*. FERTILITY, PREGNANCY AND LACTATION*:** *Pregnancy:* There are no adequate data from the use of hydroxocobalamin in pregnant women and the potential risk for humans is unknown. However, taken into account that no more than two injections of hydroxocobalamin are to be administered, the potentially life threatening condition, the lack of alternative treatment, hydroxocobalamin may be given to a pregnant woman. Health care professionals are requested to promptly report the exposure during pregnancy to the Marketing Authorisation Holder and to carefully follow-up on the pregnancy and its outcome. *Breast-feeding:* Because hydroxocobalamin will be administered in potentially life-threatening situations, breast-feeding is not a contraindication to its use. In the absence of data in breast-fed infants, breast-feeding discontinuation is recommended after receiving Cyanokit. **UNDESIRABLE EFFECTS*:** *The most frequents:* reversible red colouration of the skin and mucous membranes, marked dark red colouration of the urine. *Reported in association with Cyanokit use, without frequency estimations:* Decrease in the percentage of lymphocytes; allergic reactions including angioneurotic oedema, skin eruption, urticaria and pruritus; restlessness; memory impairment, dizziness; eye disorders such as swelling, irritation, redness; ventricular extrasystoles; transient increase in blood pressure, hot flush; pleural effusion, dyspnoea, throat tightness, dry throat, chest discomfort; abdominal discomfort, dyspepsia, diarrhoea, vomiting, nausea, dysphagia; pustular rashes (face and neck); headache; injection site reaction; peripheral oedema; artificial elevation or reduction in the levels of certain laboratory parameters. **OVERDOSE*:** Treatment is directed to the management of symptoms. **PHARMACODYNAMIC PROPERTIES*:** Antidotes, ATC code: V03AB33. *Mechanism of action:* Each hydroxocobalamin molecule can bind one cyanide ion by substituting the hydroxo ligand linked to the trivalent cobalt ion to form cyanocobalamin, a stable, non toxic compound that is excreted in the urine. **PHARMACOKINETIC PROPERTIES*. PRECLINICAL SAFETY DATA*. INCOMPATIBILITIES*:** Cyanokit must not be mixed with other medicinal products except the recommended diluant. No simultaneous administration of hydroxocobalamin through the same intravenous line with the following drugs: diazepam, dobutamine, dopamine, fentanyl, nitroglycerin, pentobarbital, phenytoin sodium, propofol, thiopental, epinephrine, lidocaine hydrochloride, adenosine, atropine, midazolam, ketamin, succinylcholine chloride, amiodarone hydrochloride, sodium bicarbonate, sodium thiosulfate, sodium nitrite, ascorbic acid. Simultaneous administration of hydroxocobalamin and blood products through the same intravenous line is not recommended. **SPECAIL PRECAUTIONS FOR STORAGE*:** Do not store above 25°C. The reconstituted solution has to be used immediately. **SPECIAL PRECAUTIONS FOR DISPOSAL AND OTHER HANDLING*:** The vial is to be reconstituted with 200 ml of diluent (sodium chloride 9 mg/ml (0,9 %) solution for injection) using the supplied sterile transfer device. The intravenous infusion set provided in the kit must then be used. **MARKETING AUTHORISATION HOLDER:** Merck Santé s.a.s., Lyon, France. **MARKETING AUTHORISATION NUMBER:** EU/1/07/420/002

*For more information, please refer to the SmPC on the EMA website.
Please always refer to full prescribing information applicable in your country, which may vary. This prescription only medicine may not be available in your country.
Production Date: March 2011.

Merck Serono

Merck Serono is a division of Merck.

3045260001

MERCK