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Brief Report

Sulpiride-Induced Tardive Dystonia

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Summary: Sulpiride is a selective D2-receptor antagonist with antipsychotic and antidepressant properties. Although initially thought to be free of extrapyramidal side effects, sulpiride-induced tardive dyskinesia and parkinsonism have been reported occasionally. We studied a 37-year-old man who developed persistent segmental dystonia within 2 months after starting sulpiride therapy. We could not find any previous reports of sulpiride-induced tardive dystonia. **Key Words:** Sulpiride—Tardive dystonia—Parkinsonism.

Sulpiride is a selective dopamine D2-receptor antagonist used in the treatment of psychosis, depression, and Huntington's disease (1–3). The drug was initially thought not to cause extrapyramidal side effects, and it was indeed reported to suppress tardive dyskinesia (3,4). Sulpiride, however, has been associated with parkinsonism and, more recently, has been implicated as a possible cause of tardive dyskinesia (3,5). Tardive dystonia, a clinical variant of tardive dyskinesia, has not been described following the use of sulpiride.

CASE REPORT

A 37-year-old man from Mexico City first noted stress-related anxiety, depression, and panic attacks early in 1986. In November 1987, he was prescribed sulpiride, 50 mg, 3 times a day. After 2 months of sulpiride therapy, he developed laterocollis to the left. Except for life-long nocturnal bruxism, he had not previously experienced any movement disorder, nor was there a family history of movement disorders.

Diagnosed as having "spasmodic torticollis," the patient was treated unsuccessfully with a variety of medications including: trihexyphenidyl, haloperidol, levodopa/carbidopa, amitriptyline, isocarboxazid, triazolam, lorazepam, diazepam/acetaminophen, doxepin, flunitrazepam, phenytoin, nortriptyline, and a barbiturate. Despite these drug trials, administered over a 3-month period, his cervical dystonia progressed into retrocollis and torticollis to the left. He also developed right shoulder elevation, trunk rotation, and dystonic posturing of the upper extremities that precluded handwriting. Prior to our initial evaluation, he was treated with botulinum toxin injections into his right neck musculature without any improvement. In July 1988, he sought the advice of an acupuncturist and was treated with three different mixtures containing arsenic, an extract of the tarantula spider, and another made from a sample of the patient's blood, urine, and saliva. He reported some improvement for approximately 2 weeks after this treatment. The patient also took sulfasalazine and sulfapyridine for ulcerative colitis and psyllium hydrophilic mucilloid as needed.

When seen at the Baylor College of Medicine Movement Disorder Clinic in October 1988, the patient was disabled by dystonic movements that included constant bruxism, right shoulder elevation, and pulling of the left shoulder forward. When walking, his right arm extended behind his back, his left arm stretched forward, and he had dystonic posturing of his fingers (video segment). He had marked torticollis and laterocollis to the left as well as retrocollis. There was marked contraction and hypertrophy of the right sternocleidomastoid, right splenius capitis, and left trapezius muscles.

Wilson's disease and other forms of secondary dystonia were excluded by appropriate tests. Sulpiride was stopped and tetrabenazine was started. He obtained moderate benefit, which has persisted and was confirmed at the last follow-up examination 3 months later. Additional improvement was noted after botulinum toxin injections into his cervical muscles.

A videotape segment accompanies this article.

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DISCUSSION

Sulpiride, a substituted benzamide, is a D2-receptor blocker that was thought to be devoid of the extrapyramidal side effects typically seen with other dopamine antagonists. Parkinsonism, however, was reported in 7 of 9 patients treated for tardive dyskinesia and in 1 of 11 patients with Huntington's disease (3). The average sulpiride doses at which these side effects were first noted ranged between 630 mg (for the patients with tardive dyskinesia) and 1,200 mg (for the patient with Huntington's disease). "Tardive dyskinesia" was reported in a 77-year-old woman with oral dyskinetic movements, akathisia, dysphagia, and mild pharyngeal spasm following 8 weeks of therapy with sulpiride. However, as her symptoms resolved within 1 week of discontinuation of sulpiride, the diagnosis of "tardive dyskinesia" is not justified. A computerized literature search failed to identify any other cases of movement disorders associated with sulpiride, and the sulpiride-induced tardive dystonia seen in our patient has not been previously reported.

Tardive dystonia, a clinical variant of tardive dyskinesia, was characterized in 1982 by Burke et al. (6). Criteria for diagnosis included a history of chronic dystonia in the setting of preceding or concurrent neuroleptic use, negative family history, and exclusion of known causes of secondary dystonia (6,7). Our patient's sustained, twisting movements of the arms and neck were consistent with these diagnostic criteria. As the onset of the dystonia was related to sulpiride, it seemed certain that his dystonia was induced by the drug.

In contrast to acute dystonia, tardive dystonia has a delayed onset and may persist indefinitely after the offending drug is withdrawan (6–9). Our patient's symptoms presented after he had taken sulpiride for only 2 months. He was continued on the drug for 12 months after the onset of the movement disorder and, during that time, the symptoms progressed in severity. Despite discontinuation of sulpiride, his sustained contractions persisted. Given the favorable experience with tetrabenazine, a monoamine-depleting and dopamine receptor-blocking agent, in patients with tardive dystonia, we used the drug in this patient (8,9). Within a few days of starting tetrabenazine (25 mg, 3 times a day), the dystonic movements markedly improved.

Sulpiride is not the first dopamine blocker initially touted to be free of extrapyramidal side effects but later associated with movement disorders. Metoclopramide, another substituted benzamide, was also initially thought to be devoid of extrapyramidal side effects and was in fact recommended for the treatment of tardive dyskinesia (10,11). It has since been associated with various movement disorders, including tardive dyskinesia, dystonia, and parkinsonism; some of these movement disorders can be life-threatening (12–16). Domperidone is an experimental dopamine-2 antagonist that was promoted as free of neurologic sequelae because it presumably does not cross the blood–brain barrier (17,18). However, dystonic reactions have already been reported following its use (17,19). Given these experiences, caution is advisable when using new drugs with dopamine antagonist activity, despite claims that they are free of extrapyramidal side effects.

LEGEND TO THE VIDEOTAPE

A 37-year-old man with sulpiride-induced tardive dystonia manifested by dystonic movements and postures involving chiefly his neck, arms, and trunk is shown.

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