Case Report

Investigating the Excessive Sweating Induced by Aripiprazole: Two Case Reports

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ABSTRACT

Background: Many drugs, including antipsychotics, cause an adverse effect, such as excessive sweating (hyperhidrosis). Hyperhidrosis occurs by drugs that act on the thermoregulatory centers in the hypothalamus, spinal, and sympathetic ganglia or on the endocrine system.

Case Report: This study reports two patients who developed hyperhidrosis while taking aripiprazole. A 38-year-old woman who had a diagnosis of obsessive-compulsive disorder and a 17-year-old boy who developed multiple motor tics continued to take aripiprazole even though they had hyperhidrosis. The dosage of aripiprazole was adjusted to reduce diaphoresis.

Conclusion: Besides the potential risks of dehydration, electrolyte depletion, and hypothermia, hyperhidrosis may be a distressing and embarrassing symptom that, if not addressed properly, can promote noncompliance with the medication. Therefore, it is imperative to create awareness of this unusual potential adverse effect of aripiprazole.

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Introduction

Aripiprazole is a third-generation atypical antipsychotic medication used for different psychiatric disorders [1]. It is a partial agonist at the dopamine D2 receptor, a partial agonist at the serotonin 5-HT1a receptor, and shows antagonistic activity at the 5HT2A receptor [2]. Aripiprazole is recognized as a stabilizer of the dopaminergic system with unique psychopharmacologic properties that may limit the hypodopaminergic state blamed for the development of neuroleptic malignant syndrome [3]. Aripiprazole is approved for the treatment of schizophrenia and schizoaffective disorder and was approved by the Food and Drug Administration (FDA) for the treatment of bipolar disorder in 2004 [4]. Given that aripiprazole is well tolerated and has few side effects, it is also used for other psychotic disorders [5]. The most common adverse effects at the suggested doses (10-30 mg/day) reported sedation, blurred vision, agitation, extrapyramidal symptoms, fatigue, headache, increased appetite, nausea, and somnolence [6]. There are few reports of diaphoresis as the adverse effect of aripiprazole [7]. Hyperhidrosis is due to cholinergic sympathetic nerve overactivity as there are no histopathologic changes or a number of the eccrine glands. On the other hand, some articles recommend aripiprazole for the anti sweating interventions [8, 9]. The reduction of sweating has been associated with the unique property of aripiprazole. Here, this study reports two patients with diaphoresis as the only prominent adverse effect of aripiprazole therapy.

Case Presentation

Case 1

A 38-year-old woman was diagnosed with obsessive-compulsive disorder. Her symptoms developed in her early twenties. The obsessions she experienced consisted of disturbing and pessimistic thoughts regarding her husband. Her compulsive behavior included cleaning and washing. She also used to check his husband's mobile phone and his movements as often as 20 times per day. Moreover, she had negative thoughts about her body, and due to her obesity, she was on a diet to lose weight; she currently has a normal body mass index. She did not have any physical health problems in her past medical history, such as hypertension, hyperlipidemia, hyperthyroidism, drug abuse, and diabetes. Also, there was no history of hyperhidrosis in her family. The general examination was completely normal (blood pressure=120/70 mmHg with a pulse rate of 72 pulse/min and temperature=37˚C). Routine blood tests did not show any abnormalities (i.e. normal white blood cell count, glucose, electrolytes, normal liver and kidney function, normal thyroid function C-reactive protein, and erythrocyte sedimentation rate). Neurological consult reported normal clinical examination and the bilaterally symmetric excessive sweating. Additional imaging investigations also did not show any abnormalities.

She was treated with sertraline and olanzapine. She recovered partially but discontinued due to weight gain. A few months later, aripiprazole 10 mg/day, fluoxetine 20 mg/day, and inderal 20 mg/day were replaced, and she started experiencing generalized hyperhidrosis. She had a normal neurological examination and stable vital signs.

After beginning the treatment with an initial 2.5 mg dose of aripiprazole, the dose was increased by 2.5 mg every 4 days up to a dose of 10mg. Hyperhidrosis started about a week after beginning 10 mg of aripiprazole. She endured sweating for several months until she went to a psychiatric clinic for examination. When aripiprazole stopped, excessive sweating disappeared in about a week. The dosage of aripiprazole was adjusted to reduce diaphoresis. She continued aripiprazole 5 mg/day, and the sweating did not completely disappear.

Case 2

The second case was a 17-year-old boy who slowly developed multiple motor tics from the age of 4 years. For the first time, he showed eye blinking and shoulder movement, imbalance in walking, and additional hand movements were added. He had no vocal tics. Also, he rarely displayed irritable moods and aggressive behaviors. The subject had subclinical hypothyroidism and nocturnal enuresis in his past medical history. He did not take medicine for his thyroid. He was a smoker but did not use illicit drugs or alcohol. Neuropsychological evaluation showed minor changes in executive functioning and other cognitive domains (attention, psychomotor speed, language). He left school at the age of 12 years. Neurological examination was normal. Laboratory tests, including complete blood count, liver, renal, and thyroid functions were normal. The family history was unremarkable for tics.

Risperidone was prescribed and the patient responded. His mother stopped taking the medication because of tic absence. He had a relapse sometime later and did not respond to risperidone again. He was treated with haloperidol and it responded. His family discontinued the treatment, which led to a relapse of the tics again.

After the third relapse, he was prescribed pimozide and had a temporary and relative recovery. Subsequently, he was treated with aripiprazole and clonidine 0.2 mg/day. His tics reduced significantly, but he started to experience generalized excessive hyperhidrosis 4-5 days after the consumption of 10 mg/day aripiprazole. Secondary causes of excessive sweating, such as various types of infections, tumors, drugs as well as endocrine diseases were excluded. He reported that about 4-5 days after stopping the drug the sweating was ended. Due to the reduction in tics and prevention of relapse, he has continued the medication for now. The excessive sweating continued with the consumption of aripiprazole.

Discussion

Diaphoresis is the excessive production of sweat needed to maintain normal homeostasis and body temperature [10]. The reported prevalence of diaphoresis is about 2.5% in the general population [11, 12]. The literature on aripiprazole-induced sweating deals almost exclusively with case reports.

This report did not evaluate which dosage of aripiprazole which was responsible for the diaphoresis; however, a review of the medical literature has shown that several cases reported diaphoresis with aripiprazole as reported by our patients. Vohra (2017) reported on two patients who developed hyperhidrosis while taking aripiprazole. Both patients discontinued the medication and the sweating stopped. In one case, generalized sweating occurred a few months after taking aripiprazole (15 mg/day), experiencing generalized excessive was started. When aripiprazole was discontinued, the excessive sweating disappeared within about a week. In another case, sweating began when aripiprazole was started at a dose of 20 mg/day and continued when it was reduced to 10 mg the sweating stopped 10 days after stopping the drug [7]. However, the patients we reported continued to take the drug. Only in one patient did the dose of aripiprazole (5 mg/day) reduced and her sweating decreased. However, the mother of the patient with tics continues to take aripiprazole due to increasing agitation by reducing its dose. Our patients report that when they discontinued aripiprazole, sweating stopped after about 5 to 7 days. Nevertheless, some studies reported that aripiprazole was applied for anti-sweating interventions, which is not consistent with our report. For instance, Lu et al. reported that in two cases, aripiprazole was prescribed together with antidepressants to modulate antidepressant-induced sweating [9]. Also, Huang et al. reported hyperhidrosis under a combination of zotepine and haloperidol improved by aripiprazole [8].

Our patients report generalized excessive hyperhidrosis due to aripiprazole, which is consistent with the medical literature showing that unilateral, asymmetric, and generalized hyperhidrosis is strongly associated with secondary causes (infections, endocrine diseases, withdrawal from drugs or alcohol, etc). In contrast, the diagnosis of primary hyperhidrosis can be supported by primary involvement of the face, hands, axillae, and feet, or by bilateral and relatively symmetrical lesions, stop of sweating during sleep, onset before 25 years old, and a positive family history [13, 14].

Various medications can affect the physiologically complex thermoregulation system by acting at multiple sites and affecting sweat production, resulting in hypo- or hyper-hidrosis. These drugs can affect the hypothalamus, particularly the medial preoptic area, and the junction between the sympathetic cholinergic nerve endings and the eccrine sweat glands [15]. Various antidepressants, such as selective serotonin reuptake inhibitors with minimal effects on norepinephrine may cause diaphoresis through the teratogenic effects on the spinal cord and hypothalamus [16]. Tricyclic antidepressants with recognized anticholinergic effects occasionally cause hyperhidrosis by inhibiting noradrenaline reuptake with stimulation of peripheral adrenergic receptors [17].

Conclusion

In conclusion, this study reported two cases of aripiprazole-induced sweating. It is difficult to understand the causative mechanism of hyperhidrosis in some patients. In addition to the potential risks of dehydration, electrolyte imbalance, and hypothermia, diaphoresis can be a distressing and embarrassing condition that if not appropriately recognized, can lead to medication non-compliance. Therefore, it is imperative to raise awareness of this unusual potential adverse effect of aripiprazole.

Ethical Considerations

Compliance with ethical guidelines

The present study was completed following the Declaration of Helsinki and the Ethical Guidelines for Medical and Health Research established by the Ministry of Health and Medical Education and the Ministry of Science, Research and Technology, Iran. The authors obtained approval from the Ethics Review Committee of Mazandaran University of Medical Sciences (No. IR.MAZUMS.REC.1402.108). The patients agreed to take part in the present study and written consent forms were signed by them. In case 2 (17-year-old boy), her mother also signed the consent form.

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Authors' contributions

Conceptualization and Supervision: Seyed Hamzeh Hosseini; Methodology: Hamed Ghazvini; Investigation: Seyedeh Masoumeh Seyedhosseini Tamijani; Writing-original draft: Raheleh Rafaiee; Writing-review & editing: All authors.

Conflict of interest

The authors declared no conflict of interest.

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