Case Report

The central anticholinergic syndrome in a three-year-old girl by accidental ingestion of a high-dose of Trihexyphenidyl

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Summary
The central anticholinergic syndrome is a known central nervous system toxicity caused by an overdose of antimuscarinic drugs. It produces clinical signs that include excitement, ataxia, hallucinations, behavioral abnormalities and drowsiness. Peripheral effects include hyperthermia hot dry flushed skin, tachycardia and urinary retention. The following account reports a three-year-old Sudanese girl who developed the syndrome by the accidental ingestion of a high dose of Trihexyphenidyl and recovered completely on paracetamol given as suppository, gastric lavage and supportive care.

Keywords: Trihexyphenidyl, anticholinergic syndrome, abuse.

Introduction
Antimuscarinic drugs e.g. Benztropine, Orphenadrine, Procyclidine, and Trihexyphenidyl (Benzhexol) are clinically used to reduce the relatively excessive cholinergic tone in parkinsonism and dystonia\(^1\). Antimuscarinic medications are known for side-effects that include pyrexia, tachycardia, confusion, euphoria, hallucinations, and are liable to abuse\(^2\). Their euphoric effects are the cause of the well documented abuse of these drugs. The central anticholinergic syndrome (CAS) produces clinical symptoms that include excitement, ataxia, hallucinations, behavioral abnormalities and drowsiness\(^3\). The antimuscarinic overdose syndrome is characterized by hyperthermia delirium myoclonic movements and choreoathetosis may be seen. Seizures, coma, and respiratory arrest may also occur\(^4\). Infants and children are especially sensitive to their hyperthermic action and elderly patients are especially sensitive to central nervous system effects\(^5\). Caution is required in psychosis\(^1\), pregnancy and breast feeding\(^2\), and in children\(^6\).

Case presentation
A 3-year-old girl was presented to the outpatient department with a sudden onset fever for one hour, delirium and disorientation associated with motor abnormalities of the hands and
feet. Although not sure, the mother suspected her child had taken some tablets, she presented a 10 tablets strip of Trihexyphenidyl with only 2 tablets remaining.

**Case history**

The mother stated that her child was well until one hour ago when she started to develop fever, was talking nonsense and was carrying a tablets strip in her hands; that her child had no history of febrile or other convulsions or any permanent disease or previous hospitalization; was not on temporary or continuous medication and no known drug allergy; that her child had normal antenatal, natal, developmental and nutritional history, and was fully vaccinated; and that there was no family history of epilepsy.

General examination showed good physique, weighed 13 Kgs. The child was conscious but not oriented, delirious in a euphoric manner; murmured and laughed but did not seem to respond to simple commands, febrile (38°C) but not pale, cyanosed or jaundiced, pulse at 110 beats per minute with normal characteristics and intact peripheral pulsations, blood pressure within normal. CNS; confused and not oriented, GCS at 12, normal posture. Cranial nerves and sensations were intact. Motor examination was normal except for twitching of the right angle of the mouth and fisting of both hands. Tone was normal and power grade 3; normal reflexes and sphincteric control. Chest and abdominal examinations were normal. Respiratory rate was 23 cycles/minute with vesicular breathing; no organomegally or ascites, intact hernial orifices and normal genitalia; no signs of chronic liver disease and no lower limb oedema.

A differential diagnosis of febrile convulsions, cerebral malaria and drug poisoning was adopted. Emergency treatment in the casualty room included paracetamol suppositories plus cold application. Immediate gastric lavage was done, fragmented tablets were retrieved by the lavage but the amount ingested or washed out could not be determined. A wide pore cannula was installed, the patient was admitted and investigations requested.

A clinical diagnosis was made of drug poisoning associated with fever and the typical CAS of excitement, hallucinations, behavioral abnormalities and motor abnormalities, due to ingestion of Trihexyphenidyl at high dose and without cardiovascular or other systemic complications.

Investigations were done including TWBC 10.23 of which 49% were lymphocytes and 40% neutrophils, haemoglobin concentration 11.2 mg/dl, MCV 72, MCHC 25, random blood glucose 97, urea 33, creatinine 0.8, Na+; 135, K+; 4.2, and a negative blood film for malaria.

She was started on six hourly paracetamol suppositories plus cold application. Drugs which improve cholinergic transmission were considered but needed continuous ECG monitoring which was not available. A watchful wait-and-see policy was decided. She started to show gradual improvement and by day 2 she made full recovery and was discharged home in a good condition.

**Discussion**

The aggressive presentation of the present case could certainly be attributed to the amount of the drug absorbed prior to the execution of the gastric lavage, the ingestion of the tablets was not witnessed and the mother suspected it only as a remote possibility and presented the almost empty tablet strip from her purse a few minutes after the presentation of the patient. Diagnosis was only ascertained after retrieval of tablets by the lavage.

The predominant signs of toxicity in the CNS can be assigned to the rapid distribution of the drug to the CNS considering that benzhexol is of high affinity and efficacy in CNS conditions such as parkinsonism and dystonia in children \(^1\). Children under 5 years are
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particularly sensitive to these effects\(\textsuperscript{7}\), however, the above statements are in disagreement with previous investigators\(\textsuperscript{8}\) who appreciated the extensive experience of Marsden and Fahn in the pharmacotherapy of generalized dystonia in children with Trihexyphenidyl or Ethopropazine and their determination that the response in children was better than in adults.

Fever, as seen in the present patient, is a recognized side effect of antimuscarinic medication by a peripheral mechanism which decreases heat dissipation.

The procedures undertaken in the handling of the present case can be divided into 3 phases the first, in the casualty department, consisted of controlling fever, and conducting gastric lavage; the second investigations; and the third included continuous follow up and observation in the ward. These procedures were adequate considering that the patient was discharged 48hrs later in a good condition, however, the oral administration of activated charcoal after the gastric lavage had been advocated in such cases by some investigators\(\textsuperscript{8}\), Anne\(\textsuperscript{9}\) stated that ‘Treatment of CNS stimulant overdose is largely symptomatic and supportive. Activated charcoal (1 g/kg) may be given; hemodialysis, hemoperfusion, peritoneal dialysis, and repeated doses of charcoal are not effective in removing antimuscarinic agents’.

The administration of physostigmine to reverse the signs of toxicity in the present patient was considered but it needed continuous ECG monitoring, so was left particularly considering the absence of cardiac or other life threatening signs in the patient. Braunwald et. al.\(\textsuperscript{8}\) stated that ‘Patients with deep coma, life threatening cardiac arrhythmias, severe hallucinations, or severe hypertension have been treated with physostigmine with some reversal of these effects; it has not been established whether physostigmine reduces mortality’.

The present investigations confirmed the final diagnoses and excluded other underlying causes of fever or disease, however, in more advanced hospital settings the continuous monitoring of plasma drug concentrations could have been of help.

The symptomatic treatment and observation strategy adopted in the present case is consistent with the recommendations of most investigators that in cases of CNS toxicity supportive environment until drug effects wear off should be instituted.

It is concluded that Trihexyphenidyl is an antimuscarinic with recognized therapeutic benefits and is a substance of abuse. The CAS is a known overdose toxicity of the drug. Management is largely symptomatic and supportive. The reversal of some of the signs of the syndrome with Physostigmine administration needs continuous ECG monitoring and is controversial.

A desire to take medicines is perhaps one of the features that characterize human behavior, this could proof detrimental considering that antidotal therapy is not usually available and sometimes not usable. The use of child proof drug bottles and packs should be advocated, in addition to educating people to keep medicines out of children’s reach and their disposal off in a correct manner. The availability of abused drugs beyond legal channels should always be checked as it may affect vulnerable persons in the community, other than the abuser, including family as has been shown in the present case.

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References