Case Report

Common Problem - Uncommon Poisoning: A Case Report

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ABSTRACT

Loxapine overdose is a rare toxicological emergency. This case report deals with an 8-year-old girl presenting in stuporous condition. She was provisionally diagnosed as suffering from acute menigoencephalitis and treated accordingly. Detailed history later revealed that it was a case of inadvertent loxapine succinate administration in place of lactulose.

The patient was treated on the lines of neuroleptic malignant syndrome, after which she improved and was discharged eleven days later.

Key Words: Loxapine succinate; Lactulose; Neuroleptic malignant syndrome

INTRODUCTION

Altered sensorium with fever in a child is always a challenge to a pediatrician. History is often the most important tool to reach a diagnosis. As accidental ingestion is common amongst children a toxicological approach is quite a necessary in this regard.

The Case: An 8-year-old stuporous girl presented to the emergency department of a tertiary care hospital in Kolkata with tonic posturing and fever with profuse sweating of 1 day duration. She was admitted to the paediatric intensive care unit (PICU). The girl had been healthy before these manifestations developed. There was no history of toxic substance ingestion, substance abuse or accidental drug overdose in the first instance. On admission, her Glasgow Coma Score (GCS) was 11, blood pressure 130/74 mm Hg, pulse 186/min, temperature 103°F. She was tachypnoeic. Both pupils were mildly dilated. Neck rigidity was present, with increased tone in all the four limbs, as well as the trunk. There was no adenopathy or organomegaly. The rest of the examination revealed no abnormality.

Initial blood glucose, calcium, creatinine and sodium were normal. Her potassium was 5.4 MEq/l, and total leukocyte count was 13,000, with increased polymorphs. Arterial blood gas analysis was normal. Dual antigen for malaria was negative. Lumbar puncture revealed normal findings. ECG revealed sinus tachycardia.

The child was provisionally diagnosed as suffering from acute menigo-encephalitis, and treated with IV fluids, cardiovascular monitoring, and IV antibiotic (ceftriaxone), and antiviral (acyclovir) therapy was also started. The next day, MRI brain was done, which revealed no abnormality.

After 48 hrs, the patient's condition remained the same. In order to find out the elusive diagnosis, we interviewed the parents again in more detail, and found that the patient had been suffering from constipation for sometime, and the day before the event she had been started on a laxative. On our request, the parents brought the medicine along with the doctor's prescription. To our consternation, we found that lactulose had been prescribed, but loxapine succinate had been dispensed in error. Instead of 10 ml lactulose, the girl had been administered 10 ml of loxapine (25 mg/ml) amounting to a total dose

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of 250 mg. Subsequently, of the additional investigations ordered, creatine phosphokinase (CPK) was found to be highly elevated (4640 U/l). We did not have the facility for serum loxapine level estimation.

A diagnosis of neuroleptic malignant syndrome was made and the child was treated accordingly. She gradually improved and was discharged after 11 days.

DISCUSSION

Loxapine succinate is a typical antipsychotic drug, which was very popular in the past but is nowadays infrequently used for schizophrenia in adults. It is not approved for paediatric age group. Mode of action is unknown, but it probably blocks dopamine at postsynaptic D2 receptors, which changes the level of excitability of sub-cortical inhibitory areas associated with tranquilization as calming effects and suppression of aggressive behaviour.[1]

With near complete oral absorption, it is rapidly removed from plasma and redistributed in tissues with a special predilection for lungs, brain, spleen, heart and kidneys, which are also responsible for its side effects and toxicity profile. Loxapine is metabolized extensively and is excreted mainly in the first 24 hrs. Metabolites are excreted as conjugates in the urine and in the faeces as unconjugates. Starting dose of loxapine is usually 20–50 mg/day with escalations of up to 100 mg/day.[2] Dosage more than 250 mg is not recommended in any circumstances.

Loxapine is not approved for the paediatric age group, and there is only one case of paediatric loxapine overdose, which presented with lethargy and ataxia.[3] In adults, loxapine overdose results in CNS depression, sinus tachycardia, hypertension, hypothermia, generalized seizures, recurrent paroxysmal atrial tachycardia and transient renal insufficiency from rhabdomyolysis.[4]

Being a first generation antipsychotic, loxapine is also a potential candidate for neuroleptic malignant syndrome (NMS), which is a potentially fatal syndrome characterized by rigidity and fever. DSM-IV criteria require two or more of the following symptoms to characterize as NMS: diaphoresis, dysphagia, tremor, incontinence, changes in level of consciousness, mutism, tachycardia, alterations in blood pressure, leukocytosis and laboratory evidence of muscle injury.

In a paediatric case series of NMS, fever was present in 78% cases and rigidity was reported in 70%.[5] Fever and rigidity together were present in 47.8% of cases. Tachycardia was reported in 74% cases, while changes in the level of consciousness were reported in 61% of cases. The diagnosis of NMS is supported by laboratory evidence of increased CPK level which is also the best prognostic marker of NMS and a surrogate marker for rhabdomyolysis.[6] Leukocytosis and high urinary myoglobin is also common. Treatment of paediatric NMS is supportive with anecdotal use of bromocriptine and dantrolene sodium being effective.[7]

CONCLUSION

This case is one of the rare paediatric loxapine overdoses reported in medical literature, and is also a rare case of NMS in the paediatric age group. But the point to be highlighted is the importance of history taking in making a correct diagnosis. A sincere history taking with heightened toxicological awareness is very much needed to clinch the right diagnosis in some cases. Also, it is high time that governmental agencies and pharma houses worked in close liaison to prevent such dispensing errors, which may be fatal in nature.

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