

## Evaluation of Patients with Metoclopramide-Induced Acute Dystonic Reaction

Metoklopramid Kullanımına Bağlı Akut Distonik Reaksiyon Gelişen Hastaların Değerlendirilmesi

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### Abstract

**Objective:** Metoclopramide is a medication used as an antiemetic in children. Its most significant side effect is acute dystonic reactions requiring emergency treatment. This study evaluates some cases in which metoclopramide-induced acute dystonic reactions developed at a pediatric emergency department.

**Material and Methods:** The study includes 11 children admitted to the Pediatric Emergency Department due to medication-induced dystonia.

**Results:** The average medication time of patients was  $40 \pm 35.35$  hours, the average development period of dystonia after medication was  $1.48 \pm 0.85$  hours and the average time to complete recovery after treatment was  $1 \pm 0.33$  hours. Two of the cases were pre-diagnosed as convulsions, two as encephalitis, one as food poisoning, one as intoxication and one as a drug reaction. All cases presented with an acute dystonic reaction upon physical examination. Torticollis was observed in all cases, oculogyric crisis in seven cases, opisthotonos in two cases, tongue protrusion in two cases and contraction and increased tonus of the arms and legs in one case. Biperiden lactate was administered to all cases and rapid and complete recovery was observed.

**Conclusion:** Dystonia can easily be mistaken for other conditions due to its infrequency in routine pediatric cases when this movement disorder is compared with developing cases. It should be considered that patients who develop movement disorders and whose history includes metoclopramide usage may have a medication-induced dystonic reaction. (*JAEM 2012; 11: 80-4*)

**Key words:** Metoclopramide, vomiting, antiemetic, acute dystonic reaction, child

### Özet

**Amaç:** Metoklopramid çocuklarda antiemetik olarak kullanılan bir ilaçtır. En sık yan etkisi akut distonik reaksiyondur. Bu çalışmada Çocuk Acil Polikliniğine metoklopramid kullanımına bağlı akut distonik reaksiyon gelişen olguların değerlendirilmesi amaçlanmıştır.

**Gereç ve Yöntemler:** Metoklopramid alımına bağlı distoni gelişmesi nedeni ile Çocuk Acil Polikliniğine başvuran 11 çocuk olgu çalışmaya alındı.

**Bulgular:** Olguların ilacı kullanma süresi  $40 \pm 35,35$  saat, ilaç alımından sonra distoni gelişme süresi  $1,48 \pm 0,85$  saat ve tedavi uygulandıktan sonra tam iyileşme süresi  $1 \pm 0,33$  saat idi. Olguların ikisi konvülsiyon, ikisi ensefalit, birisi besin zehirlenmesi, birisi intoksikasyon ve biri de ilaç reaksiyonu ön tanısıyla sevk edilmişlerdi. Fizik muayenede olguların tamamında distonik reaksiyon gelişmişti. Olguların tümünde tortikollis, 7'sinde okülojirik kriz, 2'sinde opisthotonos, 2'sinde dil çıkarma hareketi ve 1'inde kol ve bacaklarda kasılma mevcuttu. Olguların 4'ünde ilk dozdan sonra distoni gelişmişti. Altı vaka üst solunum yolu enfeksiyonu, 3 vaka akut gastroenterit ve 2 vaka intihar girişimi tanısı aldı. Tüm olgulara parenteral biperiden laktat uygulandı ve tümünde kısa süre içinde iyileşme görüldü.

**Sonuç:** Distoni çocuk hasta grubunda rutin pratikte sık görülmeyen için tanınmasında güçlükler yaşanabilmektedir. Bu nedenle sık olarak görülmeyen bu hareket bozukluğu gelişen olgular ile karşılaşıldığında başka hastalıklarla kolaylıkla karıştırılabilmektedir. Metoklopramid kullanma öyküsü olan ve hareket bozukluğu gelişen olgularda ilaca bağlı akut distonik reaksiyon akla gelmelidir. (*JAEM 2012; 11: 80-4*)

**Anahtar kelimeler:** Metoklopramid, kusma, antiemetik, akut distonik reaksiyon, çocuk

### Introduction

Metoclopramide is a dopamine receptor antagonist that is used as an antiemetic. It is commonly used in the treatment of vomiting triggered by gastroesophageal reflux and infections in infants, as it is a prokinetic agent and shortens the period of emptying the stomach (1, 2). The most common side effect of metoclopramide is extrapyramidal disorders. Acute dystonic reactions are reported to occur fre-

quently (0.2-25%) as contractions in the facial, trapezius and dorsal muscles, opisthotonos, torticollis, oculogyric crisis, dysarthria and trismus. When these dystonic reactions are not diagnosed properly, they are confused with situations like tetany and convulsion; therefore, an incorrect diagnosis may be made (3, 4).

This study reports on 11 pediatric cases with metoclopramide-induced acute dystonic reactions, and aims to draw attention to the dystonic side effects of metoclopramide commonly prescribed by physicians.



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## Material and Methods

The study was planned retrospectively with the local ethical committee's approval. Informed consent was obtained from the parents of all children. The study included 11 pediatric cases of metoclopramide-induced dystonia admitted to the Pediatric Emergency Department of the Faculty of Medicine, Gaziantep University between August 2009 and August 2011. The study used clinical monitoring data on patient demographic characteristics, the type of indications for which the drug was used, the daily dosage, the development period of dystonia, diagnosis and treatment.

### Statistical analysis

Statistical analysis was performed via SPSS for Windows (version 11.0, SPSS Inc., Chicago, IL). Descriptive statistics were evaluated as mean and percentage.

## Results

The age average of the cases was  $8.3 \pm 3.99$  years old (7 months-15 years), seven of whom were female (Table 1). Average medication time of cases was  $40 \pm 35.35$  hours (2-60 hours), average time of dystonia development after medication was  $1.48 \pm 0.85$  hours (20 min-3 hours) and complete recovery time after treatment was an average of  $1 \pm 0.33$  hours (30-90 min). Five cases were treated with medicine

by a pediatrician at a state hospital, two cases by a family physician and two cases by their mother due to vomiting. Another two cases used this medicine to attempt suicide. Four cases (36.4%) developed dystonia after the initial dose, six cases (54.5%) were diagnosed with upper respiratory tract infection, three (27.3%) as acute gastroenteritis (AGE) and two (18.2%) as a suicide attempt. The complaints of the patients manifested as muscular spasms of the neck in all cases, oculogyric crisis in seven cases, nausea and vomiting in nine cases, diarrhea in three cases, tongue protrusion in two cases and unsteady gait in one case. An acute dystonic reaction was diagnosed in all cases upon physical examination. In addition to torticollis, oculogyric crisis was observed in seven cases, opisthotonos in two cases, tongue protrusion in two cases and contraction in the arms and legs in one case (Figure 1-4).

Metoclopramide was taken by all patients, nine as an antiemetic and by two patients who attempted suicide. The pre-diagnoses were convulsion in two cases, encephalitis in two cases, food poisoning in one case, intoxication in one case and a drug reaction in one case. Of seven cases sent to our hospital with a pre-diagnosis, only one patient was considered to have developed a drug reaction. Four cases presented directly to our clinic. None of the 11 patients took metoclopramide in combination with other drugs with known neurological side effects. Complete blood count, blood biochemistry and blood gas analysis were normal in all patients. Parenteral biperiden lactate (0.04 mg/kg) was administered to all cases for the treatment

**Table 1.** Basic features of cases

Case	Age	Gender	Initiator	Pre-Diagnosis of Referral	Diagnosis	Drug dose	Starting period of complaints (hours)	Development of dystonia following initial dosage	Finding
1	7 months	Female	Family Physician	.*	URTI	0.6 mg/kg/dose	2	+	Torticollis
2	6 years	Female	Pediatrician	Convulsion	URTI	?	120	-	Torticollis, Oculogyric crisis,
3	15 years	Female	-	.*	Suicide	1.8 mg/kg/dose	2.5	+	Torticollis, Oculogyric crisis
4	5.5 years	19	Pediatrician	Convulsion	URTI	?	36	-	Torticollis, Contraction, Opisthotonus
5	10 years	Female	-	.*	Suicide	2.5 mg/kg/dose	9.5	+	Torticollis, Oculogyric crisis
6	10 years	Female	Patient's mother	Encephalitis	URTI	?	8	+	Torticollis, Tongue Protrusion, Opisthotonus
7	9 years	29	Pediatrician	Encephalitis	URTI	0.51 mg/kg/day	48	-	Torticollis, Oculogyric crisis
8	7 years	Female	Pediatrician	Food Poisoning	AGE	0.71 mg/kg/day	48	-	Torticollis, Oculogyric crisis
9	8 years	24.5	Patient's mother	Intoxication	AGE	2.4 mg/kg/day	48	-	Torticollis, Tongue Protrusion
10	13.5 years	Female	Family physician	.*	AGE	1.2 mg/kg/day	48	-	Torticollis, Oculogyric crisis
11	6 years	20	Pediatrician	Drug Reaction	URTI	1.1 mg/kg/day	72	-	Torticollis, Oculogyric crisis

Abbreviations: AGE: Acute gastroenteritis, URTI: Upper respiratory tract infection, \*. Cases who consulted directly to emergency department

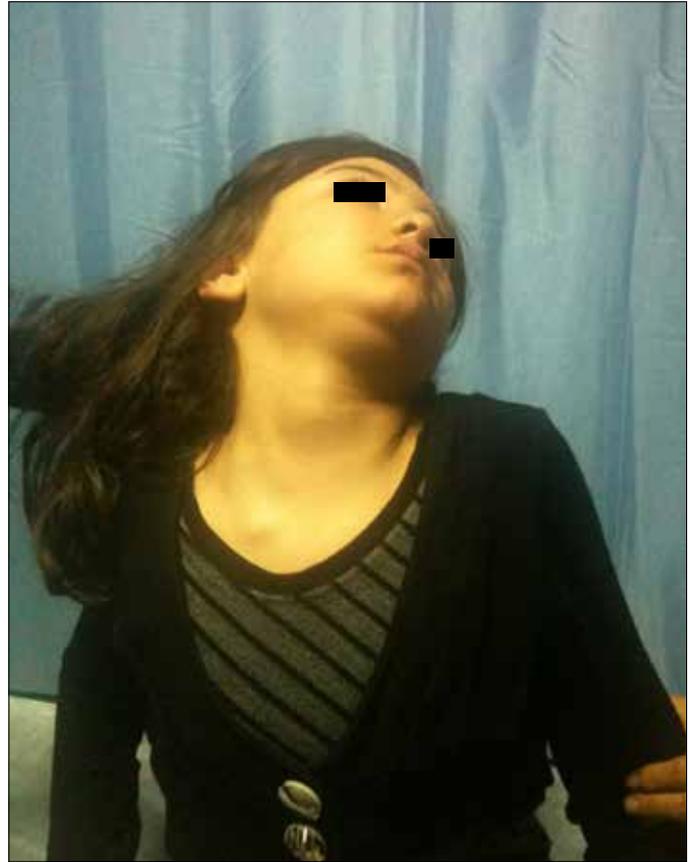


**Figure 1.** Case 1. The appearance of torticollis in neck

of an acute dystonic reaction. All cases fully responded to treatment within 30-90 minutes. All cases had normal results upon physical examination conducted 1 to 3 days later.

## Discussion

Metoclopramide is a drug used to prevent nausea by dopamine receptor antagonism in the chemoreceptor trigger zone. Its effects occur within 1-3 minutes when given intravenously and within 15-20 minutes when given orally. Its half-life is four hours (1). The advised dose of metoclopramide in children is 0.1-1 mg/kg/dose for the treatment of gastroesophageal reflux, 0.1-0.2 mg/kg/dose (intravenously at 6 and 8 hours) for postoperative vomiting and 1.2 mg/kg/dose (orally, intravenously at 2-4 hours) for vomiting due to chemotherapy (2). The adverse effects associated with the drug are idiosyncratic and do not depend on dosage; therefore, side effects may appear even at standard treatment doses. However, side effects are known to appear more frequently in overdoses and to have a cumulative effect with repeated dosing (3). Two cases in our study group took an overdose (2.4 and 2.5 mg/kg/dose), while most of the cases (six cases) took the medicine at the recommended dosage. Acute dystonic reactions have been observed in female patients more frequently than in male patients, which is also valid in our study (3, 4).



**Figure 2.** Case 10. Torticollis and oculogyric crisis in the neck

The state of a patient with involuntary movements was confused for encephalitis, tetanus, tetany and epileptic seizures when an acute dystonic reaction was ignored, which leads to diagnostic difficulties (4, 5). In parallel with the literature, several cases were referred to our clinic with pre-diagnoses of food poisoning, intoxication and drug reactions.

Metoclopramide has side effects, including irritability, dystonic reactions, hypokinesia, oculogyric crisis, vomiting and apnea. Tardive dyskinesia is a less-frequent side effect of metoclopramide observed in young children compared to dystonia and dyskinesia. High dosage and long-term usage are reported as risk factors for tardive dyskinesia (6). These cases had complaints in the neck, sight, position of the tongue and unsteady gait. Upon physical examination, dystonia findings of torticollis, oculogyric crisis, opisthotonus, tongue prostration and contraction in the arms and legs were observed. Tardive dyskinesia was not found in any cases.

While extrapyramidal reactions developed within the first 24 hours following medication in 63% of the cases (6), 36% of the cases (n=4) developed this reaction after 24 hours. Dystonia developed within the first 72 hours (1-3 days) in 94% of cases, and 90% of the cases developed dystonia within the first 72 hours. The literature also reports that dystonia may develop up to 14 days after taking medication (6). Similarly, one of our cases consulted to the clinic at a late time point (5 days).

Mixtures containing antihistamines and decongestants as well as expectorants and antipyretics containing codeine and dextromethorphan may cause acute dystonic reactions even if they are used at therapeutic dosages. In addition, epileptic children have been reported to develop dystonia following the use of phenytoin



**Figure 3.** The appearance of torticollis before (a) and after (b) treatment in Case 11



**Figure 4.** Torticollis and tongue protrusion in Case 9

and carbamazepine at treatment dosages (6-9). None of our cases took metoclopramide in combination with other drugs with known neurological side effects.

Diphenhydramine hydrochloride (1.25 mg/kg/dose, oral, intramuscular or intravascular, maximum 300 mg/day with 6 hour intervals), biperiden lactate (0.04 mg/kg, oral, intramuscular or intravascular, maximum four doses with 30 minute intervals) and benztropine mesylate (0.02-0.05 mg/kg/dose, oral, intramuscular or intravascular, maximum 2 mg/day and once or twice per day) were advised to be used in the treatment of medication-induced acute dystonia (6-10). All cases were treated with parenteral biperiden lactate. The symptoms in the cases began suddenly and accelerated rapidly; dystonia was found upon physical examination. The vital and laboratory findings of the cases were normal, the cases responded to biperiden rapidly and they were completely healthy in the pre-period. None of the cases had a history of metoclopramide usage. Therefore, these situations suggested no other reason than an acute dystonic reaction. Recovery after treatment and normal findings at the follow-up examination meant there was no need for advanced evaluation processes.

### Conclusion

Metoclopramide may cause dystonic reactions in children. When medication-induced dystonia is diagnosed, its treatment is straightforward. However, when pre-taken drugs are not examined and if dystonic movements are not recognized, difficulties in diagnosis can occur and findings may be incorrectly interpreted.

**Conflict of Interest / Çıkar Çatışması**

No conflict of interest was declared by the authors.  
*Yazarlar herhangi bir çıkar çatışması bildirmemişlerdir.*

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