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Haloperidol poisoning in pediatric patients

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Abstract

Exposing a child to a potentially toxic substance is an uncommon cause of consultation in childhood. Poisoning by drugs in this age group is commonly due to improper administration by parents or error in dosage by the doctor; also ingestion at own initiative, i.e. self-poisoning. **Case report:** *A 11 years-old male, drowsy, unresponsive, with bradypsychia, assisted ambulation without increased support arch, resting tremor; obeying orders without verbal response, isochoric pupils, difficulty opening the eyes without facial asymmetry, muscle contracture of platysma, increased muscle tone, tendon reflexes slightly increased, arrhythmic heart sounds without murmurs. On interrogation, the subject mentioned his own decision to ingest about 0.7-0.9 mg of haloperidol (0.35-0.45 ml / 7-9 drops).* **Laboratory studies:** *BUN 12 mg/dl; creatinine 0.5 mg/dl; Na 140 mmol/l; K 3.38 mmol/l; Cl 100.2 mmol/l; LDH 363 U/l; CK 130 U/l; CK-MB 13 U/l. Electrocardiogram DII length (13:00 h) with sinus rhythm, FC 100 x, corrected QT 0.57; stroke control (19:20 h) FC 70 x, QTc of 0.41 (Fig. 1). He was treated with diphenhydramine 1 mg/kg/dose with clear improvement at 12 hours after admission, so his discharge at 24 hours was decided without any additional medication.* (Gac Med Mex. 2017;153:116-9)

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Introduction

Currently, poisonings represent a growing problem in the world and they involve a broad spectrum of noxious chemical substances, the effects of which have not yet been described; however, most reported poisonings are those caused by medications.

Exposure of a child to a potentially toxic substance is an uncommon reason for medical consultation, and accounts for less than 10% of emergencies[1].

Poisoning with medications in this age group is due to incorrect administration by parents or dosing error by physicians[1-4].

Preponderant dugs in this situation are analgesics, but endless active agents for medical use can be found (neuroleptic drugs, hypnotic drugs, sedative drugs, etc.)[1-4].

Here, we present an uncommon case of self-poisoning, the causes of which are scarcely described at pediatric ages.

Clinical case

This is the case of an 11-year old male diagnosed with attention deficit-hyperactivity disorder on medical management with methylphenidate, haloperidol, fluox-

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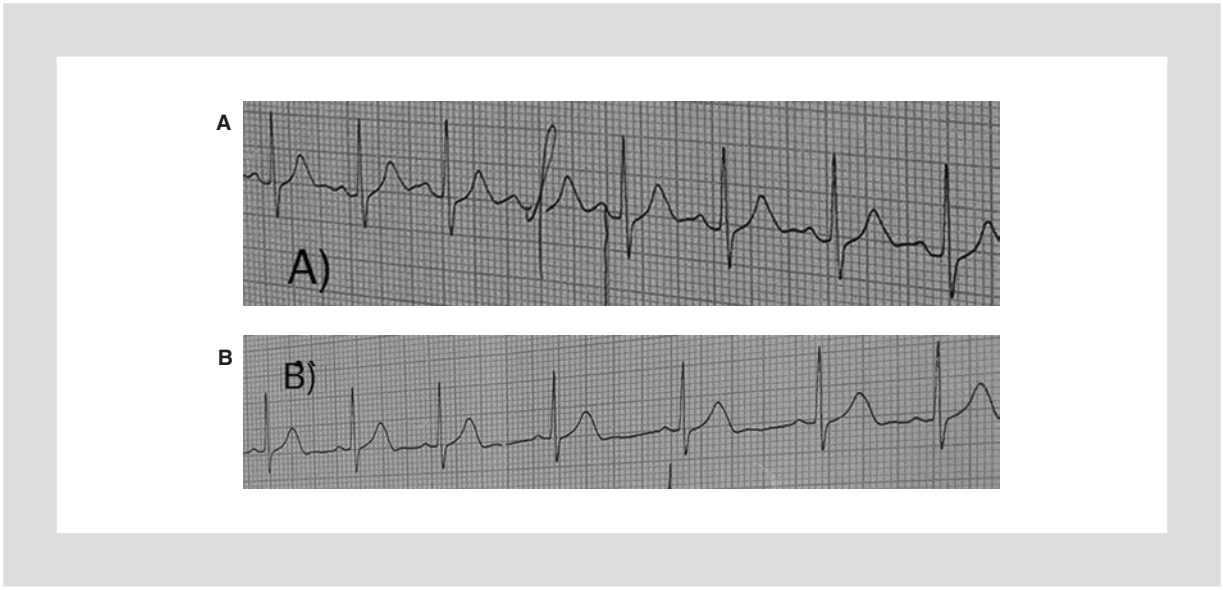

Figure 1. *Patient electrocardiogram.* **A:** *DII at admission.* **B:** *DII at 6 hours of management.*

etine and carbamazepine (parents indicated rather unspecific doses). He was brought to the department of pediatric emergencies (02:15 h) because he was experiencing chest pain and somnolence that was reduced after the ingestion of milk, as well as left side mouth corner deviation, dysarthria, masseter muscles sustained contraction (trismus), motor restlessness and opisthotonus in two occasions. On physical examination a temperature of 36.7 °C was found, as well as HR of 92 bpm, RR 22, weight 37.7 kg and SaO_2 of 94%. He was with somnolence, uncooperative, with bradypsychia, assisted ambulation without increased support arch and resting tremor. He was obeying orders without verbal response, had isochoric pupils with normal reflexes, difficulty to open the eyes, no facial asymmetry, contracture of the platysma muscle, increased muscle tone, tendon reflexes slightly increased. Heart sounds were arrhythmic without murmurs. Laboratory tests indicated BUN 12 mg/l, creatinine 0.5 mh/dl, Na 140 mmol/l, K 3.38 mmol/l, Cl 100.2 mmol/l, LDH 363 U/l, CK 130 U/l and CK-MB 13 U/l. The electrocardiogram showed DII length (13:00 h) with sinus rhythm, HR 100 bpm; corrected QT 0.57; control electrocardiogram (19:20 h) HR 70 bpm, corrected QT of 0.41 (Fig. 1).

When interviewed, the subject referred having ingested (22:50 h), at his own will, approximately 0.7-0.9 mg of haloperidol suspension (0.35-0.45 ml, 7-9 drops).

He was managed with diphenhydramine, 1 mg/kg per dose, with notorious improvement at 12 hours of admission, and discharge was therefore decided at 24 hours without further medication, after previously instructing the parents with regard to signs of alarm.

Discussion

In 2013, the Annual Report of the American Association of Poison Control Centers reported 2,188,013 cases of exposure to toxic agents, out of which 12.5% were due to therapeutic errors, with the majority (1,342,862) occurring in pediatric patients between one and 19 years of age and with a slightly higher incidence in males (52.11%)[5].

Most common causative agents in the general population were analgesics (11.5%), cosmetics or personal hygiene products (7.7%), household cleaning substances (7.6%), sedative/hypnotic/neuroleptic drugs (5.9%) and antidepressants (4.2%), whereas in children younger than 5 years analgesics were at third place, with 9.8% of cases[5].

Furthermore, mortality of 8.1% was reported, where predominant lethal agents were analgesics (acetaminophen, tramadol, etc.), cardiovascular medications (verapamil, amlodipine, etc.), antidepressants (venlafaxine, amitriptyline, etc.) and hypnotic/sedative drugs (alprazolam, benzodiazepines, etc.)[2,5].

In Mexico, in spite of the lack of updated statistical data, 1,339 deaths of all ages were reported in 2001, mostly accidental (78%), with the household being the most common place of the event[2].

According to Fernández Barocio and Sánchez-Villegas[6], the National Medical Center La Raza Dr. Gaudencio Garza General Hospital pediatric emergency department conducted a study from 1993 to 1998 that reported 2,067 poisonings, where the group aged between 12 and 23 months was predominant (34.8%), with most common drugs being benzodiazepines, carbamazepine and acetaminophen[6].

In our case, the toxic effect causative agent was haloperidol, which was wrongly taken by the subject's own decision, at a dose slightly higher than prescribed (6 drops). Its infrequency is due to the emergence of new selective neuroleptic agents and the scarce therapeutic use it has in pediatric patients.

Haloperidol is a neuroleptic drug that belongs to the butyrophenones family; with antipsychotic properties, it is used for the treatment of schizophrenia and mania in adults, while at pediatric ages its use has been described for the control of behavioral and hyperactivity disorders, as well as for La Tourette syndrome[7-9].

It is a highly potent drug that is used for the management of acute states, such as psychosis, phases of mania, hyperactivity, aggressiveness and delirium.

Haloperidol is a competitive agent with central or peripheral catecholamine neurotransmitters; in addition, it is a D1, D2, H1, H2 and alpha 1 and 2 receptor blocker, as well as of serotonin and muscarinic receptors, which causes a large number of symptoms ranging from dizziness to neuroleptic malignant syndrome[7-11]. Its absorption is entirely through the gastrointestinal tract, it is metabolized by the liver and is excreted in urine, breast milk and feces. After oral administration, plasma half-life ranges from 12 to 38 hours. It has a wide tissue distribution and crosses the blood-brain barrier.

Poisonings are mostly of acute evolution. Haloperidol overdose main manifestation is usually extrapyramidal syndrome, hypotension, respiratory distress, catalepsy and loss of alertness[7,10].

Other adverse symptoms have been less frequently described, but they are often more serious: akathisia, dystonic reactions (torticolis, retrocolis, jaw and tongue contracture, oculogyric crises and even opsithotonus), hyperreflexia and serotonin syndrome[7-13].

Arici et al.[11] mention in their study that children between 0 and 12 years of age are the most affected patient group that suffer dystonic reactions as a consequence of the use of drugs in general, among which neuroleptics are at first place, with haloperidol being the second most common causative agent, only surpassed by metoclopramide[11].

Cases of large overdosing may be complicated by shock, coma, rhabdomyolysis and ventricular fibrillation; a sign of bad prognosis is persistent hyperthermia. Chronic use, even at therapeutic doses, may cause hard-to-manage tardive dyskinesia[7,14].

Anticholinergic effects include dry mouth, constipation, blurry vision, diaphoresis and urinary retention. Cardiac effects may include hypotension, tachycardia, arrhythmias (conduction defects and ventricular fibrillation): cardiac alterations are more pronounced 10-15 hours after ingestion[4,7]. In addition, there are evidences of a relationship between haloperidol overdose and long QT syndrome and torsade de pointes[10,15,16].

Neuroleptic malignant syndrome is a rare condition that occurs as an idiosyncratic reaction to the treatment with antipsychotic drugs at therapeutic doses. It is characterized by hyperthermia, extrapyramidal syndrome, muscle stiffness, altered consciousness level and autonomous dysfunction[17].

The treatment for haloperidol poisoning includes the use of biperiden (0.04 mg/kg oral, intramuscular or intravenous, up to 4 doses at 30-munute intervals) and promethazine. Promethazine recommended pediatric dose to provide an antihistaminic effect is 0.1 mg/kg (12.5 mg maximum) by oral route every 6 hours as appropriate; however, its use is contraindicated in children younger than 2 years owing to the lethal potential due to the serious respiratory depression it causes as an adverse effect[7,9,14,18,19].

When these agents are not available, diphenhydramine usefulness stands out for the treatment of acute poisoning. It is initially slowly administered by intravenous route (1 mg/kg per dose) and, once the symptoms have resolved, it is continued by oral route for at least 72 hours[7,9,14].

In case D2 antagonism-associated adverse effects predominate, therapy implies dose reduction and addition of an antiparkinsonian agent by parenteral route, such as benztropine (0.02 mg/kg, 1 mg maximum), trihexyphenidyl and procyclidine[4,18,20-22].

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