

Aripiprazole-Induced Sialorrhea Responsive to Amitriptyline Treatment

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ABSTRACT:

Aripiprazole-induced sialorrhea responsive to amitriptyline treatment

Treatment compatibility is crucial for the psychiatric disorders. This can be provided with the low side effect profile of psychotropic drugs. Aripiprazole, a tolerable and safe antipsychotic, is used in the treatment of various psychiatric disorders. In the previous studies, sialorrhea was declared as a side effect of some antipsychotics. Furthermore, aripiprazole-related sialorrhea which was treated with diphenhydramine and trihexyphenidyl, was reported in the literature. In our case, we discussed that aripiprazole-related sialorrhea developed in a male patient who treated with amitriptyline.

Keywords: amitriptyline, aripiprazole, sialorrhea, side effect, psychosis

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INTRODUCTION

Sialorrhea is a frequent, unbearable, disturbing and persistent adverse effect of antipsychotics, especially related with clozapine, risperidone, olanzapine. This is known as dose-related adverse effect (1). This condition may be particularly socially stigmatizing and troubling for patients, resulting in treatment nonadherence or discontinuation (2). Sialorrhea may emerge all day; however, its frequency and amount that is inversely proportional with ability to swallow, increases during sleep time (3). The patients frequently complain of awakening with a "wet pillow" (2).

Aripiprazole, which is a relatively new atypical antipsychotic, has been used in the treatment of schizophrenia, depression, bipolar disorder, tic disorders, irritability, impulsivity, and obsessive compulsive disorder

(OCD) (4-6). The common adverse effect of antipsychotics such as headaches, nausea, vomiting, somnolence, difficulty with speaking, anxiety, loss of balance, insomnia, weight gain, and restlessness have been observed relatively limited in using aripiprazole compared with the other antipsychotics. This safe and tolerable profile of aripiprazole is not valid for every side effect as sialorrhea and akathisia (7).

Here, we present a case of aripiprazole-induced sialorrhea responsive to amitriptyline in a male patient with first-time psychotic episode.

CASE PRESENTATIONS

25 year-old, single, non-smoking male was diagnosed with first-time psychotic episode (Scores of SAPS and SANS were 45 and 57, respectively) and initiated aripiprazole 5 mg/day

and titrated up to 15 mg/day in the following two week. The patient psychotic symptoms were resolved gradually in three week (Scores of SAPS and SANS were 37 and 45 in the 2nd week and 23 and 32 in the 3rd week, respectively); however, he complained that he had a lot of saliva secretion coming out of his mouth after two months of taking aripiprazole. When the patient spoke, we observed his mouth was always filled with saliva. There was drooling frequently, more so in the night and after waking up in the morning from sleep the around of his mouth was wet with saliva. Daily, he was noticing over his pillow, a wet spot of around 7 cm diameter from created by the soaked saliva. During the day he was regularly trying to control the drooling, swallowing his saliva, to save him from embarrassment. A physical examination revealed no extrapyramidal symptoms such as tremor, muscle rigidity, dyskinesia or difficulty in swallowing. We consulted an otolaryngologist to examine the patient swallowing function and pharynx. There were no functional or organic abnormalities. According to the psychotic symptom relief scales scores and patient clinic, amitriptyline 10 mg/day was added to the daily treatment and sialorrhea resolved significantly within 1 week. A significant reduction in his drooling was noticed and he did not wake up with wet around of the mouth or soaked pillow.

Written informed consent was obtained from the parent (legal guardian) of the patient who participated in this case.

DISCUSSION

In this report, we presented a case of sialorrhea during aripiprazole treatment and remitted amitriptyline treatment in a patient who suffered from first episode psychotic disorder. Because of the temporal relationship between the onset of sialorrhea and use of aripiprazole, it is thought that the sialorrhea might be associated with aripiprazole. In the literature, there are two reported case, 27 year-old male patient with aripiprazole-induced sialorrhea responsive to diphenhydramine (8) and 14-year-old-boy with aripiprazole-induced sialorrhea responsive to trihexyphenidyl (9). To the best of our knowledge, this is the first case of patient with aripiprazole-induced sialorrhea responsive to amitriptyline treatment.

Antipsychotics can cause a decrease in swallowing caused by throat muscle rigidity, which is the result of

pseudo-parkinsonian bradykinesia so that drooling is a common side effect in patients treated with antipsychotics. In our case, there were no signs of esophageal dysfunction or extrapyramidal symptoms; therefore, drooling was thought to the result of sialorrhea induced by aripiprazole.

Aripiprazole acts as a potent partial agonist at D2, D3, 5-HT₁, and 5-HT_{1A} receptors and as an antagonist at 5-HT_{2A} receptors but has no clinically significant effect on the muscarinic receptors. It might seem to be a as second generation atypical antipsychotics because of differ from antipsychotics by its 5HT_{2A} receptor antagonism and weaker linking capacities and faster dissociation of D2 receptors (10).

Salivary flow is essentially under parasympathetic control and sympathetic system has a minor modifying effect in the salivary flow system. Stimulation of muscarinic receptors increases salivary flow approximately five fold (11). On human salivary gland, there are predominantly M3 receptor but M1 and M4 are fewer than it is thought that the cause of antipsychotic-induced sialorrhea can be one of these; to involve α 2-adrenergic antagonism, M4 muscarinic agonism or laryngeal peristalsis/ inhibition of swallowing reflex (2,12). In this case report, the most likely mechanism of aripiprazole induced sialorrhea is through central α 2-adrenergic antagonism as reported with risperidone (13) and clozapine (2).

In the treatment of antipsychotics-induced sialorrhea is used α 2-adrenergic receptor agonist or anticholinergic drugs (14). Amitriptyline is a tricyclic antidepressant, which blocks serotonin and norepinephrine transporters, exerts α 2-adrenergic receptor antagonism, M4 muscarinic receptor agonism, and reduces laryngeal peristalsis (15). Amitriptyline has been used to be useful in clozapine-induced sialorrhea (14,15). The treatment of sialorrhea with amitriptyline suggested to be the result of its multiple mechanisms may be responsible. In the treatment of sialorrhea with amitriptyline can be used in high doses (100 mg/day) (15).

In conclusion, it is important to be aware of the possibility of a sialorrhea being induced when starting aripiprazole therapy. Amitriptyline may be a therapeutic option for patients with aripiprazole-induced sialorrhea. We believe that these case reports serve as a base for future research to examine the relationship between using aripiprazole, onset of sialorrhea, and treatment response.

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