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CORRECTION OF PSYCHOACTIVE POISONING IN THE MANAGEMENT OF CARDIORESPIRATORY ARREST

Caroline Nascimento Menezes
Faculdade Tiradentes, Aracaju
http://lattes.cnpq.br/7917915676222437

Giovanna Brasil Pinheiro
Faculdade Tiradentes, Aracaju
http://lattes.cnpq.br/0853639987217961

Beatriz Villar Meneses Santos
Faculdade Tiradentes, Aracaju
http://lattes.cnpq.br/4842028005348466

João Matheus Góes Zedafo Ramos
Faculdade Tiradentes, Aracaju
http://lattes.cnpq.br/6979505623615516

Henrique Tetsuya Libânio Kitaoka
Faculdade Estacio, Alagoinhas

Luana Rocha de Souza
Faculdade Tiradentes, Aracaju
http://lattes.cnpq.br/8471986302764645

Victoria Maria Fontes dos Reis
Faculdade Tiradentes, Aracaju
http://lattes.cnpq.br/1849266533433847

Edenia Soares de Figueiredo Macario
Faculdade Tiradentes, Aracaju
http://lattes.cnpq.br/0178885751243711

Maria Marta Prado Lima
Faculdade Tiradentes, Aracaju
http://lattes.cnpq.br/4696911919083413

Marco Antonio Silva Robles
Faculdade Tiradentes, Aracaju
http://lattes.cnpq.br/5063057988322956

Mariana Sattler Lima Medina
Faculdade Tiradentes, Aracaju
http://lattes.cnpq.br/4878481122527810

Filipe Matias Batista Mota
Faculdade Tiradentes, Aracaju
http://lattes.cnpq.br/1517943556967941

Abstract: Introduction: Poisoning by psychoactives occurs for several reasons, among the main ones: accidental administration, attempts at self-extermination and abuse, in addition to administration errors. Among the main psychoactive drugs related to intoxication, tricyclic and tetracyclic antidepressants, serotonergic antidepressants, benzodiazepines, opioids and cocaine stand out. Acute intoxications are on the list of causes of CPA in adults and each type has its particularity and pathophysiological mechanism. The management of this condition becomes crucial for the reversal of the arrest condition, since the treatment of the causes is paramount in the approach of the patient in CPR repeatedly without success. That said, the current study aims to compendium the correction of intoxication by psychoactives in the management of CRP. **Methodology:** This is a narrative review in which Scielo, PubMed, Lilacs, UpToDate and Google Scholar databases were used to determine articles. Keywords were defined by the Health Sciences Descriptors (DeCS). For selection, the analysis was qualitative. It was up to the current study to increase articles whose discussion determined the specificities of the management of acute intoxications in order to apply them, or not, in the face of a situation of CRA. **Results:** Faced with CPA due to intoxication, the use of antidotes and increased elimination of the substance through hydration and urine alkalinization can be used. For suspected intoxication and identification of a toxic substance, one can mainly investigate non-cardiac adult patients who are admitted to the medical service in an arrest protocol. In contact with the family, it is valid to question drugs or medications ingested, time and day of ingestion and whether ingestion was accidental or via suicide attempt. Some non-specific complementary tests can be useful in the face

of generalized clinical deterioration, but as intoxication, these can be reserved for special cases. All specific treatment must be linked, without detriment, to chest compressions, application of adrenaline or amiodarone (in the indicated cycles), rhythm and pulse checking, in addition to the administration or not of electrical defibrillation. **Conclusions:** Poisoning by psychoactives has taken a relevant proportion in view of the incidence of psychiatric emergencies in the emergency room. Recognizing this possibility allows for the development of specific or supportive therapies that can support cardiopulmonary resuscitation. Despite this, its treatment must not be used to the detriment of the well-established management of CRP. After all, other causes of arrest may coexist, and some antidotes that apply to psychiatric emergencies are not necessarily recommended in the face of cardiorespiratory arrest.
Keywords: Acute intoxication. psychoactive. Cardiorespiratory arrest. Cardiorespiratory resuscitation.

INTRODUCTION

Psychoactives are, according to the World Health Organization (WHO) (1981) substances that act on the central nervous system, producing changes in behavior, mood and cognition, and leading to dependence (WHO, 1981). Medications acting on the central nervous system and drugs make up this class.

Poisoning by psychoactives occurs for several reasons, among the main ones: accidental administration, attempts at self-extermination and abuse, in addition to administration errors (GONÇALVES et al., 2017). Among the main psychoactive drugs related to intoxication, tricyclic and tetracyclic antidepressants, serotonergic antidepressants, benzodiazepines, opioids and cocaine stand out.

According to the National System of Toxic-Pharmacological Information (Sinitox), in 2003 alone, drugs were responsible for 28.2% of intoxication cases registered in the country (ANVISA, 2007). Benzodiazepines are among the most widely used. In Brazil, they are also used on a large scale and are significantly related to cases of intoxication, especially due to Clonazepam abuse.

Another reality is the cross-use of substances, such as antidepressants and benzodiazepines with alcohol. Substances can act synergistically on the same system, cause cardiorespiratory arrest, induce coma and cause death (RANG, 2007).

Complications related to substance abuse in emergency rooms represent a significant fact today, especially in the adult population. Intoxication is defined as a set of adverse effects caused by a chemical agent, due to its interaction with the biological system, triggering an imbalance in the body or a pathological state where, usually, it is revealed clinically by a set of toxic signs and symptoms that can end in cardiopulmonary arrest (CPA).

The latter is defined by the sudden cessation of systemic circulation, associated with the absence of breathing. With this diagnosis, cardiopulmonary resuscitation (CPR) cycles are initiated and, in the absence of success, the need to identify the causes of arrest increases, didactically summarized in 5 initials with "H" and 5 initials with "T" (table 1).

5 "H"	5 "T"
hypovolemia	cardiac tamponade
hypoxia	Pulmonary thromboembolism
Hypothermia	coronary thrombosis
Hyperkalemia/hypokalemia	Tension (hypertensive pneumothorax)
H+ - metabolic acidosis	Toxic (intoxication)

Table 1. Possible causes of PCR.

Acute intoxications are on the list of causes of CPA in adults and each type has its particularity and pathophysiological mechanism. The management of this condition becomes crucial for the reversal of the arrest condition, since the treatment of the causes is paramount in the approach of the patient in CPR repeatedly without success.

That said, in order to improve the prognosis of some patients, the current study aims to compendium the correction of intoxication by psychoactives in the management of CRP.

METHODOLOGY

This is a narrative review whose objective is to compend the correction of intoxications by psychoactives in the management of CRP. For this, Scielo, PubMed, Lilacs, UpToDate and Google Scholar databases were used to determine articles. Keywords were defined by the Health Sciences Descriptors (DeCS) in "acute intoxication", "psychoactives", "cardiorespiratory arrest" and "cardiorespiratory resuscitation".

For selection, the analysis was qualitative. It was up to the current study to increase articles whose discussion determined the specificities of the management of acute intoxications in order to apply them, or not, in the face of a situation of CRA. Therefore, materials whose approach did not contribute to the research detail were excluded.

There was no distinction by date or place of publication, as well as by language or country of origin.

RESULTS

The reason that most drug intoxications involved drugs that act on the central nervous system may be related to the increase in the use of this class of substance, especially due to the growth in the number of patients diagnosed with psychosomatic diseases, such as depression, anxiety, panic, among others (MOJTABAI et al., 2016). The consumption of alcohol and other drugs has also been associated with psychiatric disorders, such as intolerance to frustration, aggression, impulsivity and family problems (GALDURÓZ et al., 2010).

In the vast majority of intoxications, no further examination is necessary. However, in some situations, general tests may be necessary, such as blood count, liver function, kidney function, urine, among others. Eventually, dosage of toxic substances may be necessary through quantitative or qualitative tests.

Once the causes of arrest have been identified through clinical history and careful physical examination, care continues through volume infusion and administration of specific treatment based on the type of intoxication.

GENERAL PRINCIPLES

During the management of CPA with suspected intoxication, it is necessary to identify the toxic substance, assess its risk and the severity of the patient, stabilize it clinically considering the use of antidotes, reduce the absorption and increase the elimination of this substance, as well as prevent re-exposure through psychiatric follow-up. Reducing absorption through activated charcoal, gastric lavage, or intestinal irrigation are not viable alternatives to stopping. However, the use of antidotes and increased elimination of the substance through hydration and alkalization of the urine can be employed.

For suspected intoxication and identification of a toxic substance, one can mainly investigate non-cardiac adult patients who are admitted to the medical service in an arrest protocol. In contact with the family, it is valid to question drugs or medications ingested, time and day of ingestion and

whether ingestion was accidental or via suicide attempt.

Some nonspecific complementary tests may be useful in the face of generalized clinical degradation, but as intoxication, these may be reserved for cases with relevant comorbidities, unknown type of toxic, signs of systemic toxicity and intentional ingestion. Among them, the electrocardiogram, radiography, blood gases and urine can narrow the diagnostic hypotheses – but they participate in an evaluation secondary to the primary management of CPR.

All specific treatment for acute intoxications must be linked, without detriment, to chest compressions, application of adrenaline or amiodarone (in the indicated cycles), rhythm and pulse checking, in addition to the administration or not of electrical defibrillation.

BENZODIAZEPINES

Poisoning often related to suicide attempt in young women. It works by hindering the excitation of neurons that contain the GABAA receptor (so called because it works when the neurotransmitter gamma - aminobutyric acid, or GABA, binds to it). They are mainly represented by: diazepam, flurazepam, clonazepam, lorazepam, flunitrazepam, alprazolam and midazolam.

In this case, airway protection is essential and intubation is primarily indicated. The specific antagonist is flumazenil, which is recommended for intravenous use, at a dose of 0.1 mg in 1 minute and repeated until the desired effect (with a maximum limit of 6 ampoules). The swallowing reflex is a good parameter for reversing intoxication, since the patient will rarely resuscitate lucid and oriented.

Observational care is related to the risk of withdrawal syndrome, seizures, and use in patients with QRS interval prolongation.

TRICYCLIC AND TETRACYCLIC ANTIDEPRESSANTS

It represents another class of psychoactive drugs related to intentional abuse whose number of cases has increased in recent years due to the increased access to these medications through the higher incidence of depression diagnosis. The mechanism of action occurs through the inhibition of presynaptic reuptake of several neurotransmitters, increasing their effects in the cleft. The tricyclics are mainly represented by: amitriptyline, imipramine, clomipramine and nortriptyline, while the tetracyclics are bupropion, maprotiline and mitarzepine.

No specific antidotes are used in these cases. However, as early death usually occurs due to arrhythmias, sodium loading and serum alkalinization can be used. In this strategy, 850 mL of glucose solution must be diluted + 150 mEq of 8.4% sodium bicarbonate and start with 200 to 300 mL IV. In case of reversal of CRP, this infusion must be maintained every 1 hour with monitoring of serum pH to maintain it greater than 7.55.

There are no studies that corroborate the prophylactic use of bicarbonate, however, the basic and advanced life support guidelines, launched in 2015, brought some news about BLS and ACLS procedures, among which it is stated not to routinely use sodium bicarbonate, with the exception of in cases in which the etiology of the arrest is related to situations where bicarbonate would act as an antidote, such as intoxication by tricyclic antidepressants, acidosis or hyperkalemia previous and related to a CRP.

In case of association with benzodiazepine in this intoxication, the use of flumazenil is contraindicated, maintaining the conduct during CPR in supportive treatment with guarantee of a definitive airway.

SEROTONERGIC ANTIDEPRESSANTS

They are mainly represented by fluoxetine, paroxetine, sertraline and venlafaxine. They act by elevating serotonin in the Central Nervous System and peripheral tissue. However, their specific antidotes are rarely needed in psychiatric emergencies and avoided during the management of CPR – as the use of Cyproheptadine and Chlorpromazine are related to hypotension.

In the face of some of these toxicants, following basic management and associating supportive measures are more essential.

OPIOIDS

They act on receptors in the CNS and produce analgesia, euphoria and sedation effects. Examples include: codeine, morphine, meperidine, fentanyl, alfentanil and heroin.

Passive or even active warming must be provided, if necessary, and blood volume must be restored. A common complication is acute noncardiogenic pulmonary edema, whose specific management during cardiac arrest may be related to its resolution. Nor must the guarantee of a definitive airway be delayed.

The specific treatment well employed is the use of Naloxone; the starting dose is 1 to 4 mg. It can be administered intratracheally, intramuscularly or intravenously. Repeat doses may be necessary within 1 hour, due to its short half -life. Continuous infusion can be considered in patients who need frequent doses, at an initial rate of half the dose with which a therapeutic response has been obtained, per hour, in a solution diluted in saline.

COCAINE

Cocaine (and other sympathomimetics, such as amphetamines) acts by hyperactivating the sympathetic nervous system and has a range of administration routes, such as oral, inhaled, nasal and parenteral. This type of intoxication faces a greater challenge during PCR because the specific antagonist is a Central Nervous System depressant – a benzodiazepine -, whose action tends to prolong the patient's lowering.

That said, cardiovascular support measures, hemodynamic stabilization, and CPR follow-up are best used.

CONCLUSIONS

The management of CPR with prioritization of chest compressions, administration of adrenaline/amiodarone, and individualized application of electrical defibrillation is well established for reversing the condition and improving the patient's prognosis. However, it is known that some unsuccessful cycles suggest the identification of the possible cause for the current clinical scenario. In this sense, intoxications by psychoactives have taken a relevant proportion in view of the incidence of psychiatric emergencies in the emergency room. Recognizing this possibility allows for the development of specific or supportive therapies that can support cardiopulmonary resuscitation.

Among the main psychoactive drugs related to intoxication, tricyclic and tetracyclic antidepressants, serotonergic antidepressants, benzodiazepines, opioids and cocaine stand out, some of which are associated with each other or with the use of alcohol, whose correction during the management of CRP (Table 2) was discussed throughout the article.

Finally, despite the basic need to correct the intoxication, its treatment must not be used to the detriment of the well-established management of CRP – on the contrary, the diagnostic suspicion and the establishment of conduct must be sober

Toxicity level psychoactive	Correction during PCR
benzodiazepines	Via definitive area, Antidote: Flumazenil (0.1 mg in 1 minute, IV, with repetition)
tricyclic and tetracyclic antidepressants	general support Sodium loads and serum alkalinization
serotonergic antidepressants	cardiovascular support hemodynamic stabilization CPR follow-up
opioids	Hypothermia prevention definitive airway Antidote: Naloxone (1-4 mg, IT, IM or IV, with repeat)
cocaine	cardiovascular support hemodynamic stabilization CPR follow-up

Table 2. Correction of psychoactive poisoning in the management of cardiorespiratory arrest.

and individualized. After all, other causes of arrest may coexist, and some antidotes that apply to psychiatric emergencies are not necessarily recommended in the face of cardiorespiratory arrest.

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