

Case Report

A case of metoclopramide-induced oculogyric crisis in a schizophrenic patient under anticholinergic therapy

Antikolinergik tedavi altındaki bir şizofreni hastasında metoklopramidle indüklenmiş bir okülojirik kriz vakası

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ABSTRACT

Introduction: Oculogyric crisis (OGC) is a dystonic reaction characterized as conjugate and typically upward deviation of the eyes lasting from seconds to hours which is seen as an uncommon neurologic manifestation. Metoclopramide is a prokinetic agent that is frequently prescribed in the treatment of nausea, vomiting prophylaxis, and vomiting. One of the side effects after metoclopramide treatment is acute dystonic reactions.

Case Presentation: We report a case of metoclopramide-induced OGC despite the anticholinergic treatment in patient diagnosed with schizophrenia.

Conclusions: Metoclopramide-induced OGC and other acute dystonic reactions may be more frequent than expected. Therefore, clinicians should monitor patients closely during treatment with metoclopramide and necessary precautions should be taken for these reactions.

Keywords: Metoclopramide, oculogyric crisis, side effect, schizophrenia

ÖZ

Giriş: Okülojirik kriz (OJK), gözlerin konjuge ve tipik olarak saniyelerden saatlere kadar süren yukarı doğru sapması olarak nitelendirilen ve nadir bir nörolojik tablo olarak görülen distonik bir reaksiyondur. Metoklopramid, bulantı, kusma profilaksisi ve kusma tedavisinde sıklıkla reçete edilen prokinetik bir ajandır. Metoklopramid tedavi sonrası oluşan yan etkilerden biri de akut distonik reaksiyonlardır.

Vaka Sunumu: Şizofreni tanılı bir hastaya uygulanan antikolinergik tedaviye rağmen metoklopramidin indüklediği OJK olgusunu sunuyoruz.

Sonuç: Metoklopramid kaynaklı OJK ve diğer akut distonik reaksiyonlar beklenenden daha sık olabilir. Bu nedenle klinisyenler metoklopramid tedavisi sırasında hastaları yakından izlemeli ve bu reaksiyonlar için gerekli önlemler alınmalıdır.

Anahtar Kelimeler: Metoklopramid, okülojirik kriz, yan etki, şizofreni

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Key Points

1. The risk of metoclopramide-induced acute dystonic reactions is higher than expected.
2. Metoclopramide induced OGC is not common among acute dystonic reactions.
3. Clinicians should be careful in terms of acute dystonic reactions of metoclopramide, especially in patients treated with antipsychotics.

Introduction

Oculogyric crisis (OGC) is a dystonic reaction characterized as conjugate and typically upward deviation of the eyes lasting from seconds to hours which is seen as an uncommon neurologic manifestation [1]. Clinical symptoms and subtle eye deviation as an isolated symptom vary from very short to more severe and even painful forms accompanied by jaw opening, neck flexion, tongue protrusion, blepharospasm, and autonomic signs, such as pupillary dilation, perspiration [2]. OGC is most commonly explained as an adverse reaction to drugs such as, phenothiazines, butyrophenones, tricyclic antidepressants, carbamazepine, phenytoin, lithium, metoclopramide, α -methyl dopa, ketamine, reserpine, trimethobenzamide, diazoxide, organophosphates, phencyclidine, chloroquine and antihistamines [3]. Metoclopramide is a common prescribed antiemetic and prokinetic that the mechanism of action is on selective dopamine 2 (D2) receptor antagonist with central and peripheral antidopaminergic effects [5]. The cause of acute dystonic reaction due to metoclopramide is thought to be this mechanism. The incidence of OGC which is secondary to metoclopramide use was reported as 0.2%. In this case, we report a metoclopramide-induced oculogyric crisis despite oral biperiden treatment.

Case Presentation

A 37-year-old female patient was brought to the emergency department by her relatives for suicidal thoughts. She had been treated for schizophrenia since 2004 and had nihilistic delusions that did not respond to treatment. The patient had used clozapine for 5 years and have been using it at a dose of 600 mg / day for last 6 months. During her hospitalization, she was treated with clozapine 600 mg / day, sertraline 100 mg / day, amisulpride 400 mg / day, lithium 600 mg / day, and biperiden 4 mg / day.

On the 12th day of follow-up, the patient was consulted to general surgery department for 4-5 days of constipation. Abdominal x-ray was evaluated, and the patient was diagnosed as ileus. Oral intake of the patient was stopped by general surgery and metoclopramide 10 mg was administered intravenously (IV). After 30 minutes of the second dose of IV metoclopramide, restricted upward gaze developed and the patient became unable to look laterally, no deficits were found in neurological examination. Other systemic examinations and vitals were normal. Also, complete blood count, electrolyte values, CRP, liver, and kidney function tests were normal. The patient was diagnosed with metoclopramide-induced OGC, and metoclopramide treatment was stopped. Anticholinergic treatment was not administered because of the current ileus clinic. Within 2 hours, the patient's oculogyric crisis was improved and there was no recurrence in follow-ups.

Discussion

In this article, a schizophrenia patient diagnosed with OGC after IV metoclopramide treatment was assessed. The most important difference of this case from similar case reports is that the patient had been cured with biperiden which was a drug used for treatment of OGC when OGC occurred.

The risk factors of this case for OGC were treatment with lithium, amisulpride and metoclopramide. OGC is usually related to the dose increasing of typical antipsychotics. It is not commonly reported with atypical antipsychotics. A prospective study in psychosis patients with long-term use of atypical antipsychotic reported the incidence of OGC as 1.8%. The cases reported with atypical antipsychotics are mostly with olanzapine and risperidone, and there are rare case reports with amisulpride [7]. Mendhekar et al. reported a case of OGC developing after 400 mg / day amisulpride for 10 days and clinical improvement was observed after the amisulpride dose was reduced [8].

A small number of research suggested the relationship between lithium treatment and acute dystonic reaction. According to one case, OGC occurred while using lithium 900 mg / day. 5 days after discontinuation of lithium, the manifestation completely resolved [9].

Apart from drugs known to be risky for OGC, O'Neill et al considered that even Sertraline has a potential for laryngeal dystonia when it is used with antipsychotics [10]. Moreover, Hood et al observed a severe case of laryngeal dystonia while the patient had been receiving zuclopenthixol and sertraline. They evaluate that this interaction takes place through cytochrome P450 2D6/3A4 [11]. There are case reports of OGC's that are clozapine-induced and due to clozapine discontinuation [12, 13].

Among the drugs of the patient, IV metoclopramide added during ileus treatment was the riskiest medication for acute dystonia. Metoclopramide is a prokinetic agent that is frequently prescribed in the treatment of nausea, vomiting prophylaxis and vomiting. The most currently reported adverse effects associated with metoclopramide are diarrhea, sedation, and extrapyramidal symptoms [14]. One of the side effects after metoclopramide treatment is acute dystonic reactions. It is contemplated that acute dystonic reaction after metoclopramide is independent of dose and may occur even in therapeutic doses [5].

The risk of metoclopramide-induced acute dystonic reaction increases in female and under 30 years of age [15]. Although the duration of occurrence of side effect varies, it is usually seen in the first 24-48 hours of use. Side effects can be observed even half an hour after the administration of metoclopramide [16].

According to a case report (Koban et al.), OGC occurred in 30 minutes after the administration of 0.5 mg / kg IV metoclopramide, and these symptoms completely resolved after 1 mg / kg diphenhydramine treatment. There is also a case report in which OGC findings completely disappeared within a period of ten minutes after the administration of 5 mg intramuscular biperiden [17, 18]. Arumugam et al. cured the patient with diphenhydramine and the patient recovered completely in 12 hours [15].

Limitations

All of the drugs that this patient has been using for a long time, except biperiden, may induce an OGC. However, while this case had been using clozapine, sertraline, lithium, amisulpride and biperiden together for a long time, OGC appeared after adding metoclopramide to the treatment. This suggests that metoclopramide may primarily induce an OGC. However, drug-drug interaction, worsening of the patient's medical condition due to ileus, may have facilitated metoclopramide-induced OGC.

Conclusion

The mainstay of treatment in drug-induced OGC is anticholinergic medications. Parenteral anticholinergics or diphenhydramine are rapidly-effecting agents which are frequently used in treatment of dystonia. Benzodiazepines, including clonazepam and diazepam, may also be useful in OGC caused by neuroleptics [6, 15, 19].

In this case, OGC occurred after the addition of metoclopramide to the treatment, and the findings of examination and laboratory results that may cause OGC were normal. Although no additional treatment was applied, the symptoms of OGC was improved after discontinuation of metoclopramide treatment.

Metoclopramide-induced OGC and other acute dystonic reactions may be more frequent than expected. Therefore, clinicians should monitor patients closely during treatment with metoclopramide and necessary precautions should be taken for these reactions.

Patient's consent: Yes

Conflict of interest: The authors declare that they have no conflict of interest.

Author Contributions	Author Initials
Study Conception and Design (SCD)	HE, BAG
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