Papaverine intoxication in a newborn: an unusual case report

Zelal Kahramaner, Aydın Erdemir, Ebru Türkoğlu, Hese Coşar, Sümer Sütçüoğlu, Esra Arun Özer

Neonatology Clinic, Tepecik Training and Research Hospital, İzmir, Turkey. E-mail: eozer@deu.edu.tr
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Herbal agents are increasingly used for medicinal purposes, but there is a lack of knowledge about the content of these agents. Indiscriminate use of herbal agents may cause severe side effects and also death. We report a newborn who developed convulsions and respiratory arrest after oral intake of an opium poppy preparation containing papaverine for its antitussive effect. The infant experienced a good outcome with supportive treatment. To the best of our knowledge, this is the first time a newborn with papaverine intoxication has been described. Parents should avoid self-medication of their children, and the possibility of exposure to foreign products should be kept in mind in any seizure of a newborn with unexplained origin.

Key words: alternative medicine, intoxication, newborn, opium poppy, papaverine.

The use of alternative medicine for the treatment of many diseases is growing[1]. Herbal treatments are also known as "phytotherapy" because of their derivation from plants. Herbal agents are perceived as safe. However, these treatments may lead to side effects, including severe and life-threatening events[2].

Papaverine is a benzylisoquinoline alkaloid obtained from the opium poppy (*Papaver somniferum*)[3]. It exerts a nonspecific relaxant effect on all types of smooth muscle by inhibiting the activity of phosphodiestrase. When used clinically, it also eases respiration via bronchodilation[4].

Herbal remedies are used mostly for constipation and infantile colic in newborns and for increasing breast milk in the mothers of infants. Herein, we report a newborn who developed convulsions and respiratory arrest after oral intake of papaverine. To our knowledge this is the first such report, and we wanted to call to attention the hazards related to the indiscriminate use of herbal agents.

Case Report

An 18-day-old girl was admitted to the emergency department because of focal shaking of the left extremities. During assessment in the emergency room, she began having focal shaking of the left extremities again, and then all extremities were involved symmetrically. She remained cyanotic and unconscious. She was ventilated, phenytoin 20 mg/kg was administered as the initial dose, and she was then referred to our Neonatology Unit.

The infant was born at 40 weeks, weighing 3290 g by spontaneous vaginal delivery. Her mother was a 23-year-old gravida 2, para 1. The first pregnancy was terminated in the first trimester, reason unknown. This time, the pregnancy and labor were uneventful. The parents were nonconsanguineous and did not have a family history of seizure disorders.

On admission, her weight was 3350 g (25th–50th percentile), body length 51 cm (50th percentile) and head circumference 36 cm (50th percentile). She did not have a fever. She was hypotonic and minimally responsive on examination, with no signs of focal neurological deficit. Respiratory examination revealed bilateral crackles. She was started empirically on intravenous antibiotics (ampicillin and cefotaxime) after a full septic screen and continued on phenytoin with a maintenance dose of 5 mg/kg/day. Laboratory investigations, including a complete blood count, serum electrolytes and glucose, liver and renal function tests, blood gas analysis, and blood, urine and

cerebrospinal fluid cultures were all normal. A chest X-ray showed paracardiac densities, and a cranial computed tomography scan revealed no acute pathological findings that could have caused a seizure. A detailed history revealed that a water-based opium poppy preparation was given to the infant on the day of her seizure to cure a cough that had lasted for three days.

She was successfully extubated on day 2. An electroencephalography revealed no epileptiform activity. No additional seizures occurred during follow up, and the phenytoin dosage was gradually decreased and then stopped. Antibiotic treatment was given for ten days due to pneumonia. She was discharged home after full recovery without any sequelae. By three months of age, her physical and neurodevelopmental examination were evaluated as normal.

Discussion

Herbal agents are increasingly used for medicinal purposes. However, there is a lack of knowledge about the content of these agents. Most contain a variety of unknown substances that have undesirable effects. Some of these substances may cause severe side effects, including central nervous system symptoms (sedation, seizures, excitability) and also death[5].

The infant presented was given an opium poppy preparation by her parents for its antitussive effect. The opium poppy contains papaverine, which is an opium alkaloid causing vascular smooth muscle relaxation via phosphodiesterase inhibition[3,4]. It causes vasodilatation and bronchodilatation and has been used in the treatment of erectile dysfunction, gastrointestinal, genitourinary and biliary tract spasms, migraine headaches and cerebral vasospasm[6,7]. Papaverine is completely absorbed by the gastrointestinal tract and metabolized by the liver[8]. Side effects associated with papaverine administration frequently disappear after the discontinuation of the drug; however severe complications such as bradycardia and hypotension, hyperthermia and metabolic acidosis, intracranial pressure changes, thrombocytopenia, transient brain stem depression and transient neurological events have been reported after papaverine administration[9,10]. In this case, convulsions and respiratory depression developed after papaverine administration. This was an instance where an alternative treatment, given with unawareness of its side effects, might have led to death.

Children, especially newborns, differ from adults in terms of the absorption, distribution, metabolism and excretion of some substances; they also have developing central nervous systems, which may make them more sensitive to the adverse effects of these substances[11]. In the literature, adverse effects after exposure to papaverine have been reported in adults but not in infants. To our knowledge, this is the first case of newborn intoxication with papaverin that has been presented in the literature.

In conclusion, serious adverse effects may occur due to indiscriminate use of herbal agents, since they may include variable and unpredictable concentrations and ingredients. Parents should avoid self-medication of their children. Lastly, in any seizure of the newborn with unexplained origin, the possibility of exposure to foreign products should be kept in mind.

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