## One drop can be beneficial, one swig can be deadly: tetrahydrozoline intoxication

Muhammet Şükrü Paksu, Şule Paksu, Tuğrul Akkuş, Kemal Baysal Department of Pediatrics, Ondokuz Mayıs University Faculty of Medicine, Samsun, Turkey. E-mail: sukrupaksu@yahoo.com

SUMMARY: Paksu MŞ, Paksu Ş, Akkuş T, Baysal K. One drop can be beneficial, one swig can be deadly: tetrahydrozoline intoxication. Turk J Pediatr 2012; 54: 658-660.

Tetrahydrozoline is a commonly used imidazoline derivative with serious side effects and toxicity, particularly in small children. A one-year-old boy was admitted to the emergency department (ED) after he accidentally ingested about half a bottle of nasal decongestant solution containing tetrahydrozoline. He was unconscious, hypothermic and bradycardic on presentation. His respiration was irregular and superficial, and blood pressure was borderline hypotensive. His skin was pale and cold. Atropine was administered twice for symptomatic bradycardia, and the child was transferred to the pediatric intensive care unit (PICU). During the 12th hour of observation, vital signs returned to normal and there was no need for mechanical ventilation. Although suitable room temperature with passive warming was applied, hypothermia continued for approximately 24 hours. The patient was discharged on the second day of admission. There were no complaints one week later, and the physical examination was normal. We report a case of accidental tetrahydrozoline intoxication with life-threatening events accompanying hypothermia in a small infant.

Key words: imidazoline, tetrahydrozoline, child, intoxication, hypothermia.

Tetrahydrozoline is an imidazoline derivative with similar structure and effects to clonidine<sup>1</sup>. It is a commonly used nasal and ocular decongestant agent in our country<sup>2</sup>. Serious toxic events may develop with accidental ingestion, usually in small children<sup>3,4</sup>. We report the case of a one-year-old child who accidentally drank nasal decongestant solution containing tetrahydrozoline, resulting in serious side effects with prolonged hypothermia.

## Case Report

A one-year-old boy was admitted to the emergency department (ED) after accidentally drinking about 8 ml 0.05% of nasal solution containing tetrahydrozoline. A few minutes after ingestion, he became pale and fatigued, followed by sweating and sleepiness. His parents brought him to the state hospital ED within 30 minutes of ingestion, and 0.1 mg/kg naloxone was administered. However, no clinical improvement was achieved. Due to the patient's deteriorating condition, he was transferred to the ED of our hospital.

Admission was during the second hour of ingestion and the patient was unconscious and pale. His vital signs were as follows: blood pressure 70/40 mmHg, heart rate 60 beats/min, irregular and superficial respiratory pattern, and body temperature 35.5°C (rectal). His weight was 10 kg and height was 76 cm. On physical examination, pupils were isocoric, deep tendon reflexes were decreased, gag reflex was intact, and Glasgow Coma Scale score (GCS) was 5 (E1, V1, M3). Capillary refilling time was <3 seconds and peripheral pulses were weak. Oxygen saturation, measured by a pulse oximeter, was 92%. Chest X-ray was normal. His medical history was unremarkable. The ingestion had occurred close to his parents and no drug ingestion history was present. Laboratory investigations revealed a leukocyte count of 21900/mm<sup>3</sup>, and hemoglobin and thrombocyte counts were normal. The patient's biochemical parameters (including liver enzymes, electrolytes, renal function measurements), spot urine test, and arterial blood gas analysis were within the normal

| Tuble 1. Vital bigits of the Fatient |  |   |   |  |   |
|--------------------------------------|--|---|---|--|---|
| Respiration                          | Pulse<br>(min)   | Blood<br>pressure<br>(mmHg)   | GCS   | Body<br>temperature<br>(°C)  | Treatment   |
| Irregular<br>and                     | 60   | 60/35   | 9   | 35.4   | 0.1 mg/kg naloxone (once)   |
| Irregular<br>and<br>superficial      | 60   | 70/40   | 5   | 35.2<br>(axillary)   | 0.02 mg/kg atropine (twice),<br>oxygen by face mask, tactile<br>stimulation, and passive<br>warming   |
| Superficial                          | 100  | 105/50  | 5   | 35.5<br>(rectal)   | Oxygen by face mask, tactile<br>stimulation, and passive<br>warming   |
| Regular                              | 80   | 105/55  | 8   | 35.5<br>(rectal)   | Oxygen by face mask, and passive warming  |
| Regular                              | 78   | 90/60   | 12  | 35.5<br>(rectal)   | Oxygen by face mask   |
| Regular                              | 112  | 90/65   | 15  | 35.6<br>(rectal)   | No treatment  |
| Regular                              | 108  | 90/60   | 15  | 36.8<br>(axillary)   | No treatment  |
|                                      | Irregular<br>and<br>superficial<br>Irregular<br>and<br>superficial<br>Superficial<br>Regular<br>Regular<br>Regular | RespirationPulse<br>(min)Irregular<br>and<br>superficial60Irregular<br>and<br>superficial60Superficial100Superficial100Regular80Regular78Regular112 | RespirationPulse<br>(min)Blood<br>pressure<br>(mmHg)Irregular<br>and<br>and<br>superficial6060/35Irregular<br>and<br>superficial6070/40Superficial100105/50Regular80105/55Regular7890/60Regular11290/65 | RespirationPulse<br>(min)Blood<br>pressure<br>(mmHg)GCSIrregular<br>and<br>and<br>and<br>superficial6060/359Irregular<br>and<br>and<br>superficial6070/405Superficial100105/505Regular80105/558Regular7890/6012Regular11290/6515 | RespirationPulse<br>(min)Blood<br>pressure<br>(mmHg)GCSBody<br>temperature<br>(°C)Irregular<br>and<br>and<br>superficial6060/35935.4Irregular<br>and<br>superficial6070/40535.2<br>(axillary)Superficial100105/50535.5<br>(rectal)Regular80105/55835.5<br>(rectal)Regular7890/601235.6<br>(rectal)Regular10890/601536.8 |

Table I. Vital Signs of the Patient

GCS: Glasgow Coma Scale.

range. As the cause of the poisoning was evident, no urine toxicology screen was done. The patient had sinusal bradycardia in the electrocardiogram, PR was 0.16 sec, and QTc was 0.40 sec. Atropine 0.02 mg/kg was administered twice in 10-minute intervals due to symptomatic bradycardia, and the child was transferred to the pediatric intensive care unit (PICU). In the PICU, heart rate never fell below 100 beats/min, oxygen saturation was never less than 92%, and the patient remained in a normotensive state. He did not require mechanical ventilation; however, he had a tendency to apnea, which was reversed with intermittent tactile stimulations. Four hours after admission, the patient began to breathe normally. He was conscious at the 12th hour, GCS was assessed as 15, and neurological findings were normal. The only pathological finding at that point was hypothermia, which continued for 24 hours following admission (Table I). The patient was discharged on the second day of admission. On follow-up one week later, he was found to be doing well with no symptoms.

## Discussion

Tetrahydrozoline, an imidazoline derivative,

shows its effects at the  $\alpha$ -2 adrenoreceptors by decreasing the secretion of norepinephrine (sympatholytic effect)<sup>5,6</sup>. Although it has toxic side effects when ingested, topical use can also cause similar effects. In early childhood, even low doses may cause serious problems<sup>5</sup>. Our patient had the risk factors for intoxication, these being young age and oral intake of a high dose. Toxic side effects generally occur within 15 minutes to 4 hours after ingestion, and resolve in 24 hours<sup>7,8</sup>. In the early hours of intoxication,  $\alpha$ -2 receptor stimulation resulting in short-term hypertension can be observed<sup>5,9</sup>. This is followed by weakness, hypotension, bradycardia, and changes in regular respiration pattern related to central sympathetic depression<sup>3,4,10</sup>. Central nervous system depression occurs in a cyclic pattern, and ranges from lethargy to coma, in which the patient can respond only to strong tactile stimulation. Bradypnea and apnea are more frequent if the central regulation of respiration is influenced<sup>9</sup>. In the early periods of intoxication, our patient was pale, probably as a result of peripheral vasoconstriction. This was followed by serious toxic findings, including symptomatic bradycardia, hypotension, and depression of respiration and consciousness.

In addition, hypothermia, which is seen only in serious cases, occurred in our patient<sup>3-5,11</sup>.

Supportive treatment is the mainstay of care. Gastric lavage is not recommended, but if the patient is conscious and only a short time has passed since ingestion, one dose of active carbon can be administered<sup>5</sup>. Generally, mechanical ventilation is not required, and interestingly, apnea attacks can be terminated with periodic tactile stimulations<sup>11</sup>. On admission, our patient had 92% oxygen saturation and did not require mechanical ventilation. In the absence of bradycardia and hypotension, atropine is not recommended; however, in this situation, the drug of choice is atropine, alone or in combination with dopamine<sup>12</sup>. Symptomatic bradycardia caused by hypotension was seen in our patient, and atropine administration dramatically corrected the vital signs, except for hypothermia. In this case, there was no need for additional inotropic treatment. Although there is no conventional antidote for tetrahydrozoline, some reports recommend naloxone for imidazoline intoxications, and imidazoline has similar clinical effects to opioid agents; however, the use of naloxone in this setting is controversial<sup>5,13</sup>. Naloxone was also applied to our patient, but had no beneficial effect. Since tetrahydrozoline has a short half-life (1.2-4 hours), nearly all cases of intoxication will resolve in 24 hours, although the cardiovascular effects may be prolonged for up to 36 hours<sup>2,7,8</sup>. Our case is similar to those reported in the literature, except that our patient had prolonged hypothermia, a finding rarely reported. Prolonged hypothermia should be kept in mind as a possible transient feature of tetrahydrozoline intoxication.

## REFERENCES

- 1. Lowry JA, Garg U. Serum concentrations in three children with unintentional tetrahydrozoline overdose. Clin Toxicol (Phila) 2011; 49: 434-435.
- Spiller H, Griffith J. Prolonged cardiovascular effects after unintentional ingestion of tetrahydrozoline. Clin Toxicol (Phila) 2008; 46: 171-172.
- Daggy A, Kaplan R, Roberge R, Akhtar J. Pediatric Visine (tetrahydrozoline) ingestion: case report and review of imidazoline toxicity. Vet Hum Toxicol 2003; 45: 210-212.
- Tobias JD. Central nervous system depression following accidental ingestion of Visine eye drops. Clin Pediatr (Phila) 1996; 35: 539-540.

- Tomassoni A, Wallace K. Imidazoline, guanidine, and oxazoline antihipertensives and decongestants. In: Brent J, Wallace KL, Burkhart K (eds). Critical Care Toxicology Diagnosis and Management of the Critically Poisoned Patient. Philadelphia: Mosby; 2005: 441-447.
- van Zwieten PA, Chalmers JP. Different types of centrally acting antihypertensives and their targets in the central nervous system. Cardiovasc Drugs Ther 1994; 8: 787-799.
- Liebelt EL, Shannon MW. Small doses, big problems: a selected review of highly toxic common medications. Pediatr Emerg Care 1993; 9: 292-297.
- Mahieu LM, Rooman RP, Goossens E. Imidazoline intoxication in children. Eur J Pediatr1993; 152: 944-946.
- Michael JB, Sztajnkrycer MD. Deadly pediatric poisons: nine common agents that kill at low doses. Emerg Med Clin North Am 2004; 22: 1019-1050.
- Jensen P, Edgren B, Hall L, Ring JC. Hemodynamic effects following ingestion of an imidazoline-containing product. Pediatr Emerg Care 1989; 5: 110-112.
- Rangan C, Everson G, Cantrell FL. Central alpha-2 adrenergic eye drops: case series of 3 pediatric systemic poisonings. Pediatr Emerg Care 2008; 24: 167-169.
- Maggi JC, Iskra MK, Nussbaum E. Severe clonidine overdose in children requiring critical care. Clin Pediatr (Phila) 1986; 25: 453-455.
- Holmes JF, Berman DA. Use of naloxone to reverse symptomatic tetrahydrozoline overdose in a child. Pediatr Emerg Care 1999; 15: 193-194.