

CASE REPORT

Domperidone-induced dystonia: a rare and troublesome complication

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SUMMARY

Domperidone is a commonly prescribed antiemetic drug but its side effects are rarely seen. Extrapyramidal side effects are a very rare complication of the drug occurring in 1/10 000 population. They usually occur in infants and very young children due to a poorly developed blood–brain barrier. We report a case of acute dystonia in a 13-year-old boy induced by domperidone. The boy was treated for viral fever and was started on domperidone 30 mg/day, sustained release form (0.7 mg/kg/day), for persistent vomiting along with other supportive treatment. On the fourth day of treatment, although the fever and vomiting subsided, the child developed oromandibular dystonia despite giving the drug in the recommended dose. Fortunately, drug-induced dystonias are a reversible condition and the child improved in 7–8 days after discontinuation of the drug. There was no recurrence at 1 month follow-up. Usually, dystonic reactions do not threaten life but are troublesome and life altering, so judicious use of the drug is advised.

BACKGROUND

Domperidone is a commonly prescribed antiemetic drug. Its extrapyramidal side effects are rare since it does not cross the blood–brain barrier under normal circumstances.¹ It is a dopamine receptor antagonist and is usually prescribed in a dose of 30 mg/day but a maximum of 80 mg/day can be given. The recommended dose for children is 0.25–0.5 mg/kg, three to four times per day, maximum dose being 2.4 mg/kg/day.² Various drug interactions leading to increase or decrease in blood levels of the drug have been reported. Important drugs listed in this category are the azole group of antifungals, a few antimalarials, fluoroquinolones, macrolides, salbutamol, valproic acid, carbamazepine, anticholinergics, monoamine inhibitors, tricyclic antidepressants, selective serotonin reuptake inhibitors, etc.³

Domperidone is a commonly prescribed drug in day-to-day clinical practice. Rare side effects (1 in 1000) as described are loss of libido, gynaecomastia in men and amenorrhoea in women. Very rare side effects (1 in 10 000) are anaphylaxis, extrapyramidal symptoms, agitation, nervousness, convulsions, sleepiness, headache, urinary retention, life-threatening ventricular arrhythmia and sudden cardiac death.²

Acute dystonias, parkinsonism, akathisis and tardive dyskinesias are various extrapyramidal symptoms and are usually side effects of dopamine antagonist antipsychotic drugs.⁴ The most common

drug in this category is haloperidol.⁵ These movement disorders are also caused by selective serotonin receptor inhibitors,⁶ antidepressants such as amitriptyline, amoxapine, sedatives such as midazolam, antiemetic drugs such as metoclopramide, prochlorperazine, anticonvulsants such as carbamazepine or phenytoin and other drugs such as lithium, promethazine and calcium channel blockers such as verapamil.⁷ Other secondary causes of extrapyramidal symptoms are encephalitis, meningitis,⁸ Parkinson's disease⁹ and Wilson's disease or head trauma. This is manifested as involuntary contraction of various muscles resulting in abnormal postures or slow repetitive movements.¹⁰ They are classified depending on the area of involvement or as syndromes based on their patterns. Oromandibular dystonia is a focal dystonia that causes involuntary spasm of the jaw, lips and tongue muscles. It can also affect speech and swallowing. There can be difficulty in chewing.^{7 11} This can also mimic temporomandibular joint disorder.¹² The boy in our presentation developed acute dystonia, a very rare neurological complication of this drug despite giving the drug in the recommended dose. Coadministered antibiotic cefixime (100 mg twice daily) is not reported to cause any interaction with domperidone.

CASE PRESENTATION

A 13-year-old boy, weighing 42 kg, from Raipur, Chhattisgarh (India) presented in the medicine outpatient department with fever and chills, headache, bodyache and persistent vomiting for 2 days. There was no significant history, drug history or family history of any neurological disease. He was conscious, oriented and febrile (39.4°C), pulse was 104/min, regular and BP was 100/70 mm Hg. There was no pallor, icterus, cyanosis, clubbing, pedal oedema or lymphadenopathy. His cardiovascular, respiratory, per abdomen and genitourinary system did not display any abnormality. Central nervous system examination was normal. On further evaluation, his haemoglobin was found to be 11 g, TLC 10 200, DLC P40%, L55%, M3% and E2% with normal platelet counts. Other tests such as liver function test, kidney function test, random blood sugar and urine analysis were normal. His blood culture was sterile and malarial antigen test was negative. On the basis of lymphocytosis and his clinical presentation, diagnosis of viral fever was made and he was treated symptomatically with paracetamol and domperidone 30 mg/day, sustained release form (0.7 mg/kg/day) before food. An antibiotic of the cephalosporin group



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(cefixime) 100 mg twice daily was also started. On the fourth day of starting this treatment his fever subsided and vomiting stopped; however, his parents noticed that the child's speech was slurred and he was making strange movements of his lips and tongue. He had neither difficulty in swallowing nor any respiratory distress. Neurologist opinion was sought and after detailed neurological examination diagnosis of acute dystonia, probably domperidone induced, was made. There was no history of head trauma or similar history, nor any family history of such illness. There was no history of intake of domperidone in the past. There were no tremors at rest to suggest parkinsonism and no clinical features in favour of Wilson's disease. Signs of meningeal irritation were absent. His complete blood count, liver function tests, kidney function test and urine tests were repeated, and were normal. His cerebrospinal fluid analysis and MRI with contrast were performed to rule out meningitis and encephalitis, and were normal. This further strengthened the diagnosis of drug-induced extrapyramidal symptoms. He was advised to discontinue the culprit drug immediately and promethazine 25 mg, three times a day for 5 days was prescribed. With that, in 7–8 days his speech became normal with disappearance of abnormal movements of lips and tongue and there was no recurrence in 1 month follow-up.

OUTCOME AND FOLLOW-UP

The child improved in 7–8 days with discontinuation of domperidone. There was no recurrence at 1 month follow-up.

DISCUSSION

Domperidone is a commonly prescribed antiemetic drug with rare side effects. However, its judicious use has been advised by Health Canada in March 2012 due to its possible lethal side effects such as sudden cardiac death and serious arrhythmias especially when prescribed in doses greater than 30 mg/day to individuals over 60 years old.^{13–15} Extrapyramidal side effects such as dystonias, parkinsonism, akathisia and tardive dyskinesia which are side effects of dopamine antagonists, usually antipsychotic drugs, are very rare side effects of domperidone and are either seen in infants and very young children due to poorly developed blood–brain barrier or in older individuals with dementia. We report a case of domperidone-induced oromandibular dystonia, a type of focal dystonia in a 13-year-old child. This child improved after discontinuation of the culprit drug. On literature search, we found few case reports of domperidone-induced extrapyramidal symptoms especially dystonias^{16–17} and tardive dyskinesia.¹⁸ The diagnosis of drug-induced dystonia is usually clinical and is made on the basis of history of intake of a drug known to cause this extrapyramidal symptom. So awareness of even rare side effects of a drug is important to make this diagnosis. Proper physical examination with good medical history especially of a drug or drugs taken by the patient in the near past and any history of similar side effects to drugs is essential. A negative family history of similar symptoms is also helpful to exclude primary dystonia. To establish the causal relationship between domperidone and dystonia we applied the Naranjo algorithm and a score of five indicated a 'probable' relationship in our case. With WHO Uppsala Monitoring Centre criteria, this adverse reaction had 'certain' relationship with domperidone administration. The temporal relationship between administration of domperidone and onset of dystonia and its disappearance with discontinuation of the drug suggested this relationship. We did not try rechallenge with domperidone due to the troublesome nature of this reaction. Fortunately, drug-induced acute dystonias are usually

reversible.¹⁹ Their treatment is mostly simple and very effective. Parenteral administration of anticholinergics such as beztropine or diphenhydramine is reported to reverse drug-induced dystonias promptly. Antihistamines having anticholinergic action are also, such as promethazine, helpful; they inhibit the neurotransmitter acetylcholine level in the brain. In some cases benzodiazepines are found to be useful. Usually, anticholinergic drugs are continued for a week to prevent recurrence.^{20–21} Injecting botulinum toxin in affected muscles to relieve spasm, pallidotomy or deep brain stimulation are other modalities of treatment in refractory dystonias.¹¹ The child in our presentation improved after discontinuation of domperidone and was prescribed promethazine 25 mg three times a day for 5 days. Drug-induced dystonia usually quickly improves with medication and this child recovered gradually in 7–8 days. There was no recurrence at 1 month follow-up. Sustained release form possibly prolonged the action of domperidone. Although dystonias are not usually life threatening,¹⁹ they are life altering and troublesome for patients and family members, so judicious use of the drug is advised.

Learning points

- ▶ Domperidone is one of the most commonly prescribed drugs. Its complications are rare and extrapyramidal symptoms such as dystonias are very rare but troublesome complications.
- ▶ Lowest effective dose of the drug should be used and sustained release preparation should be avoided in children and elderly individuals in view of possible extrapyramidal symptoms.
- ▶ Drug-induced dystonias are usually reversible; although not life threatening, unlike serious cardiovascular complications of the drug, they are life altering and disturbing to patients and their family members, so judicious use of the drug is required.
- ▶ Awareness of the potential for certain drugs to cause dystonic reactions is important in making diagnosis of this movement disorder.

Competing interests None.

Patient consent Obtained.

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