

CASE REPORT

Ebastine overdose in a child

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To the Editor

A three-year-and-eight-month-old child, 14.5 kg, was brought to our emergency room (ER) 40 min after involuntary ingestion of six 10 mg ebastine film-coated tablets (total intake: 60 mg). The child's clinical history revealed no chronic diseases, past acute infectious events, and no intake of other drugs. The mother related the onset of her child's drowsiness after the ingestion of the tablets. Impairment of consciousness lasted 20 min followed by sudden recovery. The child did not complain for headache, dizziness, dryness of the mouth, palpitations, or any abdominal symptoms. The mother reported the absence of any treatment attempts before arriving at our ER. The child appeared in good general conditions at physical examination, with neither behavioral changes nor altered state of consciousness, no cardiorespiratory, or abdominal abnormalities. Vital signs were normal: heart rate 91 beats per minute with normal electrocardiogram (ECG) and QTc values, sinus rhythm, 100% oxygen saturation (SaO₂) in room air and spontaneous breathing, body temperature 36.6°C. Red cells, white cells, platelets, creatinine, albumin, and alanine transaminase were normal. The patient presented normal values for venous blood gases. In agreement with the advice of the poisoning center, the child was hospitalized with oxymetry monitoring

Key Clinical Message

The lack of side effects after acute ingestion of a high dose of ebastine in our child aging 44 months suggests an overall safety profile of ebastine; it could suggest less time of hospitalization for children who are subjected to this event.

Keywords

Antihistamines, ebastine, emergency medicine, overdose, pediatrics, toxicology.

for 48 h. Five grams of activated charcoal was administered. ECG, complete blood count (CBC), and blood chemistry tests, repeated after 24 h, remained normal. During hospitalization, the child did not suffer from neurological, cardiorespiratory, or gastroenterological symptoms; diuresis was normal. No fever during the hospitalization. The child was discharged in good general conditions 48 h after her arrival in our ER.

Ebastine is a second-generation antihistamine, used for symptomatic treatment of allergic rhinitis and urticaria [1].

It binds to the H₁ histamine receptor, preventing its activation determined by an allergic reaction.

Ebastine 10 mg tablet (the type of the formulation taken by the child) is not allowed to children under 12 years; in fact, the safety and efficacy in these patients has not been studied [1].

Due to this evidence, the use of ebastine tablets is allowed only for subjects over 12 years of age.

Most guidelines report that appropriate dosage is 10 mg tablet once a day. An intake of 20 mg/day is reported to be tolerated [1].

In children, the formulation allowed in some countries is the syrup; in particular, guidelines have authorized its use in children aged 6–12 years at the dosage of 5 mg/day. Furthermore, different guidelines have allowed the use in children aged 2–5 years at the dosage of 2.5 mg/day [2].

Potency of ebastine, at the dosage of 10 mg, is less powerful than cetirizine and terfenadine [3]; instead, ebastine has more potency than fexofenadine and loratadine. Ebastine 20 mg tablet has higher efficacy in comparison with cetirizine (10 mg) or loratadine (10 mg) [4].

Antihistamines overdose represents an important problem in pediatric age. In the literature, we found multiple cases of children who experienced a first-generation antihistamines overdose, particularly diphenhydramine [5]. Some adverse effects resulting from the use of these drugs are due to the fact that they provoke a poorly selective action on H1 receptors, because they can also interact with no histamine receptors (mainly serotonergic, cholinergic, and alpha-adrenergic). Specifically, the most serious effects of overdose are due to abnormalities in signal conduction and heart rhythm (consequent to the block of potassium channels that control the phase of cardiac repolarization [6]) and to neurological involvement (due to the accumulation of the molecule, dispensed to high doses and highly lipophilic, within the CNS) with convulsions which may be followed (at high doses) by states of coma, occasionally irreversible [7].

The second-generation antihistamines have many advantages over first-generation antihistamines, in particular a low lipid solubility, which determines a reduced capacity, to normal dosages, to cross the blood-brain barrier. Consequently, second-generation antihistamines bind exclusively to the H1 receptor, characteristic which determines the lack of occurrence of all adverse reactions due to the binding to the nonhistamine receptors.

The risk of nonsedative antihistamines overdose, including ebastine, is represented by tachycardia, abnormal behavior, headache, dizziness, oliguria, and gastrointestinal disorders [1, 8]. These symptoms are explained by the fact that second-generation antihistamines are metabolized in the liver by the cytochrome P450. So they arise in two types of events: first of all, their overdose: It takes to a saturation and consequently to an inhibition of this system and secondly, their concomitant consumption (particularly terfenadine or astemizole) with drugs which are able to inhibit cytochrome P450. These two side effects can cause an abnormal accumulation of these agents and their metabolites in the body with the risk of possible side reactions, especially at cardiac level (i.e., tachyarrhythmia, torsades de pointes, QT prolongation) [6].

Concerning ebastine overdose, there are few clinical studies in the literature involving only adults, and to the best of our knowledge, we did not find any study including children. Moss *et al.* showed no clinically relevant effect of the drug on QTc interval at the recommended doses of 10 and 20 mg/day in adults. Besides, when it is

administered at ordinary doses, with ketoconazole or erythromycin (also metabolized by the cytochrome P450), the overall effect on the QTc interval does not appear to be clinically significant [9]. The same was reported when ebastine tablets were administered in the amount of 60 mg/day (three times the recommended dose) for a week or 100 mg of ebastine in a single dose [10].

Starting from this case report and the limited information on second-generation antihistamine overdose, it could be possible to consider new strategies for its treatment. The actual treatment of this condition consists of administering activated charcoal to patients presenting within an hour of ingesting substantial amounts of this type of antihistamines. Cardiovascular monitoring is also important. Because of their capacity to cause tachycardia and the uncertainty about the potential of antihistamines to cause arrhythmias in overdose, an ECG should be performed and the QRS and QT intervals assessed. Patients with abnormal ECGs or signs of evolving toxicity should undergo ECG monitoring. Furthermore, it has been suggested that adults that did not develop any adverse reactions from ebastine overdose in the first six hours after ingestion have no risk of later symptoms [8]; our findings suggest that this might be the case also in young children.

The lack of side effects after acute ingestion of a high dose of ebastine in our three-year-and-eight-month-old child suggests an overall safety profile of ebastine at the maximum dosage of 60 mg.

Actually, there are few scientific studies regarding second-generation antihistamines overdose, very few studies regarding it in children, and no study regarding ebastine overdose in children.

In conclusion, this case report could be helpful because a strategy of toxicological management of antihistamine overdose has been proposed and it could lead to new questions about the use of ebastine in children: Also, it could increase the variety of second-generation antihistamines available to the pediatrician in allergic rhinitis and urticaria and reduce the time of observation when children, without clinical signs, take an overdose of ebastine.

Authorship

LP: is the main author, pointed out the idea, revised the literature, and drafted the article. GP: contributed to the idea development, searched the literature, and approved the article. AP: drafted the article, developed the idea, searched the literature, and approved the manuscript in the final form.

Conflict of Interest

None declared.

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