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Case Report

Accidental Trihexyphenidyl Intoxication in a Seven-Year-Old Child: A Case Report from Senegal

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Abstract

Trihexyphenidyl or Artane® /Parkinane® is an anti-cholinergic drug belonging to the antimuscarinic class. It is used in the treatment of Parkinson's disease and widely in psychiatry for the management of extrapyramidal side effects of neuroleptics. Its overdose leads to a central and peripheral anti-cholinergic syndrome. We report here the case of a seven-year-old Senegalese boy who developed signs of intoxication due to accidental ingestion of a high dose of trihexyphenidyl and recovered completely after administration of parenteral antipyretic, gastric lavage and supportive care in a paediatric setting.

Keywords: Trihexyphenidyl; Intoxication; Emergency; Senegal

Introduction

Trihexyphenidyl is an anti-cholinergic drug belonging to the antimuscarinic class. Marketed in French-speaking countries as Artane® or Parkinane®, trihexyphenidyl is clinically used to reduce excessive cholinergic activity in Parkinson's disease and dystonia [1]. It is also used for the management of various extrapyramidal side effects of neuroleptic treatments [2,3]. Its mode of action is to inhibit the effects of acetylcholine by blocking its binding to muscarinic cholinergic receptors at neuroreceptor sites in smooth muscle, cardiac muscle and gland cells in the peripheral ganglia and central nervous system [2]. Susceptible to abuse [4], trihexyphenidyl overdose results in peripheral signs of parasympathetic blockade (dilated pupils, hyperthermia and dry skin, facial flushing, foul breath, hyperthermia, tachycardia, cardiac arrhythmias, These may include a decrease in bowel sounds and urinary retention, and neuropsychiatric signs such as delirium, disorientation, anxiety, hallucinations, delusions, confusion, verbal incoherence, agitation, hyperactivity, ataxia, memory loss, and convulsions [5]. This condition can deteriorate into stupor, coma, paralysis, cardiac and respiratory arrest and ultimately death [6]. Children are particularly sensitive to the hyperthermic action of Artane® [7], so its use in their case is subject to great caution. Trihexyphenidyl intoxication in children is rarely described in the literature. We report the case of a seven-year-old child who presented signs of accidental trihexyphenidyl intoxication.

Case Presentation

Doudou is a seven-year-old Senegalese boy from a modest background who was brought by his paternal uncle to the psychiatric emergency room of the National Psychiatric Centre of Thiaroye because of the sudden onset of incomprehensible speech, disorientation and psychomotor agitation marked by disordered hand gestures. According to the observations of those around him, the first disorders began about two hours before the consultation, and the young boy suddenly showed psychomotor instability with incessant walking back and forth in the yard and uncontrolled manual movements. This picture of instability is completed by incomprehensible words associated with a frantic demand for water to quench his thirst. The adult who brought him to the psychiatric clinic, his maternal uncle, told the doctors that Doudou had been complaining of headaches since the morning. Faced with this condition, his maternal grandmother, who is illiterate and has been under psychiatric care for more than 10 years, gave him two 5mg trihexyphenidyl tablets (Artane®) which she had taken from her personal stock of medicines, thinking they were paracetamol tablets. A few hours after accidentally taking this medicine in a domestic context, the child began to become agitated, making comments that were incomprehensible to the family. His uncle, who is a nurse and had done a training course in psychiatry, decided to take him to a psychiatric emergency room to ensure better care.

Doudou had no personal psychiatric history, no febrile convulsions, no chronic illnesses, had never been hospitalised before and had no drug allergies. His uncle reports that his nephew has never had any medical problems since birth. His vaccination record is up to date and his psychomotor development is normal. Among his family history, we note that his maternal grandmother, hypertensive and diabetic, has been under psychiatric care for several years for psychotic disorders. Her mother is hypertensive and her father is a smoker and alcoholic.

The clinical examination in the psychiatric emergency room showed that Doudou was in good general condition, that he was confused, his attention was impaired and he was disoriented with psychomotor agitation and an inability to stay in place. He was delirious in a euphoric way, answering questions to the side, and kept asking for water to drink. The mucous membranes were anicterically coloured. He had no cyanosis or oedema of the lower limbs, and no folds of dehydration or malnutrition. His weight was 21 kg for a height of 120 cm. Doudou was afebrile with a temperature of 38°C, his blood pressure was normal for his age (110/70mmhg), the peripheral pulses were palpable and synchronous with the heart sounds with a heart rate of 100 beats/minute. The respiratory system was normal with a respiratory rate of 24 cycles/minute. Neurologically, apart from confusion, the Glasgow score was 13/15. Posture was normal with no motor or sensory deficit. The tone was normal, the cranial nerves intact and the reflexes preserved, except for the corneal reflex

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with pupils that were dilated and reactive to the approach of the light beam. The rest of the clinical examination was unremarkable.

Given this clinical picture, two diagnostic hypotheses were evoked: trihexyphenidyl intoxication and neuromalaria. In the psychiatric emergency room, a rapid diagnostic test for malaria (RDT) was performed and came back negative. Doudou was treated with a parenteral antipyretic before being referred with us to the paediatric emergency department of a hospital in Dakar.

On arrival at the paediatric emergency department of Pikine Hospital in Dakar, Doudou was admitted to a common ward. A good-calibre venous line was placed and blood samples were taken for biological tests (blood count, C-reactive protein, uraemia, creatinemia, blood ionogram and blood sugar). A thick drop with parasite density was also requested. A gastric lavage was performed and fragmented tablets were recovered. He was given 5 mg of diazepam intramuscularly to calm agitation. Biological examinations revealed the following results: White Blood Cell (WBC) count 4.6 109/L, 49% lymphocytes and 40% neutrophils, haemoglobin concentration = 12.2 mg/dl, fasting blood glucose = 0.97g/l, urea = 3.3 mg/l, creatinine = 0.8mg/dl, Na^+ = 135 mEq, K^+ = 4.2mmol/l. The thick blood drop was negative.

Doudou received paracetamol infusions (Perfalgan® 1g at a rate of 1.5 ml/kg four times a day) and infusion solutions in the observation room of the paediatric emergency department. He also received intramuscular diazepam injection (Valium® ampoule 10mg), activated charcoal based on Eucarbon® tablet (one tablet twice a day). Close monitoring of alertness, vitals and agitation was decided. The evolution was marked by a clear improvement of the clinical picture after 72 hours, so his exeat was decided after full recovery.

Discussion

This clinical case is illustrative of acute trihexyphenidyl intoxication prior to admission to the paediatric emergency department and gastric lavage. The accidental ingestion of Artane® tablets was confirmed by the child's grandmother, who mistook Artane® in her personal pharmacy for a box of painkillers as she wanted to relieve the young patient of the headache he was complaining of. Following this family self-medication, the diagnosis was made in the psychiatric emergency room. First of all, thanks to the questioning carried out with the parent - a nurse by profession - who was accompanying the child and who had some experience in psychiatry. By showing the doctors the Artane® platelet, he helped to orient this diagnostic hypothesis, which was also reinforced by the presence in the young patient of a predominant central anti-cholinergic syndrome made up of agitation, delirium, confusion, amnesia, hallucinations and ataxia. Peripheral anti-cholinergic symptoms such as dry mouth with a constant demand for water, tachycardia with a heart rate of 100 beats/minute and visual disturbances with bilateral mydriasis were also recorded in Doudou. The predominance of toxic symptoms in the central nervous system could be attributed to the rapid distribution of the drug within the central nervous system as trihexyphenidyl rapidly crosses the blood-brain barrier and has a high affinity for the central nervous system [1]. It is important to note that trihexyphenidyl has a high dose to lethal dose ratio. In other words, most of its effects are dose-dependent for their occurrence and intensity.

Furthermore, for the same dose, trihexyphenidyl can produce symptoms of varying intensity depending on the individual sensitivity of each patient. Therefore, children seem to be particularly susceptible to these effects [8]. The fever of 38 degrees, which the young patient presents, is a symptom of central anti-cholinergic syndrome [9]. Indeed, anti-cholinergic products are very likely to block the thermoregulatory centre located in the rostral part of the hypothalamus, which contains many cholinergic synapses, and consequently disrupt the thermolysis mechanisms [10]. This dangerous complication cannot be attributed to a single cause, especially in the context of the malaria endemic in Senegal, even though our country has seen a strong reduction in the disease in recent years [11]. Therefore, with the symptoms presented by our patient, the diagnosis of neuromalaria was evoked, but it was eliminated due to the absence of plasmodiums in Doudou's blood in the thick blood drop.

The therapeutic management of the patient took place in two phases. The first, in the psychiatric emergency department, with the administration of an antipyretic and referral to a specialised department. The second phase, which was carried out in the paediatric emergency department, consisted of gastric lavage and monitoring in an isolated room. This procedure proved to be effective and appropriate as the patient was discharged 72 hours later having recovered/returned to good health.

In addition, during his hospitalisation in the paediatric emergency room, Doudou received treatment with activated charcoal and para-clinical examinations. Activated charcoal is recommended in such situations of intoxication after gastric lavage [12]. This drug inhibits the systemic absorption of the toxic product in the gastrointestinal tract and accelerates their digestive elimination. It is effective against most drug intoxications if administered within two hours of ingestion [13].

However, other researchers such as Anne [14] believe that repeated doses of charcoal are not effective in eliminating anti-muscarinic agents. She advocates the administration of physostigmine salicylate to reverse the signs of brain toxicity. Physostigmine is a tertiary cholinesterase inhibitor which allows an increase in brain acetylcholine concentration. The onset of action of physostigmine is rapid (0.5-3 minutes) in cases of intoxication with anticholinergic drugs such as trihexyphenidyl, but its initiation requires monitoring with continuous electrocardiogram follow-up [15]. In our patient, the administration of physostigmine was not retained given the inaccessibility of the product in the Senegalese context, the absence of morbid danger for the patient and other complications. Braunwald E et al. [12] had reported that patients with deep life-threatening coma, severe hallucinations or severe arterial hypertension had been treated with physostigmine with some reversal of its effects. This was not the case with Doudou. The therapeutic strategies adopted in this patient were in accordance with the recommendations developed by most authors in the management of intoxication with anticholinergic drugs such as trihexyphenidyl [12,13].

Conclusion

Trihexyphenidyl (Artane®) is an antimuscarinic known for the treatment of Parkinson's disease and the extrapyramidal side effects

of neuroleptics. Recognised for several years as à substance of abuse, trihexyphenidyl intoxication leads to a central and peripheral anticholinergic syndrome which can be lethal in children if not treated early. This management requires hospitalisation with régula follow-up and symptomatique treatment with the use of antidotes, which is unfortunately rare in the context of the observation presented here. The hospitalisation of this child reveals two important issues: the question of self-medication and the control of domestic pharmacy which must be kept out of the reach of children and subjects who do not have the skills to use them wisely and with precaution. In order to reduce the risk of drug poisoning within families, the role of prescribing physicians and pharmacists is essential in the psycho-education of their patients and their carers. All the more so as self-medication is a frequent practice [16] in a population that is still insufficiently educated and in a precarious situation [17], with little or no coverage by the Couverture Maladies Universelles (CMU), and which avoids health costs by foregoing medical care. Living in the Dakar region and having a relative who is a nurse with good knowledge of the health system, the child was also able to benefit from an efficient health service, which might have been more difficult to find in other regions of the country.

Author Contributions

Diagne I: conception and writing of the article. Petit V: improvement in the drafting of the manuscript in its overall form. Boiro D: improvement of the manuscript in the discussion.

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