760 atropine ampules used to treat a patient with severe pesticide intoxication in a low resources setting

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Abstract

We reported the case of a 24-year-old male patient that arrived unconscious; with no identifiable vital signs, a complete lack of response to pain stimuli and presented an extremely myotic pupils. Due to the report of his relatives we diagnosed an acute self-induced organophosphate (OP) intoxication through the ingestion of a full bottle of malathion. Endotracheal intubation, chest compressions, and manual ventilation were performed until the heart monitor showed slow myocardial activity. The patient was treated with atropine in the absence of specific antidote (pralidoxime). A continuous peripheral IV infusion of atropine was started at a rate of 2 mg IV every 3 min. Given the constant decline in the patient's heart rate, the dose was constantly increased according to the vital sign chart until complete atropinization was achieved (heart rate over 120'). After administering a total of 760, 1 mg/ml ampules within 12 hours, a significant improvement was observed. The patient was discharged from the hospital 8 days later with no further complications.

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Resumen

760 ampollas de atropina utilizadas para tratar a un paciente con intoxicación grave por plaguicidas en un entorno de bajos recursos

Reportamos el caso de un paciente de 24 años de edad, admitido a un centro hospitalario de segundo nivel en la ciudad de Quito. El paciente ingresó en malas condiciones generales sin signos vitales identificables, ausencia total de respuesta a estímulos dolorosos y pupilas extremadamente mióticas. Cuando un familiar refirió la ingesta de pesticida se diagnosticó como una intoxicación aguda por organofosforados (OP). Luego de la intubación endotraqueal, compresiones torácicas y ventilación manual, el paciente mostró una actividad miocárdica irregular y bradicardia significativa. El paciente fue tratado con atropina IV a dosis altas debido a la ausencia de pralidoxima como antídoto específico. La infusión de atropina se inició a una velocidad de 2 mg IV cada 3 min. Sin embargo, debido a la disminución constante de la frecuencia cardíaca del paciente, la dosis se incrementó hasta alcanzar niveles de atropinización completa (frecuencia cardiaca superior a 120/minuto). Después de administrar un total de 760 ampollas de atropina de 1 mg/mL dentro de las 12 primeras horas de admitido el paciente, se observó una mejora significativa. El paciente fue dado de alta del hospital 8 días después, sin mayores complicaciones.

Palabras clave: Intoxicación por organofosforados, Tratamiento farmacológico, Atropina, Ideación suicida, Malatión, Reporte de caso

Introduction

According to the World Health Organization (WHO), more than two million people try to commit suicide ingesting pesticides worldwide every year and from these attempts more than 10% result in death [1]. In addition to suicide, other negative effects of this type of chemical can be found, especially non-intentional poisoning, higher incidence of birth defects and water sources contaminations represent a major health problem in countries where these products are widely used [2-4]. In Ecuador the National Institute of Census and Statistics registered 21.583 cases of organophosphate intoxication in a 10 years' period, according to this data, there is an increment of more than 37% since 2001 to 2010 [5].

Organic derivatives of phosphorus-containing acids are organic substances first developed as insecticides in 1940 [6]. The chemical structure of organic phosphorus-containing substances makes them highly soluble in lipids and its volatile compounds facilitate their absorption by short dermal exposure times, inhalation or ingestion [7]. Once the substance is absorbed, the acid containing particle combines with the cholinesterase enzyme (AChE) also known as acetylcholinesterase, creating a highly selective, competitive and irreversible union [8-10]. This combination disables the normal function of the enzyme and prevents the hydrolysis of acetylcholine to choline and acetic acid within the nerve endings synapses [11].

Once the acetylcholinesterase upturns, intense toxic cholinergic manifestations are visible, classified in muscarinic and nicotinic effects that affect the entire nervous system, from the superior cortex to the peripheral synapses [11]. In most cases, organophosphate poisoning causes evident clinical manifestations within the first three hours after oral consumption, while skin exposure may be delayed up to 12 hours [12, 13]. In general terms, most of patients will have most of the following clinical manifestations: acute intoxication period characterized by altered state of consciousness, neuromuscular alterations, dyspnea, sweaty cold skin, excessive gastrointestinal, bronchial, parasympathetic innerved glands secretions and pin-point (constricted) pupils [14]. A further symptomatology that occurs 24 to 48 hours after exposure is weakness of muscles at the extremities, with compromised respiratory function, decreased or absent reflexes; and, additionally, a late neurotoxicity symptomatology can occur up to 4 weeks after exposure [15, 16]. Diagnosis can be made based on clinical manifestations, although ideally laboratory tests, by measuring serum acetylcholinesterase or butyrylcholinesterase concentrations are the gold-standard to confirm organophosphate intoxications [17, 18].

Initial treatment begins with support of circulation, airway and breathing (CAB) [19]. The patient under cardiac arrest is managed in accordance with the current standards of care, including Advanced Cardiovascular Life Support (ACLS) and other necessary measures [20]. Once the patient is stable and spontaneous circulation is achieved, a complete removal of any sources of the substance is compulsory, including clothing removal and skin cleaning with tap water or saline solution [21]. Aggressive antidote treatment, fluid resuscitation, gastric and mucous suctioning, urethral catheterization, vital signs monitoring as well as complete lab test and toxicological screening should be started as soon as possible. Specific medical therapy includes anticholinergic drugs (atropine or glycopyrrolate) and specific antidotes like pralidoxime should be promptly administered [21-23]. Benzodiazepines may also be used in order to prophylactically decrease neurocognitive dysfunction and to reduce patient's stress [24].

When available, pralidoxime should be administered. This molecule acts as an acetylcholinesterase enzyme activator, binding the inactivated portion of the enzyme, and liberating the phosphate group, thus, muscarinic and nicotinic symptomatology will be progressively reversed [21, 25]. In low-resource settings where pralidoxime might be hard to obtain, anticholinergic drugs, such as atropine, is the only option to improve pulmonary ventilation and to reduce intrapulmonary secretions [26]. Atropine should be initiated promptly at a rate of 1 to 2 mg IV bolus, repeating administration every 3 to 5 min, or intravenous continuous perfusion until atropinization is achieved: heart ratio >120/min, systolic blood pressure >80 mmHg, pupils dilated, presence of bowel sounds, and absence of fasciculation or seizures [27, 28].

Case Report

A 24-year-old farmer was brought at 10:30 am to the emergency department of Hospital Pablo Arturo Suarez in Quito, Ecuador. At the moment of arrival, physical examination vital signs were not identified; the patient did not respond to any pain stimuli, there was so much oral secretions, the skin felt diaphoretic; and his pupils were extremely myotic (pin-point pupils) without reactivity. The patient was managed with advanced life support, vasoactive agents such as epinephrine, defibrillation for one time and endotracheal intubation. After that the heart monitor showed slow activity and pulmonary crackles were heard; Glasgow Coma Scale improved from 3 to 6/15.

After stabilizing the patient, relatives attested that while celebrating New Year's Eve at home; patient was passing out and for an autolytic intention he drunk approximately 500 ml of a pesticide's bottle which seemed to contain Malathion; consequently, acute self-induced organophosphate (OP) intoxication was diagnosed. Blood samples were drawn and atropine infusion was administered. Infusion started at a rate of 1 mg IV every 3 minutes while controlling vital signs. Ten minutes later, due to the fact that the patient's heart rate fluctuated within a range of 30-40 beats/min with presence of bronchial secretions, the dose of atropine was increased up to 1 mg IV per minute for near of 50 minutes. Next, the patient did not achieve atropinization yet and due to his persistent

bradyarrhythmia and abundant bronchial secretion, the dose of atropine was increased to 2 mg IV per minute diluted in saline solution administrated through the pump as we aimed to achieve a heart frequency of about 100-120 beats/min. Lab results of blood biometry, blood chemistry, and electrolytes were reported; the values altered were glucose 171 mg/dl and blood sodium 167mEq/l. While the patient was in the Emergency Intermediate Care Unit the continuous vital signs monitoring showed that after 6 hours the team could not reach the atropinization umbral. At the end of the day, around 17:30 approximately the patient's vital signs began to stabilize and his pupils reacted slowly to direct light stimulation. After eight hours of continuous motorization, the umbral of atropinization was achieved, the amount of bronchial secretions decreased, pupil diameter improved and the heart ratio ranged from 110-130 beats/min. at this moment the dose of atropine was decreased to 1 mg every five minutes with continuous monitoring. Finally, twelve hours later having used all the atropine ampules from the hospital, nearby pharmacies and relatives having obtained 400 additional ampules with a total of seven hundred and sixty 1 mg/ml atropine ampules, the patient aroused from his stupor, asked us with signals that the endotracheal tube was bothering him and after checking his vital signs and his fight against the ventilator the team decided to withdraw the mechanical respiratory assistance. After discussed this episode with the patient and his relatives and after observing his improvement, an alert and regretful patient with a Glasgow of 15/15 was discharged from the ER 24 hours later. He was admitted to the internal medicine ward to complete the psychiatry evaluation and the follow up for his intoxication, however after eight days of normal results and behavior no further complications were reported.

Discussion

Worldwide, pesticide poisoning specially those caused by organophosphate (OP) and its derivate are the main cause of pesticide induced suicide [1, 2, 29]. Regardless the number of cases reported each year, the treatment of acute self-induced organophosphate intoxication usually relies in the rapid administration of specific antidote and a correct treatment and still causes several thousand deaths every year around the globe [30]. In low resource setting specially those located in developing countries where the economy its driven by agriculture the availability of this products is extensive. In those locations usually the list of essential drugs approved by the World Health Organization is not always available, making difficult to health care providers to accomplish the international guidelines [31].

In that situation when pralidoxime is not available, higher doses of atropine could save the life of the patients with life-threatening intoxication [26, 32, 33]. The international guidelines are clear, pralidoxime should be used as the first line of treatment for OP intoxication, however, in real life situations where the health care access is not fully achieved and the lack of resources is evident, desperate measures should be considered [34]. In the situation the medical team experienced many years ago the goal of the treatment was to revive the patient, decrease muscarinic related symptoms although the dosage used have never been described before in such a level the final outcome very positive.

We do not recommend this type of treatment when proper measures are available, however around the globe specially in the poorest regions in the world patient with acute, severe, self-induced organophosphate intoxication, using more than 760 ampules of atropine 1mg/dl over eight hours of treatment could potentially save someone's life. The international guidelines recommend us to treat the patient with 1 mg ampules per 3 minutes, but with continuing monitoring of heart ratio and bronchial secretions it was realized that the usual doses was not enough after ten minutes of treatment [25, 35]. Then high doses of atropine were administered with continuous perfusion initially with 1 mg per minute for 50 minutes that only helped with decrease of bronchial secretions and finally continuous perfusion achieved 2 mg per minute for six hours. With this dosage heart ratio remains in a range of 40 to 60 beats per minute and bronchial secretions almost disappear, condition known as atropinization [36]. Once the patient reached atropinization infusion was decreased to 1 mg atropine per each 3 minutes, patient was kept under observation in case of further complications.

In clinical practice, dosage regimens are usually designed according to severity of poisoning and to the signs of atropinization [26]. Abedin et al. in 2012, reported that individualized incremental bolus dose followed by continuous infusion, the same regimen used in this case, has several advantages over conventional incremental bolus doses alone [26].

Conclusion

In low resources settings, a severe phosphorus-containing acid (organophosphate) intoxication, self-induced or not, is a therapeutic challenge, especially when the specific antidote pralidoxime is not available. After performing CPR and ABC vital support measures, high doses of atropine or atropine in continuous perfusion can save the life of patients presenting potentially life threatening organophosphate intoxication.

Conflicts of interest

The authors declare that there is no conflict of interest of any kind.

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Author contributions

The authors contributed equally in this report.

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