

NEUROLOGICAL SIDE EFFECTS ASSOCIATED WITH UNNECESSARY USE OF METOCLOPRAMIDE IN CHILDREN

Abdullah Abdulaziz Al Zaben, MBBS, DCH, FRCPC; Abdullah Solaiman Al Herbishi, MBBS, FRCPC, FAAP

Incidence of side effects of metoclopramide is 20%.¹ Neurological symptoms such as oculogyric crisis and involuntary contractions of the eye muscles leading to upward conjugate gaze occur in about 1% of patients.² Children and young adults are more prone to develop these symptoms, even after a single dose.^{3,4} Despite the fact that these effects disappear spontaneously and completely after discontinuation of this treatment, they create unnecessary anxiety for the patient, parents and health care personnel. This problem would not have emerged without the uncontrolled, and most of the time unnecessary, prescription of metoclopramide to young children. In this study, over a one-year period, we analyzed the clinical data of 24 children who presented with these manifestations after being prescribed metoclopramide for an acute illness.

Material and Methods

Clinical data and hospital course of children presenting over a one-year period (starting July 1991) to the emergency room of the Pediatric Department of the Riyadh Medical Complex with neurological symptoms due to metoclopramide (primperan or plasil) were analyzed. The number of admissions to this emergency unit was 30 to 50 children per day with various acute pediatric problems. Age, weight, indicating symptoms for prescribing metoclopramide, dose given, frequency and route of administration were all recorded. The specific neurological symptom and/or sign, e.g., oculogyric crisis defined as involuntary contractions of the eye muscles resulting in upward conjugate gaze, dystonia, drowsiness, etc. was elicited at presentation and its course thereafter was followed. Some children were given diazepam to abort or lessen these symptoms and the rest resolved spontaneously.

From the Department of Pediatrics (Dr. Al-Zaben), Riyadh Medical Complex, and Department of Pediatrics (Dr. Al-Herbishi), King Khalid University Hospital, Riyadh.

Address reprint requests and correspondence to Dr. Al-Herbishi: P.O. Box 90533, Riyadh 11623, Saudi Arabia.

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Results

Twenty-four children presented with clinical data fulfilling the criteria. They represent zero to one case of 30 to 50 admissions per day during the period of the study with estimated prevalence of 0.6% among total admissions. Nine were males and 15 were females. Metoclopramide was prescribed as plasil in 11 and as primperan in 13 children. Most of these children were young; 10 were below six months of age, three between six and 12 months of age, nine were between one and six years and two were above six years of age (Table 1). The dose ranged from one to 10 mg given three to four times daily. Suppositories were prescribed in five cases and oral preparation (drops or syrup) in the rest. Indicating symptoms were vomiting in 19 cases, cough in 17 cases and wheezing in two cases. The drug was taken accidentally in one case and was mistakenly prescribed as an antipyretic in another case (Table 2). All 24 children presented with neurological symptoms and/or signs. Nineteen children showed the typical oculogyric crises. Dystonia manifested in 13; lethargy in two, sleepiness in one and drowsiness in two. One child was ataxic; four showed tonic-clonic movements described as seizures (Table 3). The duration of symptoms ranged from 0.5 to 72 hours (mean 10). Diazepam 0.3 mg/kg/dose intravenously was used once in 13 children. All children were admitted and observed in the hospital.

Discussion

Metoclopramide, a dopamine receptor antagonist that possesses central antiemetic and peripheral gastrointestinal motility effects, is widely used.¹⁻⁴ It has been used in the pediatric age group for various indications, e.g., gastroesophageal reflux,^{4,5} chemotherapy-induced emesis,⁶ ureterolithiasis,⁷ surgery-induced emesis,⁸ and many other indications. Its use as an antiemetic for acute illness, e.g., gastroenteritis, is rarely if at all indicated. On the contrary, it may mask helpful symptoms and signs in the evolving acute illness. Furthermore, the value of metoclopramide, even for the above-mentioned indications, is recently debated.⁶⁻¹⁰ Despite all of this, metoclopramide remains a popular antiemetic, used widely in developing countries as it is readily accessible to patients and physicians. The

estimated prevalence of neurological side effects in our study of 0.6% represents only the tip of the iceberg, as we feel that mild symptomatology may be overlooked by patients and parents.

Neurological deficits are more hazardous in young children, especially infants and neonates, where it can precipitate apnea and death.¹¹ Unfortunately, our study showed a predominance of the use of metoclopramide in young infants (less than six months). All of our patients presented with acute illness without prior indication of an antiemetic. The most common neurological sequela of metoclopramide was oculogyric crisis (19 out of 24 or 79%). This percentage certainly reflects a high frequency when compared to other neurological sequelae. In addition, dystonia was the second highest precipitating symptom in the emergency room. Extrapyramidal symptoms were reported in 1% to 5% of metoclopramide users.^{2,12} Obviously these symptoms are frightening to the patient and the parents. Less frequent symptoms such as ataxia, aphasia, and decreased level of consciousness are also worrisome. The presence of these symptoms in young children and infants may predispose to even more respiratory compromise, namely apnea, in addition to the previously reported symptoms of restlessness, anxiety and sudden death.^{2,9,11} Most of our patients received doses of

the drug that were more than the recommended therapeutic dose of 0.15 mg/kg/dose⁶ or 0.7 mg/kg/day.⁹ However, even with standard therapeutic doses, neurological side effects were reported.⁴

The absorption of metoclopramide is rapid throughout the gastrointestinal tract with variable peak plasma levels according to the route of administration.¹³ In our patients, there was no statistical difference between oral and rectal routes, either in terms of duration of symptoms or severity of symptoms.

Most of these symptoms resolve spontaneously. Some do require treatment with 1 mg/kg of intravenous diphenhydramine. Fifty-four percent (54%) of our patients were given diazepam, which abolished symptoms immediately.

In conclusion, we feel that antiemetic agents such as metoclopramide are overused in children without scientific basis. We recommend that the existing practice of uncontrolled prescription of these agents should decline. We emphasize the role of senior pediatricians in publicizing this among their junior colleagues in various institutions.

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TABLE 1. Number of children according to age.

Age (years)	Number of cases
0-0.5	10
0.5-1	3
1-6	9
>6	2
Total	24

TABLE 2. Indicating symptoms of prescribing metoclopramide.

Symptom	No. of children
Vomiting	19
Cough	7
Wheezing	2
Accidental	1
Error	1

TABLE 3. The presenting neurological symptoms in the children presented.

Presenting manifestation	No. of children
Oculogyric crises	19
Dystonia	13
Tonic-clonic seizures	4
Drowsiness	2
Lethargy	2
Aphasia	2
Sleepiness	1
Ataxia	1