Metoclopramide-induced acute oculogyric crisis treated with biperiden: A case report

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ABSTRACT

Metoclopramide is an antiemetic prescribed in general medical practice. The drug can cause acute dystonic reactions. Here, we described the case of a 23-year-old young woman with a chief complaint of blurred vision and later dystonic, oculogyric-type crisis. She underwent laboratory tests and neuroimaging then was hospitalized in the Neurological Department. Treatment with intravenous biperiden interrupted the oculogyric crisis. Only a thorough drug history and correct clinical examination can discover the use of metoclopramide-induced adverse drug reaction such as oculogyric crisis.

Keywords: *Acute dystonia, Extrapiramidal reaction, Metoclopramide, Neurology.*

Drugs with dopaminergic antagonistic properties are known for their ability to cause side effects of the extrapyramidal type. Drugs that may cause acute dystonic reactions are antiemetics, antimalarials, antipsychotics, antidepressants and antiepileptics [1]. Metoclopramide, a dopamine-2 receptor antagonist is one of the most commonly prescribed antiemetic drugs but has the propensity to cause several extrapyramidal movement disorders [2]. One of those extrapyramidal types of side effects caused by metoclopramide is oculogyric crisis which is a type of acute dystonia.

We report the case of a 23-year-old young woman with an oculogyric crisis caused due to the metoclopramide drug in order to draw the attention towards the frequent occurrence of metoclopramide-induced movement disorders so that the drug should be prescribed with caution by general practitioners.

CASE REPORT

A young woman of 23-year-old presented to the emergency room with complaints of blurred vision in both eyes and difficulty in closing her eyes for 2 days. The woman gave a history of fever and tonsillitis 3 days back for which she was examined by her family doctor and he prescribed antibiotic therapy (clarithromycin) and metoclopramide at a dose of 10 mg three times a day for the prevention of nausea and vomiting associated with the antibiotic. She had taken the above-mentioned drugs three times a day for 1 day. After 1 day, the patient started to develop blurred vision and difficulty in closing the eyes, for which she came to us.

On examination, the vitals were stable. The neurological evaluation showed that the patient was alert, cooperative, oriented in space and time, and can walk independently without pathological connotations. There was no cranial nerve palsy, sensory or cerebellar deficit. The tendon reflexes were normal and there were no signs of the suffering of the pyramidal and extrapyramidal tract. The patient was evaluated by an eye specialist and on local examination, the eyes were normal. Persistent conjugate upward and lateral deviation of the eyes (oculogyric crisis) and neck stiffness were observed (Fig. 1). The patient could bring her eyes back to the primary position with extreme effort, and the eyes resumed their eccentric position within seconds. The rest of her examination was unremarkable.

The patient was advised for computerized tomography (CT) scan of the brain and the findings were normal. The results of complete blood count, liver and kidney function test, and electrolytes were normal. Based on the above-mentioned history and clinical findings, a diagnosis of oculogyric crisis induced by metoclopramide was made.

The patient was admitted to the Neurology Department and the oculogyric crisis induced by metoclopramide was treated with slow intravenous infusion of 2 mg biperiden. The symptoms

Figure 1: Oculogyric crisis in the patient.

disappeared after about 30 minutes of the therapy without relapse. The patient remained under observation for 48 hours without further recurrences. Treatment with metoclopramide has been stopped and a follow-up visit 2 weeks later was unremarkable.

DISCUSSION

Acute dystonic type reactions are due to an impaired balance between dopaminergic activity and acetylcholinergic in nigrostriatal pathway. In particular, drugs that may cause acute dystonic reactions are antiemetics, antimalarials, antipsychotics, antidepressants and antiepileptics [1]. Drugs that block the dopamine D2 receptor would lead to a sudden increase in cholinergic tone in the striatum through a mechanism that can be independent of dose.

Metoclopramide, a benzamide dopamine-2 receptor antagonist, is one of the most commonly prescribed antiemetic drugs. The antiemetic properties of metoclopramide were attributable to its blocking action of the central and peripheral dopamine receptors. The most common type of extrapyramidal symptom associated with metoclopramide is acute dystonic reactions, that can occur with approximately 0.2% of patients (1 in 500) treated with 30 to 40 mg of metoclopramide per day [3]. The symptoms of acute dystonic reactions include involuntary limb movements, facial grimacing, torticollis, oculogyric crisis, rhythmic protrusion of the tongue, bulbar type of speech, trismus, opisthotonus, etc. [4]. Oculogyric crisis, a type of acute dystonic reaction is characterized by bilateral sustained upward elevation of visual gaze with hyperextension of the neck [5].

The risk of such reactions is increased between 10 and 29 years and a female preponderance is shown with 70% of the cases [6]. In an epidemiological study, Bateman et al showed 455 reports of acute dystonic adverse reactions, 318 (70%) of which were reported in women [7]. Tianyi FL reported the case of a 16-year-old female who had dystonic reactions from metoclopramide. The drug was discontinued and was administered with 8 mg oral chlorpheniramine [8]. In our case also, the patient was a female and of young age. Acute dystonic reactions due to the metoclopramide drug occurred within the first 24 hours in 63% of the patients and during the first 72 hours in 94% of the cases [7]. The most common differential diagnosis of acute dystonia is encephalitis, complex partial seizures, tetanus, strychnine poisoning and hypocalcemic tetany [2,9,10].

The most rapid treatment of an acute dystonic reaction caused by metoclopramide is the intravenous or intramuscular administration of anticholinergics or antihistaminic drugs such as 2mg iv biperiden, 50mg oral diphenhydramine, benztropine, and diazepam [4]. The choice of the route of the drug depends upon the severity of the case. Usually, the intravenous route is the route of choice and most reliable as it can resolve signs and symptoms within 10 min. The intramuscular route is an alternative of iv route but it takes minimum 30 minutes to be absorbed. The oral route is the most unreliable as it undergoes first-pass metabolism in the gastrointestinal tract with a bioavailability of as low as 25% and a mean peak time of up to 4 hours [11]. In the present case, iv biperiden drug was successfully used to treat the patient.

The biperiden drug is a weak peripheral anticholinergic agent that has the capacity of reducing the imbalance between dopamine and acetylcholine which would be the likely mechanism underlying dystonic reaction. The molecule is characterized by a marked central anticholinergic action, due to the interaction with muscarinic acetylcholine receptors of type M1. The prompt discontinuation of the drug and the administration in the emergency room of biperiden iv determines the disappearance of the symptoms within 30 minutes. A case report published by Karagoz G et al also used 2mg biperiden drug intravenously for the treatment of metoclopramide-induced acute dystonic reaction in a 25-year-old female [4].

Although acute dystonic reaction induced by metoclopramide is self-limiting and rarely causes permanent damage, the drug should be used with caution especially in young female patients. Also, a thorough drug history should be taken in individuals that are suspected with acute attacks of oculogyric crisis for rapid diagnostic assessment and appropriate treatment.

CONCLUSION

General practitioners widely prescribe metoclopramide for the treatment of gastrointestinal disorders such as nausea and vomiting. The dystonic-dyskinetic reaction occurs in most cases within 72 hours from the beginning of the treatment and especially in younger female subjects. The oculogyric crisis is successfully treated with intravenous biperiden. The correct diagnosis in the emergency room is very important as it may avoid hospitalization.

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