

# Cyproheptadine poisoning, importance of good interrogation: report of a case

## Summary

**Introduction:** Cyproheptadine (CH) is a nonspecific antiserotonergic drug with antihistamine, anticholinergic and sedative properties, used as an orexigenic. It is important to know that CH is considered a safe medication in children and adolescents, since the most frequent side effect is sedation that gradually disappears with cessation of the drug.

**Clinical Case:** Female preschooler of 4 years and 8 months of age, who developed a current illness characterized by ataxic gait, dysarthria, disorientation and acute confusional state, of sudden onset, progressively. A new multivitamin medication had been started which has CH as its active ingredient. She was kept under medical supervision for 6 hours, where improvement of the symptoms was evident.

**Conclusion:** Although the indication of orexigenics in pediatric patients is a common practice, it should be carefully evaluated by parents and physicians, and accidental poisoning should be suspected when administering new medications to pediatric patients.

**Keywords:** cyproheptadine, intoxication, appetite stimulant, orexigenic

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## Introduction

Cyproheptadine (CH) is a non-specific antiserotonergic drug with antihistaminic, anticholinergic and sedative properties, used as an orexigenic agent, in allergy, pruritus and in the treatment of migraine and other vascular headaches.<sup>1</sup> In gastroenterology practice, CH has been considered the most commonly used drug of choice for appetite stimulation, weight gain and food intolerance in young children with feeding disorders.<sup>2</sup> CH has long been considered the antidote drug for serotonin toxicity (ST), due to its non-selective antagonist properties for 5-HT receptors, especially for the 5-HT-2A receptor and has been useful in relieving ST symptoms.<sup>3</sup>

In a review published in the literature, CH is considered the safest pharmacological treatment in relation to other non-selective 5-HT antagonists, taking as a reference a safe dose in pediatric patients of 0.25 mg/kg/day.<sup>4</sup> Cases have been reported on the pharmacological action of CH in cases of atopic dermatitis, and cases of intoxication by antidepressant drugs, resulting in good resolution of associated symptoms.<sup>5-7</sup> It is exceptionally notable the use of CH in appetite stimulation, combined with multiple vitamin mixtures, as a therapeutic target in recovery and nutritional stimulation.<sup>8</sup>

It is important to know that CH is considered a safe drug in children and adolescents, since the most frequent side effect is sedation, which gradually disappears with the cessation of the drug.<sup>9</sup> Although described as safe and effective, orexigenic drugs in healthy children are a common medical practice, however, they are not exempt from more or less serious adverse risks, even when administered in correct doses.<sup>10</sup>

The case of a 4-year-old female preschooler is presented. After a detailed physical examination and targeted questioning, she was diagnosed with drug poisoning due to suprathreshold ingestion of CH, in a pharmacological combination with a multivitamin. This led the medical staff to direct a correct therapy and satisfactory clinical

evolution, and also to encourage health education for family members and patients about the ingestion of harmful medications that are within reach of children.

## Clinical case

Female preschooler, 4 years and 8 months old, from Las Lomas, Valera municipality, Trujillo state, who began her current illness 30 minutes prior to her admission, characterized by ataxic gait, dysarthria, disorientation and acute confusional state, of sudden onset, progressive, accompanied by generalized itching with cutaneous rash predominantly on the palms and soles, for which reason the mother went to the pediatric emergency service of the "Dr. Pedro Emilio Carrillo" University Hospital (HUPEC), where it was decided to admit her. The patient had no significant medical history, however, the mother reported exhaustive control in a well-child consultation, for short stature and lack of appetite. One month before her current illness, the mother mentioned that she had started a new multivitamin medication called Ciproheptadine, which has cyproheptadine hydrochloride as its active ingredient, with supplements of B vitamins and vitamin C (Figure 1).



Figure 1 Apetivon BC®, a drug used as an appetite stimulant.

On physical examination upon admission to HUV, heart rate: 135 bpm, respiratory rate: 23 rpm, temperature: 37.4°C, blood pressure: 87/55 mmHg (10th percentile for age), arterial oxygen saturation: 99%. Weight: 15,000 gr, height: 98 cm. The patient was in regular clinical condition, with mild cutaneous-mucosal pallor, tachycardic, normothermic to the touch in the extremities, eupneic, tolerating ambient oxygen, generalized cutaneous rash was evident, predominantly on the palms and soles, pruritic. Rhythmic heart sounds, no murmurs were auscultated. Audible respiratory sounds, symmetrical, without aggregates. No signs of respiratory distress were evident. Soft, depressible abdomen. No visceromegaly was palpated and there were no signs of peritoneal irritation. Symmetrical, mobile limbs, without edema. Neurological: disoriented, dysarthric, in acute confusional state, with ataxic gait and emission of incoherent phrases, little cooperative to the physical examination, preserved muscle strength with Daniels scale 4/5. No signs of meningeal irritation, did not present ictal events, pupils with tendency to mydriasis, normoreactive to light.

The mother was questioned about the corresponding dose, who reported administering 5 ml/day, so she was asked to bring the container and the box to corroborate the dosage, expiration date and to know its composition. Upon arrival, it was verified that the medication was open, empty, and its correct dosage for the patient's age was 2.5 ml/day (each ml has approximately 0.8 mg of CH). Directed questioning was carried out on the preschooler, who confessed to having ingested the entire bottle, because it had "good flavor" (the medication has a caramel and cherry flavor), therefore drug poisoning by cyproheptadine was confirmed. Parenteral hydration was prescribed, with lactated Ringer's at 10 ml/kg, repeating a second dose, a dose of glucocorticoid (hydrocortisone at 10 mg/kg/dose) and a consultation with the pediatric neurology service was requested.

The patient was kept under medical supervision for 6 hours, where improvement of the neurological symptoms was evident, with a physiological gait, coherent sound emission, and absence of rash after 4 hours of administration of the glucocorticoid. Regrettably, in view of the absolute improvement, the mother demanded discharge against medical advice, taking responsibility for the complications and/or consequences related to her daughter's health, so the follow-up, clinical assessment by pediatric neurology, as well as a possible indication for neuroimaging could not be carried out.<sup>11-18</sup>

## Discussion

CH has been described as a nonspecific antiserotonergic drug, with antihistamine and anticholinergic properties, for orexigenic purposes; a dose of 0.25 - 0.4 mg/kg/day has been recommended, with a maximum of 12 mg/day.<sup>10</sup>

There are multiple medical indications where CH has had very good benefits, as described by Zuñiga,<sup>13</sup> in the article on the management of atopic dermatitis, cyproheptadine is a first generation sedative antihistamine, which may be beneficial in patients with pruritus, although the dose and duration of treatment have not been determined. Although the exact amount of CH over-administration ingested by the patient presented is unknown, a cutaneous reaction with pruritus is evident, secondary to intoxication, where there was only improvement after the administration of the glucocorticoid.

According to the Spanish Association of Pediatrics,<sup>1</sup> the most frequent side effects in the pediatric population after the

administration of CH are sedation, drowsiness, coordination disorders, hallucinations, mydriasis, tachycardia and hypotension; as occurred in the case presented, the patient presented neurological manifestations of anticholinergic symptoms caused by mydriasis, as well as ataxic gait, dysarthria and disorientation.

Medical treatment using CH has been beneficial in the pediatric population that has difficulties in increasing appetite, as described by Philco,<sup>9</sup> however, this drug, having antiserotonergic and antihistamine properties, has been used as an appetite stimulant in children with gastrointestinal, oncological, psychiatric and autoimmune pathologies. In the case of the patient studied, the indication of the pharmacological mixture that included CH as an appetite stimulant, and its accidental ingestion, exceeding therapeutic doses, led the patient to present a decrease in neurological functions for her age.

Although the indication of orexigenics in pediatric patients is a common practice, with the therapeutic goal of increasing the weight-height curve appropriate for age, it should be carefully assessed by parents due to imminent adverse effects. On the other hand, physicians should suspect accidental poisoning when administering new medications to pediatric patients, as well as provide health education to encourage parents and guardians not to leave them within reach of children, causing possible adverse events.

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## Conflicts of interest

The authors declare that they have no conflict of interest in this Clinical Case.

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