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Case Report

Atropine Intoxication in a Child after Accidental Ingestion of 200 mg Atropine Sulfate - A Case Report

Elvin Aliyev[1], Ömür Görgülü[1], Zerrin Yalvaç[2], Suat Biçer[2*], Ebru Türköz Acar[3], Mohammad Charehsaz[3], Ayça Vitrinel[2]

[1]*Yeditepe University, Faculty of Medicine, 6th grade Medical Student*

[2]*Yeditepe University, Faculty of Medicine, Department of Child Health and Pediatrics,*

[3]*Yeditepe University, Faculty of Pharmacy*

[*]**Corresponding author:** Suat Biçer, Yeditepe University Hospital, Devlet Yolu Ankara Cad No: 102-104. 34752, Ataşehir-İstanbul; Tel: +90 216 578491; E-mail: suatbicer@yahoo.com

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Abstract

Atropine systemic toxicity may causes the anticholinergic toxidrome including pupillary, mucous membranes, skin, urinary, gastrointestinal, cardiac, and central nervous system symptoms. A 6-year-old boy admitted to the emergency department with agitation, vomiting, and fever with a suspect ingestion of atropine sulfate solution. The patient was hospitalized, intubated, sedated with midazolam and mechanically ventilated. Gastric lavage was performed. After treatment with active charcoal, neostigmine and afterwards physostigmine were administered. Atropine sulfate was detected in the blood sample by using high-performance liquid chromatography-diod array detector method. Patient had supportive care until his symptoms resolved. At the end of the fourth day, patient was discharged in a healthy state except bilateral mydriasis which may continue for a week.

Key words:

Anticholinergic toxicity; Atropine sulfate; Child; HPLC-DAD; Intoxication; Physostigmine

Background

Anticholinergic (antimuscarinic) agents may be classified by their source (natural, semisynthetic, or synthetic) or structure (tertiary amine or quarternary ammonium compounds). Atropine sulfate is an anticholinergic drug which historically was used as a cycloplegic and mydriatic agent. Because of its long mydriatic action (7 - 12 days) shorter acting agents are now being preferred [1]. Its active substance is atropine which is obtained from Atropa Belladonna, a tertiary amine with half-life of 2.6-4.3 hours [1, 2]. Dose dependent symptoms arised by atropine poisoning are listed in Table 1.

Not all the characteristics of anticholinergic toxidrome should necessarily be present in each poisoning, but the clinical picture is often dominated by a toxic psychosis with hallucinations, disturbance of orientation and psychomotor agitation, aggression or anxiety.

Dose	Symptoms
0.5 mg	Slight dryness of nose and mouth; bradycardia
1 mg	Greater dryness of nose and mouth, with thirst; slowing then acceleration of heart rate slight mydriasis
2 mg	Very dry mouth; tachycardia with palpitation, mydriasis, slight blurring of near vision; flushed, dry skin
5 mg	Increase in above symptoms plus disturbance of speech; difficulty in swallowing; headache, hot, dry skin; restlessness, with asthenia
≥ 10 mg	Above symptoms to extreme degree, plus ataxia, excitement, disorientation, hallucinations, delirium, and coma
65 mg	May result in fatality

Table 1: Dose dependent symptoms arised in atropine poisoning

The interpersonal variation in relation to atropine toxicity is demonstrated by cases of death that have been reported following doses of 100 mg or less for adults (and 10 mg for children), while on the other hand, people have recovered from intoxication with a 1 g dose of atropine [3]. Children have special susceptibility, and even small amounts can produce central nervous system manifestations [4]. Atropine toxicity symptoms are associated with doses as low as 0.5 mg in children. We report a child with oral atropine poisoning who was treated with decontamination methods and antidote.

Case Report

A 6-year-old boy with agitation, vomiting, and fever was brought to our pediatric emergency department by his mother. His symptoms appeared for the last fifteen minutes. He was unresponsive to verbal stimuli, with flushing, and his body temperature was 37.5°C. First physical examination revealed bilateral mydriasis with equal and mildly reactive pupils, decreased response to painful stimuli with disturbance of consciousness, the Glasgow coma scale was evaluated as 9/15 points. A rash was present on his face. His fundoscopic examination was normal, deep tendon reflexes were equally brisk, involuntary movements were observed in all extremities, and meningeal irritation signs were negative. He was hemodynamically unstable, heart rate was 160 beats per minute, capillary refill time was normal. He was mildly tachypneic at 38 cycles per minute. His breath sounds and ventilation of lungs were normal bilaterally. Bowel sounds were decreased. The patient was considered as acute encephalopathy, and was monitored. His arterial oxygen saturation was 99%. He was healthy until the last 15 minutes. Patient was using methylphenidate for his attention-deficit hyperactivity disorder. There was no history of trauma or poisoning. Patient was sedated with intravenous midazolam (3 mg) to decrease his agitation and involuntary movements in the pediatric emergency unit. The blood chemistry, complete blood count, C-reactive protein, erythrocyte sedimentation rate, and blood gases of patient were normal. Sinusal tachycardia was detected on electrocardiogram (ECG), however, other possible ritm abnormalities were nothing. After several attempts of questioning, an empty blue-colored vial was found at the house of the patient's cousin who was a student in pharmacy school. This vial was filled with atropine sulfate, mydriatic ophtalmic solution which was full in the morning.

Consequently, the patient was considered atropine poisoning in the first hour of admission, and hospitalized in intensive care unit. He was intubated with cuffed endotracheal tube after being deeply sedated with midazolam 4 mg and relaxed with rocuronium, and mechanically ventilated with SIMV mode. Gastric lavage was performed and approximately 30 mls of purple-red colored gastric fluid was aspirated. Active charcoal (1 gr/kg) was administered by orogastric tube. Two antidote drugs, first neostigmine (single dose, 0.75 mg), secondarily physostigmine (three dose, total 2 mg) were used to antagonize atropine. Pupillary response was increased but mydriasis continued. His tachycardia (180/min.) was treated with esmolol in the form of infusion for a period of 12 hours. Due to increasing requirement of midazolam it was discontinued and replaced with propofol. After the initiation of propofol treatment, the sedative state continued without awakenings.

Three blood samples (first at 11th hour after admission, other 2 samples at 13th hour) were drawn and sent to Pharmacology laboratory of our university for analysis, 1.93 μg/ml of atropine sulfate (cut-off value: 0.40 ug/ml) was detected in the first sample by high-performance liquid chromatography-diod array detector (HPLC-DAD) method. Other sample concentrations were below the limit of quantification of the method. These undetectable levels of atropine sulfate were accordant with patient's clinical status.

Patient was hemodinamically stable at the end of the 24th hour and the propofol dose was decreased. Patient was extubated after the propofol treatment was stopped. His clinical status was stable after extubation for the next 24 hours. He was discharged at the end of the fourth day with bilateral mydriasis.

Discussion

Atropine is a belladonna alkaloid with anticholinergic effects. Atropine systemic toxicity causes the features of anticholinergic toxidrome including dilated pupils, dry mucous membranes, dry skin, urinary retention, and tachycardia, other features are tachypnea, elevated body temperature, and central nervous system (CNS) stimulation marked by restlessness, confusion, psychotic reactions (i.e. aggression, psychomotor agitation, and delirium) and occasionally seizures [4-6]. Agitation and vomiting were initial symptoms in our patient. In severe intoxication, central stimulation may cause CNS depression, coma, circulatory and respiratory failure, and death [7]. These anticholinergic symptoms are caused by block of the muscarinic receptors (cholinergic block) [1, 7]. Our patient with atropine sulfate solution ingestion was severely ill and needed immediate treatment and observation in the intensive care unit. A facial rash may appear on the face or upper trunk as in our patient at initial examination. Mydriasis may persist for one week as it was with our patient [8].

Diagnosis of anticholinergic toxicity may be difficult and generally based on history, because specific laboratory tests are not routinely available and the wide range of signs and symptoms may not be present in each case [9]. Additionally, signs and symptoms of anticholinergic toxicity (i.e. altered mental status and hallucinations) may occur in other cases such as hypoglycemia, intracranial infections, intracerebral hemorrhage, sepsis, psychiatric disorders, and other poisonings [4, 10]. Differential diagnosis of intoxication is important for early treatment and prognosis. Fortunately, detecting atropine levels in the plasma is possible but it is a time-consuming process. Hence test results of our patient were achieved after seven days. Blood samples were sent for analysis of atropine levels before and after the initiation of antidote treatment. HPLC-DAD method was used in determination of atropine in the blood sample [11]. Only in the first of three samples atropine sulfate was detected.

We had to evaluate methylphenidate overdose for its similar effects. The manifestations of methylphenidate toxicity are consistent with those of typical sympathomimetic agents [12]. In overdose, the patient may present with mydriasis, agitation, anxiety, tremor, hyperreflexia, confusion, hallucinations, delirium, paranoia, movement disorders, and seizures. Cardiac effects are primarily tachycardia and hypertension. Patients may complain about chest pain and palpitations [13]. All of these symptoms were present in our patient. After thorough questioning of his pharmacy-student-cousin, atropine poisoning became first-line diagnosis. The improvement of patients' clinical status after treating with physostigmine also supported atropine poisoning.

Initial treatment choices for atropine poisoning are gastrointestinal decontamination and antidote treatment. Gastric lavage may be useful especially during the first hours of poisoning. Decontamination with activated charcoal may be effective for poisons which are known to be absorbed by charcoal in the first hour of ingestion [14, 15]. However, it may be administered after one hour in patients who were taken anticholinergic drugs orally for delaying gastric transition [1, 16]. Our patient was decontaminated by gastric lavage and activated charcoal at the second hour after intubation with cuffed endotracheal tube because of the risk of aspiration of activated charcoal in patients with altered mental status and other central nervous system symptoms [17, 18].

Cholinesterase inhibitors, mainly physostigmine and neostigmine are used to relieve anticholinergic symptoms of atropine. Neostigmine may be useful in relieving peripheral anticholinergic symptoms in case physostigmine is not available. Since neostigmine doesn't cross blood-brain barrier it is not effective for central symptoms [2, 19]. Both peripheral and central anticholinergic symptoms may be treated by physostigmine, it's a reversible cholinesterase inhibitor and the preferred agent for the control of peripheral and central anticholinergic symptoms including agitation and delirium [2, 20]. Neostigmine was used initially in our patient because physostigmine was not available in our hospital at the time. This antidote is available only in "National Drug and Pharmacy Center" in our country. Also benzodiazepines may be used to resolve CNS stimulation as adjunctive therapy to cholinesterase inhibitors, especially neostigmine [2, 20]. Burns et al. showed that physostigmine is more effective and safer than benzodiazepines for the treatment of CNS stimulation including agitation and delirium caused by anticholinergic drugs [20]. Benefits of using physostigmine in patients with anticholinergic poisoning such as decreasing the neuromuscular hyperactivity, eliminating the cranial imaging and lumbar puncture, shortening the duration of toxicity, and allowing to earlier discharge from hospital are the cause of choosing for the first line therapy. An initial physostigmine dose of 1 to 2 mg (0.5 mg in children) given intravenously over three to five minutes is recommended [5, 16, 20]. If the response is incomplete, additional doses of 0.5 to 1 mg every five minutes should be given until delirium resolves or cholinergic signs (diaphoresis, salivation, vomiting, and diarrhea) occur. A prolonged PR (> 200 ms) or QRS (> 100 ms and not related to bundle branch block) interval on ECG are considered as only contraindications for physostigmine use [20]. It is crucial that if there is a suspencion about atropine intoxication, antidote treatment should be administered before the obtained absolute results of the blood atropine levels, as in our patient. By administering these agents,

our patient recovered from his symptoms and was discharged with only mydriasis which may continue for a week [8].

Conclusion

Cases of atropine sulfate poisonings may be confused with metabolic, infectious, psychotic or brain disorders. Anticholinergic toxidrome should be beared in mind in cases with agitation, vomiting, fever, flushing, and mydriasis. Gastric decontamination, cholinesterase inhibitors, and benzodiazepines with supportive care including endotracheal intubation were effective to treating with no sequel of the poisoned patients with atropine sulfate. Atropine sulfate can be detected in blood samples by using HPLC-DAD method.

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