

Metoclopramide Induced Intermittent Opisthotonos in Infant

Case Report

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Abstract: Metoclopramide is widely used as an antiemetic and a prokinetic agent. Both the antiemetic properties and side effects of the drug are the result of dopamine receptor antagonism within the central nervous system. Therapeutic doses of metoclopramide can produce adverse effects. A 5-month-old girl was referred to our emergency department with the pre-diagnosis of afebrile convulsion. In her medical history, she was mistakenly given 2 mg/kg metoclopramide within a 24 h period, after which she became hypertonic and exhibited intermittent opisthotonos. Complete blood count, electrolytes, liver and renal function tests, blood gas analysis, and urinalysis were all within normal limits. Electroencephalogram, brain CT and cerebrospinal fluid examination were normal. Metoclopramide treatment was discontinued and she was treated with biperiden, which led to an improvement in symptoms after 15 minutes and complete remission in 60 minutes. Intermittent opisthotonos may be confused with convulsion in infant and thus lead to an unnecessary hospital admission. Physicians should be aware that metoclopramide is widely used in the pediatric population and children are susceptible to the side effects of metoclopramide and the side effects may present as "intermittent opisthotonos" as observed in our patient.

Keywords: *Intermittent Opisthotonos • Infant • Metoclopramide*

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1. Introduction

Metoclopramide, a member of the chlorobenzamide group, is widely used as an antiemetic and a prokinetic agent in general practice and hospitals. The antiemetic effect of the drug is the result of dopamine receptor antagonism in the chemoreceptor trigger zone. Another effect is to increase the gastrointestinal transit. Both the therapeutic and side effects are the result of anti-dopaminergic feature of drug [1,2]. The side effects of metoclopramide include neuroendocrine (galactorrhea), neurological (asthenia, sleepiness), extrapyramidal

dyskinetic reactions, myoclonic jerking and rarely intermittent opisthotonos [1,2]. Both the therapeutic and toxic doses of metoclopramide can produce adverse effects, which are usually seen within the first 24-72 hours of drug exposure. The infants are more susceptible to the side effect of metoclopramide [3].

In this article we report an infant who had an intermittent opisthotonos that was induced by metoclopramide treatment.

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2. Case Report

A 5-month-old girl was referred to our emergency department with the pre-diagnosis of afebrile convulsion. She was prescribed metoclopramide 0.5 mg/kg/day by her general practitioner for her two-day duration of nausea and vomiting. Nevertheless she had mistakenly been given 2 mg/kg metoclopramide within 24 h period, after which she became hypertonic and exhibited intermittent opisthotonos.

On the initial assessment, she was minimally responsive to verbal and painful stimuli. Acute dystonia of the extensor muscles of the neck, back, and both extremities was present as well as jaw-rigidity, horizontal nistagmus, and uncontrolled movements of the tongue. On physical examination, she revealed a rectal temperature of 37.1°C, pulse rate of 140/min, respiratory rate of 30/min, and systolic arterial pressure of 78 mmHg. The examination of other systems was unremarkable.

Laboratory studies revealed blood count, electrolytes, liver and renal function tests, blood gas analysis and urinalysis within normal limits. Electroencephalogram, computed tomography of brain and cerebrospinal fluid examination were normal. No significant change was observed in repeated blood analysis.

Metoclopramide treatment was discontinued and she was treated with biperiden 5 mg IM, which led to an improvement in symptoms after 15 minutes and complete remission in 60 minutes. The symptoms of the patient did not reappear during the one year follow-up.

3. Discussion

Opisthotonos is a relatively rare and challenging neurological symptom of spasticity or dystonia that most often results from extended asphyxia in children. This clinical picture is most frequently seen after an extensive lack of oxygen in the brain, for example after near-drowning, after cardiac arrest or suffocation. These patients show a combination of spasticity and a tendency to go into dystonic posture. This dystonic posture is often referred to as opisthotonus (Greek: opistho=behind; tonos=tone). In addition, the lower limbs go into extension and the upper limbs into flexion [4].

Metoclopramide is a commonly used drug to treat gastroesophageal reflux disease in infants. In many practices, metoclopramide has become the standard of care without a rigorous approval process. Although the prevalence of metoclopramide use in infants across

inpatient and outpatient settings is ill-defined, it is clear that it is commonly prescribed for infants and children. In the United States, more than 7 million prescriptions for metoclopramide were dispensed in 2004 [5].

Both therapeutic and toxic doses of metoclopramide can produce the adverse effects. Cezard *et al.* reported that there is no dose-effect correlation and sex has no influence on the occurrence of neurological symptoms [6]. Bateman *et al.* reported that there was no difference in plasma concentration of metoclopramide of children with dystonia when compared to those without these side effects [7]. Hyser *et al.* reported that metoclopramide clearance is reduced in renal failure, and myoclonus or other neurologic complications may be precipitated in such patients by usual doses of this drug [3]. In this patient, there was no risk factor precipitating the seizure. We did not detect electrolyte imbalance, hypoglycemia, hypocalcemia, history of head trauma, infection, renal failure, metabolic abnormality of proteins, carbohydrates and/or lipids.

Some drugs used in childhood may cause dystonic reactions. Crosley *et al.* reported that carbamazepine caused dystonia in three children with brain damaged [8]. Methylphenidate, a stimulant drug used in management of the hyperkinetic reaction in children, caused dyskinesia and dystonia when the simultaneous use of methylphenidate and a phenothiazine was followed by withdrawal of the phenothiazine [9]. Acute dystonia usually occurs three to five days after antipsychotic therapy begins or the dosage is increased [10]. Although there was a history of metoclopramide overdose in our patient, it is reported that there was no difference in plasma concentration of metoclopramide of children with dystonia when compared to those without this side effects [7]. Our patient did not receive any other drug other than metoclopramide.

The children with acute dystonia usually referred to the pediatric emergency units with the presumptive diagnosis of central nervous system diseases such as meningitis/encephalitis and convulsion. Yis *et al.* reported two children with acute dystonia related with metoclopramide. One of them referred to their units with presumptive diagnosis of encephalitis another with tetany [11]. These conditions may lead to unnecessary invasive procedures such as lumbar puncture, unnecessary hospital admission and drug administration. The patient referred to our emergency unit pre-diagnosis of afebrile convulsion. Use of metoclopramide should be questioned in patients presenting with acute dystonia. Metoclopramide-induced dystonia is frightening both for the patient and family. Particular care is required when prescribing metoclopramide preparations for children, as the side effects may occur not only with an

accidental overdose but also with very slight overdose, as demonstrated in our patient. Intermittent opisthotonos may be confused with convulsion in infants and thus lead to an unnecessary hospital admission. Physicians

should be aware that metoclopramide is widely used in the pediatric population and children are susceptible to the side effects of metoclopramide and may present as “intermittent opisthotonos” as observed in our patient.

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