Nomifensine-induced dyskinesia

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Nomifensine maleate, a tetrahydroisoquinoline derivative, has recently been introduced as an antidepressant in Canada. In clinical trials it has been shown to be as effective as amitriptyline hydrochloride.[1] Side effects are infrequent, and in two trials involving almost 1400 patients dyskinesia associated with nomifensine was not reported.[2,3]

Case report

An 81-year-old man was evaluated for depression associated with dementia of unknown cause for about 1 year. He had a history of bipolar affective disorder, for which he had been treated fairly effectively with lithium carbonate for 21 years. He was taking 600 mg of the drug per day but, despite adequate serum lithium levels, began to complain of lack of energy, apathy and depression. He had never been given neuroleptics or other dopamine agonists or antagonists.

After therapy with nomifensine, 50 mg three times a day, was started, the patient's mood stabilized and his energy increased without signs of hypomania. By the 24th day of treatment mild rhythmic buccolabial movements appeared, and on the 31st day buccolabial and lingual dyskinesia were obvious. Therapy with nomifensine was stopped, and the dyskinesia gradually disappeared over the next 4 weeks, while the depression returned. Therapy with methylphenidate hydrochloride, 20 mg/d, was begun to treat the primary symptom of fatigue. One week later, buccolabial dyskinesia was again observed.

Owing to failure of response to methylphenidate the patient was admitted to hospital. Nomifensine was again given, with subsequent symptomatic improvement and reappearance of dyskinesia.

Comments

"Second-generation" antidepressants, including nomifensine, are increasingly being prescribed. Nomifensine's advantages include lower anticholinergic and antihistaminic potency, more specificity in target receptor activity, less cardiotoxicity and low lethality in overdoses.[4,5] It is thus well suited to the elderly, who tend to be more sensitive to anticholinergic, antihistaminic and cardiotoxic effects of drugs. It is also recommended in retarded depression, especially in the elderly, as it has an amphetamine-like effect.[4]

Nomifensine strongly inhibits the uptake of both norepinephrine and dopamine in rat brain synaptosomes.[4] In theory, dyskinesia associated with long-term use of neuroleptic medications is due to functional postsynaptic denervation that results in elaboration of dopamine receptors in the mesolimbic and nigrostriatal regions. When the blockade is removed, the increase in the number and size of dopaminergic receptors leads to postsynaptic hyperactivity, since the receptors are sensitive to even small amounts of dopaminergic stimulation.[6-8]

It is surprising that there have been no reports of dyskinesia associated with nomifensine. Perhaps my patient was a "susceptible host": his early dementia represented a process that had caused loss of dopaminergic neurons, with subsequent elaboration of postsynaptic dopaminergic receptors. This hypothesis is further borne out by the fact that methylphenidate, a strong dopaminergic agonist, produced buccolabial dyskinesia in the patient.

Although dyskinesia may prove to be a rare side effect of nomifensine, patients with early organic dementia who receive the drug may be at higher risk for the development of dyskinesia.

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