

Acute dystonic reaction induced by a single dose of clebopride

A case report

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Abstract

Rationale: Clebopride is known as a dopamine antagonist used for alleviating emetic symptoms with minimal side effects. Herein, we report a case of acute dystonic reaction possibly caused by administration of clebopride in a young male.

Patient concerns: A 19-year-old with no special medical conditions, visited a local clinic complaining of abdominal discomfort, associated with nausea and vomiting. The patient was prescribed with tiropramide, clebopride, simethicone, and mosapride citrate, only to visit the emergency department for abrupt neck pain followed with dystonic reactions upon oral administration of the drugs. The patient suffered involuntary movements of the neck to the right, while maintaining voluntary motor controls of the neck to the left.

Diagnosis: Vital signs and neurological exams showed no abnormality and the preliminary blood workup (a complete blood count and measurement of electrolytes, inflammatory marker levels, copper concentration, etc) were all within normal ranges. Additional imagery tests including brain computed tomography (CT), neck contrast-enhanced CT, and magnetic resonance imaging failed to prove any focal lesion pertinent to the condition. Drug screening was done and then clebopride was suspected to be the cause of the dystonic reactions.

Interventions: Benztropine (1 mg) was administered orally.

Outcomes: The patient's symptoms improved after 1 hour, and he was observed for 6 more hours for possible recurrences before he was discharged. The patient was referred to an outpatient neurology department for 1 month, during which he had no recurrence or other extrapyramidal symptoms.

Lessons: Although it is uncommon to experience extrapyramidal symptoms by clebopride, its chemical closeness to metoclopramide may induce such symptoms under certain clinical situations. Therefore, physicians should take in consideration of this effect and dwell in caution upon prescribing the drug.

Abbreviation: Etc = et cetera.

Keywords: acute dystonic reaction, antiemetic, clebopride, dopamine antagonist

1. Introduction

Dopamine is a catecholamine that acts on the central and peripheral nervous systems and is involved in hormone synthesis and secretion and blood pressure control.^[1] This important drug is used to treat diseases such as Parkinson's disease and schizophrenia.^[2] Dopamine D2 receptor antagonists, such as metoclopramide, domperidone, clebopride, levosulpiride, and

bromopride, act on the gastrointestinal tract and are commonly used as antiemetic agents.^[3] Many of these drugs are known to be relatively safe. However, in rare instances, similar chemical compositions can cause side effects, such as extrapyramidal symptoms. Here, we report the case of a young male with acute dystonic reaction following only a single oral dose of clebopride and provide a supporting video.

2. Case presentation

A 19-year-old male with no special medical or family history visited the local medical center due to abdominal discomfort, nausea, and vomiting. He was prescribed tiropramide 100mg, clebopride 0.68mg, ranitidine 150mg, bismuth 100mg, and mosapride 5mg for the conservative treatment of gastroenteritis symptoms. He took 1 dose of the prescribed medication orally and visited the emergency medical center within 1 hour presenting with cervical pain and involuntary cervical rotation to the right. The patient was constantly complaining about his neck turning to the right. Although he was able to turn his neck to the neutral position and the left, the cervical pain was exacerbated during rotation (Video 1, <http://links.lww.com/MD/D19>).

The patient showed no abnormal vital signs or other neurologic deficits. There were also no abnormal findings in any of the tests conducted that included a complete blood count

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and measurement of electrolytes, inflammatory marker levels, copper concentration, and so on to detect electrolyte imbalances and infection and brain (nonenhanced) and neck (contrast-enhanced) computed tomography to detect radiologic abnormalities of the head and neck.

An oral dose of 1 mg benztropine was administered based on the diagnosis of acute cervical dystonic reaction induced by clebopride. After 1 hour of taking benztropine, the symptoms improved and did not recur during 6 hours of observation. The patient was discharged without additional medicines from the emergency department after being told to stop taking the suspected drugs and chose to make follow-up visits to the neurology outpatient department. The patient was followed up for 1 month, during which he experienced no recurrence or any other extrapyramidal symptoms. Brain magnetic resonance imaging showed no specific findings aside from multiple, small, non-specific T2 hyperintensities in the subcortical white matter of both cerebral hemispheres.

3. Discussion

All D2 receptor antagonists, including domperidone, that cannot easily pass the blood–brain-barrier can cause extrapyramidal reactions.^[3] Clebopride is a nonselective benzamide that has high affinity for the Dopamine D2, D3, and D4 receptors and also acts on the dopaminergic receptors of the gastrointestinal tract.^[4,5] Clebopride is 10 times more potent than metoclopramide^[6,7] and is associated with reversible Parkinsonian-like symptoms (involuntary movements of the tongue and mouth, blepharospasm, trismus, torticollis, resting tremors, rigidity, and bradykinesia in both the arms and legs) and potentially irreversible tardive dyskinesia.^[3] In acute drug-induced movement disorders, the neck and craniofacial area are most commonly affected and the onset of occurrence is within 48 hours for 50% of patients and within 5 days for 90% of patients.^[8,9] Other case reports have also shown that acute drug reactions are common in younger people, presumably due to the immature blood–brain-barrier,^[10–12] while other risk factors include a higher potency and dose of the drug and psychiatric illness.^[12]

Although previous cases of clebopride-induced extrapyramidal symptoms were co-administered with a number of different drugs, clebopride has been considered as the major offending drug eliciting adverse neurologic effects due to its pharmacodynamic peculiarity. The co-associated drugs were mainly second generation antihistamines, antispasmodic agents which would make it highly unlikely for these drugs to exert such extrapyramidal effects other than the dopamine antagonist, clobepride. In align with the previous cases, the drugs, in our case, among tiropamide (antispasmodic agent), ranitidine (antihistamine), bismuth (antidiarrheal agent), and mosapride (5-hydroxytryptamine receptor agonist), clebopride is likely the responsible drug for the dystonic symptoms based on the pharmacological mechanisms.

In regards to the treatment, most of the reported cases had shown improvements with benzodiazepines or anticholinergics. The onset of the symptoms varied from 2 to 14 days after clebopride.^[10,11] Patients suffering from cervical dystonia improved after 7 days of clonazepam (0.25 mg, twice a day), eperisone (50 mg, twice a day), and benztropine (1 mg, twice a day).^[11] Other cases showed oculogyric crisis where the symptom was relieved after intravenous injection of lorazepam (2 mg).^[10]

In similar nature, the patient in our case was well responsive to 1 mg of oral benztropine.

Although acute drug-induced movement disorders are rare, life-threatening laryngeal dystonia and respiratory dyskinesia have been reported,^[9] and this case report shows that these symptoms can occur following just 1 dose of clebopride. Therefore, physicians need to be careful when administering Dopamine D2 receptor antagonists and should advise patients to immediately stop taking any suspected medications if symptoms occur. Furthermore, the use of anticholinergics (such as benztropine), diphenhydramine, and benzodiazepine should be considered as well as the prophylactic use of antipsychotics over the long term.^[9,13,14]

4. Consent for publication

Informed written consent was obtained from the patient for publication of this case report and accompanying images.

Author contributions

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