Acute Hemifacial Dystonia Possibly Induced by Clebopride

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Abstract: Dystonic reactions produce twisting and repetitive movements or abnormal posturing. Severe dystonic reactions have been shown to occur in concert with numerous medications. This report details the case of a patient who developed hemifacial dystonia as acute side reaction from administration of clebopride for dyspeptic prophylaxis. When the drug was immediately stopped, the dystonic posture disappeared completely within 2 weeks. The use of clebopride may be associated with not only a reversible or persistent parkinsonism syndrome but also hemifacial dystonia; therefore, attention must be drawn to this possible side effect.

Key Words: clebopride, acute dystonia, parkinsonism syndrome

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Dystonias are considered an extrapyramidal effect that is most typically thought to arise from decreased dopamine (DA) activity in the basal ganglia.[1] There are primary forms with unknown etiology and secondary forms, including those related to several drugs.[2] Benzamide derivatives are antidopaminergic gastrointestinal prokinetic drugs that enhance gastric motility and are exploited clinically for the management of dyspetic syndrome. The prokinetic effect is mediated through the blockade of enteric inhibitory DA-D_2 receptors, which are likely to interact with other receptors (serotoninergic and α-adrenegic).[3] The antagonism of central D_2 receptors may cause both therapeutic (prokinetic activity) and adverse (including extrapyramidal reactions) effects.[4]

We present an old woman who showed right orofacial dystonia possibly related to clebopride use. Severity of dystonia was rated using the Oromandibolar Dystonia Rating Scale (ODRS) and Disability Scale (DS).[5]

CASE REPORT

An 83-year-old woman, without a family history of movement disorders, assumed for self-medication of clebopride at a dosage of 1.5 mg/d (mean dosage) for constipation. Four hours later, she developed abnormal hemifacial posture without any disturbances of consciousness, involving the masticatory and tongue muscles causing difficulties in speech and mastication. The neurological examination performed at the third day of therapy showed a dystonic posture of the face, with torsion and mouth deviation. Severity of dystonia rated using ODRS is 28 (0 = normal and 43 = maximum), whereas using DS, it is 3 (0 = normal and 4 = maximum). A cranial and neck magnetic resonance imaging and electroencephalography showed no abnormalities. Electrocardiography resulted in a slight prolongation of QT interval. She did not take any other drug. The dosage of clebopride was immediately reduced to 0.5 mg/d, but on follow-up after 3 weeks, it was found that there was no improvement of the dystonic effect. Only when the drug was completely discontinued that the abnormal posture disappeared within a few days (approximately 2 days).

DISCUSSION

Clebopride is relatively a nonselective benzamide, behaving as an antagonist on 5-HT_2 receptor and on the α_2-adrenergic receptor with lower affinity, as well as having high affinity for not only D_2, but also D_3 and D_4 sites.[3] Indeed, clebopride interaction with DA-D_2 receptors is viewed as a clinical liability, causing increased prolactin release[6] and extrapyramidal effects.[4] The plasma half-life is 2.1 to 2.7 hours for clebopride and 5 to 6 hours for its major metabolite, *N*-desbenzyl-clebopride.[7] The pathogenesis may involve dysfunction of the basal ganglia, although the exact mechanism remains to be elucidated. It has been suggested that serotoninergic neurons may contribute functionally to the inhibition of DA and noradrenaline systems in the control of motor behavior.[1] In fact, the role of 5-HT_3 and 5-HT_4 receptors in the modulation of DA and acetycoline[8,9] release has been suggested; moreover, a role of both 5-HT receptors subtypes in locomotor activity has been observed in young mice sensitive to audiogenic seizures.[10] This is also consistent with the localization of 5-HT receptors in the nigrostriatal system of laboratory animals and the human brain.[11] We propose, as for other types of benzamides, that this mechanism can also be applicable to clebopride, and it could be correlated both with DA receptors blockade and also with agonist activity on 5-HT receptors subtypes (5-HT_3 and 5-HT_4).[3] We have reported a case describing a woman who developed acute hemifacial dystonia, possibly related to overmedication of clebopride. Other articles have reported extrapyramidal disease after short- and long-term treatment[4] with clebopride; nevertheless, hemifacial dystonia is an unusual side effect especially after acute administration. Lopez Rois[12] has described acute extrapyramidal reactions after administration of clebopride only in children. After discontinuation of the drug, the patient did not show any abnormal posture, and the motor development was completely normal. On the contrary, we observed no significant improvement with a reduction of clebopride dose (0.5 mg/d; ODRS at baseline = 23; ODRS after 3 weeks = 22; DS at baseline = 3; DS after 3 weeks = 3); this suggests a supersensitivity of the nigrostriatal system, rather than a dose-dependent effect. Hemifacial acute dystonia should be added to the spectrum of movement disorders possibly seen in patients receiving clebopride, such as tardive dyskinesia and parkinsonism.

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