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Brief Report

Can Trazodone Induce Parkinsonism?

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Trazodone, a triazolopyridine compound chemically unrelated to tricyclic or tetracyclic antidepressants, which is widely used in Italy for its combined antidepressant and tranquilizing properties, is believed to elicit few CNS adverse reactions (1). Among these, sedation is the symptom most frequently encountered (2). We have observed the case of a woman who developed reversible parkinsonism shortly after starting trazodone hydrochloride, and recovered completely from extrapyramidal symptoms within 1 year after discontinuance of the drug.

A 74-year-old white woman first reported in July 1984 to the outpatient clinic for extrapyramidal disorders. Her personal medical history revealed only chronic asthma. Neurological history was uneventful until October 1983, when she lost a sister with whom she lived. She developed a reactive depression and in November 1983 she started trazodone hydrochloride 150 mg b.i.d. This was the only drug therapy she had taken for the previous 5 years. It was effective in gradually improving mood. However, around January 1984, parkinsonian symptoms became apparent: The patient first noted the onset of resting tremor of the left forearm, then slowing of movements and masked face, and, finally, slowing of gait and mentation.

Upon examination, the patient displayed a typical parkinsonian picture, with prevalence of symptoms on the left side. A masked face was evident. Bradykinesia involved all movements of limbs and trunk. Resting tremor was present on the left side, especially in the forearm. Mild bilateral muscular rigidity was detected; the cogwheel sign was present at the left wrist and elbow. No cranial nerve abnormalities were present; sensation and deep tendon reflexes were normal; Babinski signs were absent. Standard electroencephalogram and routine blood and urinary examinations were normal. Trazodone hydrochloride was withdrawn.

Neurological examination performed 2 months after discontinuance of trazo-

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done revealed that akinesia and rigidity were markedly improved; the cogwheel sign was undetectable, tremor was only evident at the left arm, and gait was still impaired. The tremor disappeared 6 months later, and gait and muscle tone were rated normal after 10 months. Fourteen months after discontinuance of trazodone, no extrapyramidal signs were detected.

The present case is, to our knowledge, the first report that trazodone can induce parkinsonian symptomatology. This is supported by the following data: (a) The patient did not take any other therapy whatsoever, (b) a definite temporal relationship existed between administration of trazodone and the onset of symptomatology, and (c) the presence of idiopathic Parkinson's disease was ruled out by follow-up.

Chemically induced parkinsonism is a well-known and still poorly explored field. In addition to neuroleptic drugs and pethidine derivatives (3,4), other chemicals have been reported in recent years to cause parkinsonism: they include flunarizine and cinnarizine (5,6), metoclopramide (7), and phenytoin (8). It is currently believed that such extrapyramidal symptomatology may develop in the elderly and in genetically predisposed individuals as a side effect of several different classes of drugs (9); trazodone hydrochloride also appears to be a candidate for such adverse reactions. Since drugs capable of producing parkinsonism belong to different classes, it is generally difficult to draw clear relationships between chemical formulae and clinical symptomatology. However, it is interesting to note that trazodone shares two important features with calcium entry blockers (e.g., flunarizine and cinnarizine), such as the presence of a propylpiperazine sequence in the chemical structure, and a selective antiserotoninergic activity. In addition, trazodone has no known monoamine oxidase inhibiting or dopaminergic activity.

Interestingly, a 65-year-old woman who displayed choreic and myoclonic symptoms after receiving relatively high doses of trazodone (600 mg/day) has been reported recently (10). This patient was also being treated with lithium salts, and recovered from extrapyramidal symptoms after trazodone was reduced to 400 mg/day. Taking together this and our observations, it can be assumed that trazodone is a suspected candidate for extrapyramidal adverse reactions, including parkinsonism. The infrequent occurrence of the reported extrapyramidal reactions is probably related to the recent introduction of this drug in the English language pharmacopoeia.

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