Orijinal article

Side Effects of Metoclopramide: Does It Deserve to Prescribe For Nausea, Vomiting?

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ÖZET

Metoklopramid komplikasyonları: bulantı ve kusma için değer mi?

Metoklopramid antiemetik olarak kullanılan dopamin reseptör antagonistidir. Önerilen tedavi dozlarında da görülebilen ekstrapiramidal etkiler çocuklarda sık görülen akut yan etkilerdendir.

Kırıkkale Üniversitesi Tıp Fakültesi ve Sağlık Bakanlığı Kırıkkale Çocuk Sağlığı ve Hastalıkları Hastanesi acil polikliniklerine Mart 2006-Mart 2007 tarihleri arasında metoklopramid kullanımı sonrası ortaya çıkan yan etkileri ile başvuran 19 olgu retrospektif olarak değerlendirildi.

Çalışmadaki hastaların yaşları 4 ila 174 ay arasında değişmekte olup 10 (%52,7)'u kızdı. Görülen yan etkiler; distonik reaksiyon, okulogirik kriz ve konvülsiyon idi. Tüm hastalarda semptomlar metoklopramid kullanımını takip eden ilk üç günde ortaya çıkmıştı. 17 hasta tek doz biperidene yanıt verirken bir hastaya ikinci doz uygulanması gerekmişti. Bir hastada konvülsiyon nedeniyle tedaviye midazolom eklenmişti.

Klinisyenler metoklopramide kullanımı sonrası yan etkiler açısından dikkatli olmalıdır.

Anahtar Kelimeler: Çocukluk çağı, distonik reaksiyonlar, metoklopramid, yan etkiler

ABSTRACT

Metoclopramide is a dopamine receptor antagonist which is used as an anti-emetic. Extrapyramidal reactions which could be seen even at recommended doses are the most common acute side effects in children.

This retrospective study, evaluated adverse reactions of metoclopramide in 19 patients who had attended to the emergency departments of Kırıkkale University School of Medicine and Ministry of Health Kırıkkale Children's Hospital between March 2006 and March 2007.

Patients in our study were between 4 and 174 months of age and 10 (52.7%) of them were females. Observed adverse reactions were dystonic reaction, oculogyrics crisis and convulsion. In all patients symptoms arised within the first to 3rd days of metoclopramide usage. All 17 patients responded to one dose Biperiden administration except one, who needed the second dose. One patient had convulsion and midazolam was added to the treatment.

Physicians must be aware of adverse reactions caused by metoclopramide.

Key Words: Childhood, dystonic reactions, metoclopramide, side effect

INTRODUCTION

Metoclopramide is clorobenzamide which was used commonly as an anti-emetic agent. The antiemetic effect of the drug is a result of dopamine receptor blockage in the chemoreceptor trigger zone[1]. Even optimum doses of metoclopramide could be associated with variety of adverse effects on the central nervous system in children[2].

Extrapyramidal reactions are the most common acute side effects and these include particularly dystonic reactions like muscle contractions[3]. These dystonic reactions could be seen as pharyngeal and laryngeal dystonia, musculer contractions of face and neck, opistotonus, torticollis, trismus, oculogyric crisis, akathisia, ataxia, agitation, irritability, nystagmus and convulsion[3].

In this paper we aimed to focus on adverse central nervous system effects of metoclopramide when used as an antiemetic.

MATERIAL AND METHODS

Between March 2006 and March 2007, 19 children who were admitted to the emergency unit of Kirikkale University School of Medicine and Ministry of Health, Kirikkale Children's Hospital were retrospectively evaluated.

Hospital records were used to collect informations about demographic characteristics, presenting symptoms, clinical signs and that were administered.

All data were entered by using SPSS 11.5 software package for the statistical analysis. The definitions were provided as numbers and percentages for discrete variables and mean and standard deviations for continuous variables.

Table 1. Characteristics of the patients

Patients	Sex	Age	Dosage (mg) Route of administration	Symptoms Started (day)	Initial presentation
1	female	4 month	25 (po*)	3.day	Convulsion
2	female	12 year	30 (po)	1.day	Acute dystonia
3	male	5 year	15 (po)	1.day	Acute dystonia
4	male	9 year	10 (v**)	2.day	Acute dystonia
5	female	10 month	10 (po)	2.day	Oculogyric crisis
6	female	11 year	20 (po)	1.day	Acute dystonia
7	female	14 year	30 (po)	1.day	Acute dystonia
8	female	9 year	60 (po)	3. day	Acute dystonia
9	male	15 year	30 (po)	1.day	Acute dystonia
10	male	10 year	60 (po)	2.day	Acute dystonia
11	male	8 year	20 (iv)	2.day	Acute dystonia
12	male	11 year	40 (po)	2.day	Acute dystonia
13	female	8 year	50 (po)	2.day	Acute dystonia
14	female	18month	15 (po)	3.day	Acute dystonia
15	male	9 year	20 (po)	1.day	Acute dystonia
16	male	13 year	60 (po)	2.day	Acute dystonia
17	female	9 year	30 (po)	2.day	Acute dystonia
18	male	3 year	10 (po)	1.day	Acute dystonia
19	female	13 year	50 (po)	2.day	Acute dystonia

*po:peroral ** iv: intravenous

RESULTS

Mean age of the 19 children was 90±51.64 months (min 4 months-max 174 months) and 10 (52.7%) were females. Symptoms started averagely within the three days of start of metoclopramide treatment in our patients. Initial symptoms were acute dystonia in 17 patients, oculogyric crisis and convulsion in other two patients respectively.

Only two children received metoclopramide treatment via intravenous route, where all others received orally. In all cases the drug was prescribed by a physician for nausea and vomiting due to respiratory tract infection or gastroenteritis. In all patients drug was used within recommended doses (Table 1).

After reserving a full history and carrying out a complete physical examination, metoclopramide adverse reactions were diagnosed in 18 cases. In one of the patient who was 4 months of age and had admitted to the hospital with fever, vomitting and convulsion the initial diagnosis of menengitis was suspected. Menengitis was excluded in this patient with normal lumbar puncture and CT imaging findings and with detailed history, usage of metoclopramide was learned as the etiological factor for convulsion.

Metoclopramide treatments were stopped in all patients and intramuscular biperidene lactat (1.2 mg/m^2) was administered. In 17 of all patients symptoms dissappeared within 6 hours. But one of the patients needed additional dose of biperidene as no improvement was observed in her dystonic movements. Midazolam was also administered to one patient who had admitted with convulsions.

In all cases parents were distressed by dramatic and sudden nature of adverse affects. All patients were hospitalized and were observed for 24 hours. As there were no relapse in dystonic reactions and were no abnormal signs and symptoms. Children were discharged from the hospital.

The only case stayed in the hospital for seven days who was suspected and searched for menengititis.

DISCUSSION

Metoclopramide is used in children especially for the treatment of gastroeosophageal reflux, nause and vomiting. The antiemetic effect of the drug is related to dopamine-2 receptor antagonism in the chemoreseptor trigger zone[4]. The prokinetic effect is secondary to increased motility in upper gastrointestinal tract. It also increases the resting tone of the lower eosophageal sphincter[5].

Secondary blockage of spesific postsynaptic dopamine receptor in basal ganglia metoclopramide may produce acute dystonia. The acute reactions are usually self limited or respond well to treatment[6]. Children and young adults, particularly females are more sensitive to extrapyramidal effects of this medication. Oculogyric crises develop most commonly in female patients[6]. In our study oculogric crises was seen in only one female patient and 10 of 19 patients were female.

Acute dystonic reactions usually occur within the first 24 to 72 hours of treatment[3]. In all our patients metoclopramide adverse reactions

developed within 3 days of begining of the treatment.

At higher doses of metoclopramide higher incidence of extrapyramidal reactions in children and adults were reported in retrospective studies in literature. Metoclopramide usage is restricted under the age of 20 years in England due to its side effects[6]. Extrapyramidal reactions could be seen even at recommended doses[2]. In our cases metoclopramide was used within recommended doses.

Prescription of metoclopramide is not recommended in children except for severe intractable vomiting. If vomiting is associated with radiotherapy and as a premedicational agent before starting diagnostic procedures metoclopramide can be administered[6]. In our study the drug was prescribed in all cases for nausea and vomiting due to respiratory tract infection or gastroenteritis.

The side effects create a great panic and horror in parents and anxiety in children. Physicians must be aware of the adverse reactions caused by metoclopramide usage. They should never forget about the possibility of development of these reactions that can easily be confused with other diseases and blur the clinical picture of the patient. If physician intented to prescribe metoclopramide the precise dose and possible side effects should be discussed with the parents before starting the agent.

Because of its extrapyramidal side effects, physicians and especially pediatricians should prescribe metoclopramide for only certain indications mentioned above. In regard of the possibility of development of side effects and trauma of these side effects on families and children, pediatricians should be very cautions before prescribing metoclopramide.

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