

Acute Metoclopramide Toxicity in Children

M.M.A. Faridi, M.D., D.C.H., V.K. Gandhi, M.D.
Delhi, India

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Abstract

Vomiting is a common symptom in children and is usually treated with phenothiazines. A new dopamine antagonist, metoclopramide, considered relatively safe, is widely used as antiemetic. The development of extrapyramidal symptoms is a well known manifestation of phenothiazine toxicity. During an epidemic of gastroenteritis, we encountered 18 patients who had received metoclopramide and developed extrapyramidal symptoms. All patients improved with diphenhydramine therapy. Our experience suggests that the development of extrapyramidal symptoms after intake of metoclopramide may not be uncommon.

Key words: *Gastroenteritis, metoclopramide, vomiting, extrapyramidal symptoms.*

Emesis, an important symptom of varied etiology, is frequently encountered in pediatric age group. Having peripheral as well as central action on chemoreceptor trigger zone,¹ metoclopramide is being increasingly used for symptomatic relief of vomiting in children because of its availability in pediatric dose regimen, economy, palatability and better safety record as compared to phenothiazines; the latter are known to produce severe acute extrapyramidal symptoms.²⁻⁴ We came across several cases of acute metoclopramide toxicity during the recent epidemic of acute gastroenteritis and cholera in East Delhi in the month of August 1988. The clinical profile of these cases is presented in this communication.

Material and methods

A detailed clinical presentation of 18 cases, who

reported to Special Diarrhoea ward, with acute extrapyramidal symptoms following recorded administration of metoclopramide, was studied as regards to age, sex, duration of illness, prescriber, route of administration, dosage schedule, total drug intake, intake of any other antiemetic and response to oral diphenhydramine hydrochloride (12.5 mg/teaspoonful, as syrup Benadryl).

All children were suffering from loose motions and vomitings for 1-3 days. They were diagnosed as cases of acute gastroenteritis with mild to moderate dehydration but no child was in peripheral circulatory failure. They had not passed urine for 6-16 hours. The possibility of cholera was ruled out in all cases by physical characteristics and microscopic examination of stools by "hanging drop" method and later on confirmed by culture studies.

All children were initially managed by intravenous fluid therapy and syrup Benadryl in doses of 5 mg/kg/24 hours in 3 divided doses orally for 2-3 days. After correction of dehydration, oral rehydration solution (ORS) was given ad lib and antibiotics, where indicated.

Results

All patients were between 4-12 years of age but majority of them (72.2%) were 8 years old with slight male preponderance M:F:1.2:1. To all but one patient (94.4%) metoclopramide was prescribed either by private practitioner (qualified and quacks) or by

*From the Department of Pediatrics
University College of Medical Sciences
and Guru Tegh Bahadur Hospital
Delhi, India*

*Reprint Requests: Dr. M.M.A. Faridi
Department of Pediatrics
University College of Medical Sciences
D-18, GTB Hospital Campus
Delhi-110095.*

Table 1. Symptoms and signs of acute metoclopramide toxicity in 18 children.

Symptoms/signs	% of cases
1. Oculogyric crisis, facial grimacing/Neck retraction	94.5
2. Torticollis, Protrusion of tongue, opening of mouth	66.6
3. Ataxia/unsteady gait	61.1
4. Hypertonia	61.1
5. Stare look, nystagmus	33.3
6. Akinesia	27.7
7. Dystonia/Abnormal posture	27.7
8. Akathesia/Tremors	Nil

dispensary doctors alone or in combination. About 77.7% prescribers were qualified doctors of whom 21.4% were Pediatricians. In one case (5.6%), the child developed drug reaction 1 hour after oral intake of metoclopramide syrup (0.2 mg/kg as single dose) in our hospital. This child did not have any record of medication but some injection had been given to her by the private practitioner for the complaint of vomiting 8 hours before admission to this hospital.

All children were hospitalised within 2 hours of development of extra-pyramidal symptoms. About 2/3rd cases received parenteral medication but none of the patients developed toxicity after single dose. Majority of them (83.3%) developed reaction after 2 or 3 doses of drug given over a period of 12-24 hours. Total dose intake varied from 0.6 mg/kg to 2.25 mg/kg in 12 to 24 hours. History of taking injection triflupromazine (Siquil) in addition was elicited in one case in the dose of 0.4 mg/kg as single dose.

Oculogyric crisis and facial grimacing with neck retraction were observed in all except one case irrespective of age and sex. Torticollis, protrusion of tongue and opening of mouth were the next common features (66.6%) followed by ataxia and unsteady gait (61.1%). Akathesia was not observed (Table 1).

All cases showed improvement within 6-8 hours with oral intake of syrup Benadryl. The oculogyric crisis and facial grimacing were first to go followed by neck retraction, stare look and hypertonia in that order. Within 24-36 hours all symptoms subsided without any neurological deficit or recurrence of symptoms, but few children complained of headache and sleepiness. All the patients were discharged within 24 hours following complete recovery.

Discussion

Metoclopramide (methoxy-2-chloro-5 pro-cainamide) is a new generation dopamine antagonist and is chemically related to procainamide. It has a potent central antiemetic effect by virtue of its ability to block dopamine receptors in chemoreceptor trigger zone.¹ Dystonic and dyskinetic reactions, similar to those occurring with phenothiazine, may occur

with metoclopramide, more commonly in children than adults.⁵ The symptoms of acute metoclopramide toxicity have been reported with a dosage of 1 mg/kg/day and occur 1-3 days after oral administration.⁶ In our study group total dose varied from 0.6 mg to 2.25 mg/kg in 12 to 24 hours. The early onset of toxic symptoms in our series might have been due to (i) parenteral administration of the drug in majority of cases (ii) impaired renal excretion leading to accumulation of drug in the body since all children were suffering from dehydration and oliguria. This might have prolonged the half life of the drug.⁷⁻⁹ In our series, notwithstanding age, sex, route of administration and dosage, the symptoms and signs of metoclopramide toxicity were striopallidal in nature as has been observed by other workers in toxicity with phenothiazines^{2,3,4,10} and with metoclopramide.¹¹ But unlike other workers^{5,8,11} we did not observe akathesia. Generalised dystonia too was infrequent.

The dopamine mediated synaptic neurotransmission in the basal ganglia is antagonised by metoclopramide resulting in increase of the cholinergic activity and imbalance between cholinergic and dopaminergic receptors leading to dystonic and dyskinetic symptoms. Diphenhydramine hydrochloride by virtue of its anticholinergic property reverses this imbalance. This results in prompt amelioration of distressing extrapyramidal symptomatology.^{4,12} All our children fully recovered without any sequelae by oral diphenhydramine hydrochloride therapy.

As nausea and vomiting are usually short-lived, indiscriminate use of metoclopramide should be discouraged. Since dehydration is a risk factor, drug must be used cautiously and in appropriate doses with anticipation of toxic reactions in these circumstances.

References

1. Pinder RM, Brogdon RN, Sawyer PR, et al: Metoclopramide: a review of its Pharmacological properties and clinical use. *Drugs* 1976; 12:81-131.
2. Gupta JM, Lovejoy FH: Acute phenothiazine toxicity in childhood: A five year old survey. *Pediatrics* 1967; 39:771-4.
3. Knight ME, Roberts RJ: Phenothiazine and butyrophenon intoxication in children. *PCNA* 1986; 33:209-307.
4. Sharma M, Gandhi VK, Taluja RK, Mathur PS: Acute phenothiazine Reaction. *Ind Pediat* 1988; 25: 571-2.
5. Lancaster R: Metoclopramide. In: *Pharmacology in clinical practice*. First edition, London; William Heinemann Medical Books Ltd., 1980: 384.
6. Daele MC, Jaeken J, Schueren PV et al:

Dystonic reactions in children caused by metoclopramide. Arch Dis Child 1970; 45: 130-3.

7. Albiloi R, McCallum RW: Metoclopramide: Pharmacology and Clinical application. Ann Int Med 1983; 98: 86-95.
8. Piper DW, Carle DJ, Doe WF et al: Nausea and vomiting. In: Speight TM, ed, Avery's Drug Treatment. Principles and practice of clinical pharmacology and Therapeutics. Edinburg: Churchill Livingstone, 1987; 756-8.

9. Bateman DN: Clinical Pharmacokinetics of metoclopramide. Clin Pharmacokin 1983; 8:523.
10. Mittal MM, Gupta SK, Misra RC: Extrapyramidal manifestation following phenothiazine therapy. J Assoc phys India 1970; 18:691-6.
11. Bateman DN: Extrapyramidal reaction with metoclopramide. BMJ 1985; 291: 930-2.
12. Singh RP, Sachdev HPS: Metoclopramide. Ind Pediat 1988; 25: 993-6.