Sialorrhea in an Adult Taking Aripiprazole

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After five months of treatment with aripiprazole, this patient developed excessive sialorrhea, an extremely uncommon adverse effect.

FDA approved in 2002, aripiprazole is the newest atypical antipsychotic drug on the market. Compared to other antipsychotics, aripiprazole has the advantages of a minimal effect on weight gain, no cardiac effects, and a low risk of extrapyramidal adverse effects.

The drug does have adverse effects, however, the most common of which are headache, nausea, vomiting, akathisia, tremor, and constipation. As with any new medication, postmarketing experience plays a key role in uncovering other possible adverse effects.

Thus far, there has been one case report in the medical literature of sialorrhea, or drooling, associated with aripiprazole use.[1] It describes a six-year-old child who received two doses of the drug and subsequently developed lethargy, sialorrhea, and flaccid facial muscles. These symptoms improved with administration of diphenhydramine. In this article, we present what we believe to be the first case report of aripiprazole-induced sialorrhea in an adult.

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INITIAL EXAM AND PATIENT HISTORY

A 58-year-old man was admitted to a VA hospital following acute onset of depressive symptoms (including tearfulness, decreased motivation, lack of energy, and insomnia) that had progressed gradually to encompass prominent psychotic features. Specifically, the patient was experiencing delusional guilt and ruminations about past transgressions, which he said had resulted in several individuals persecuting him and speaking to him in his sleep and in person. He was convinced that a horrible fate was going to befall him. Fearing this event, and because he said that his persecutors had told him to sit without moving, he had stopped taking medications and eating, instead confining himself to his room, huddled by the air conditioner—the only place that he felt somewhat safe.

The patient had a medical history of hypertension; diabetes; hyperlipidemia; anemia; sleep apnea, requiring bilevel positive airway pressure; and a cerebrovascular accident that had occurred several years ago and resulted in residual right-sided hemiplegia. Prior to his stroke, he had no history of psychiatric illness other than alcohol dependence, which was in remission for almost 40 years. Upon hospital admission, the patient's prescribed medications included: mirtazapine 15 mg per day, simvastatin 20 mg per day, metformin 850 mg twice a day, and benazepril 40 mg per day.

Further review of the patient's records revealed that he had undergone cognitive testing approximately six months prior to admission, the results of which had revealed substantial cognitive deficits in language and visuospatial ability but average memory and attentional abilities. Clinicians detected a hint of psychotic thinking, though the patient was guarded in general.

Several months later, he was referred to geriatric psychiatry, where he scored 29 out of 30 on the Folstein Mini-Mental Status Exam and did not appear overtly depressed. When his depressive symptoms escalated, however, he was prescribed citalopram 10 mg. This was followed one month later by trazodone 50 to 100 mg at bedtime as needed to aid in sleep and alprazolam 0.25 mg twice daily to augment treatment of agitation. Two months later, citalopram, trazodone, and alprazolam were discontinued—due to treatment failure and poor appetite with citalopram. The patient was switched to mirtazapine 7.5 mg nightly.

Mirtazapine therapy had been selected because it was thought that it would help the patient sleep, improve

his appetite, and decrease his depressive symptoms, which were very mild at the time. The mirtazapine dose eventually was increased from 7.5 to 15 mg nightly with some signs of improvement. He worsened, however, and subsequently was admitted to the VA hospital following his caregiver's reports that he no longer was eating or leaving his room.

Given the patient's symptoms and his medical and psychological history, he was diagnosed with severe psychotic depression. This condition was believed to be related both to his stroke and to his feelings regarding his mother's death from a stroke three months prior to the hospital admission.

TREATMENT COURSE

Upon admission, his mirtazapine dose was increased to 22.5 mg at bedtime. Oral quetiapine 25 mg was added at bedtime to target his psychotic depression. This drug was then titrated up to 100 mg. The patient continued to resist taking his medications, however, principally because of his fear of being sedated and thereby "losing his protective vigilance."

After the patient had been receiving mirtazapine for two months, a decision was made to discontinue mirtazapine and quetiapine and switch to aripiprazole. The latter medication was chosen in the hopes that it would be less sedating while still targeting his psychotic depression. His response was not optimal, however, despite titration from 5 to 10 mg daily.

Shortly thereafter, treatment with electroconvulsive therapy (ECT) was begun. With the ECT, the patient became more adherent to his medications and improved clinically. He continued taking oral aripiprazole monotherapy (10 mg daily) for the next five months, along with his other medications (including simvastatin, metformin, benazepril, and aspirin-dipyridamole).

During this time, the patient began to drool excessively. The aripiprazole dose was decreased to 5 mg, and then the drug was stopped completely. Following discontinuation of aripiprazole, the drooling subsided.

The patient has experienced no further drooling since the discontinuation of aripiprazole. Currently, his only treatment for his psychiatric symptoms is maintenance ECT. The patient's mental health status, however, is contingent on his agreeing to continue routine ECT to control his symptoms.

ABOUT THE CONDITION

Aripiprazole's mechanism of action is mixed dopamine-serotonin agonist-antagonist activity. It binds to D2 receptors and is a partial agonist at the 5HT1a receptor, but it is an antagonist to the 5HT2a, H1, and alpha 1 adrenergic receptors. Although the drug may cause an increase in salivation in approximately 2% of patients,[2] the reaction was surprising in this patient after such a long duration of treatment with the drug. Sialorrhea is observed more commonly in patients taking clozapine, as a result of muscarinic receptor agonism.

Saliva is produced and secreted by the six major salivary glands. Together, they secrete approximately 1.5 L of saliva per day. Saliva functions to keep the mouth clean and to aid in food digestion.

When saliva flow becomes too high, though, it can have negative effects. For example, people with sialorrhea may develop chapped or dry skin around the mouth and lips—which puts them at risk for infection. In addition, sialorrhea during sleep may increase a patient's risk of aspiration. There also is a negative social stigma associated with sialorrhea.[3]

Saliva secretion is induced largely by the parasympathetic nervous system. To a lesser extent, the sympathetic nervous system induces saliva secretion by increasing its protein content. All antipsychotic drugs have the potential to induce drooling—due to the fact that they can cause a decrease in swallowing, which results from pseudoparkinsonian bradykinesia. The typical antipsychotics, such as haloperidol, are more likely to cause these symptoms, however.

The blockade of alpha-2 adrenergic receptors additionally may cause drooling. Furthermore, there has been one case report of sialorrhea in a patient who was being treated with olanzapine but showed no clinical signs of parkinsonism. Olanzapine, like clozapine, is a direct agonist at the M4 receptor, suggesting yet a third mechanism for antipsychotic-induced sialorrhea.[4] ●

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