DOI: 10.14744/DAJPNS.2024.00254
Dusunen Adam J Psychiatr Neurol Sci
2024;37:164-165

LETTER TO THE EDITOR

Osmotic-release oral system methylphenidate-induced hyperhidrosis in an adolescent boy: A dose-dependent side effect

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Dear Editor,

Attention Deficit Hyperactivity Disorder (ADHD) is one of the most common childhood disorders. Its symptoms affect cognitive, academic, behavioral, emotional, and social functioning. Stimulants are the most common type of prescription medication for ADHD. Methylphenidate (MPH) is the main stimulant. Studies have shown that treatment doses of MPH cause adults to sweat significantly (1). They have also indicated that high doses of MPH lead to excessive sweating in children (2). However, no studies or cases have demonstrated that treatment doses of MPH cause hyperhidrosis in children and adolescents. This letter presents the case of an adolescent who complained of dose-related excessive sweating. It occurred after he took a normal treatment dosage of Osmotic Release Oral System (OROS) MPH for his ADHD. The patient and his parents provided consent for this report.

We diagnosed a 15-year-old boy with combined ADHD after he exhibited signs of attention deficit. We initiated treatment with OROS-MPH at a dose of 27 mg/day and increased it to 36 mg/day after ten days. The patient showed some improvement in attention deficit symptoms, according to the outpatient clinic exam and reports from parents and teachers. We did not observe any side effects at 27 mg/day. However, he complained of mild sweating on his face, arms, and chest at 36 mg/day. We increased the drug dose to 54 mg/day. Reports indicated notable gains in ADHD symptoms and school performance upon examination. We compared the improvement to the first visit. However, the patient reported that his sweating had increased. This situation was making him very uncomfortable, as he was experiencing social embarrassment and emotional stress.

We reduced the patient's medication dose to 36 mg/day, and his complaint of sweating significantly decreased. However, his attention deficit symptoms worsened. Consequently, we increased the drug dose back to 54 mg/day. The patient's excessive sweating recurred at this dose. Nonetheless, the effective treatment dose for this patient's attention deficit symptoms is 54 mg/day. He was not receiving any medication other than OROS-MPH, and he had no comorbidities. His medical history and workup, including blood tests, were unremarkable. We attributed the hyperhidrosis to the use of MPH. The patient and his parents said they wanted to continue the current treatment at a dose of 54 mg/day. He continued his treatment at this dose without seeking treatment for his excessive sweating. We advised the child to adopt some behavioral measures, including showering daily, avoiding sweat-inducing clothing, drinking plenty of water, limiting caffeine intake, and using deodorant.

How to cite this article: Durak M, Isik U. Osmotic-release oral system methylphenidate-induced hyperhidrosis in an adolescent boy: A dose-dependent side effect. Dusunen Adam J Psychiatr Neurol Sci 2024;37:164-165.

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Received: May 21, 2024; **Revised:** July 16, 2024; **Accepted:** August 22, 2024

Studies show that adults sweat significantly at treatment doses of MPH (1). However, no studies or cases demonstrate that treatment doses of MPH cause hyperhidrosis in children and adolescents. There is a study documented in the literature about hyperhidrosis caused by toxic doses of MPH in children (2). The children in this study took excessive amounts of MPH either accidentally, due to a dosing error, or intentionally. The dose of MPH in our case was within the therapeutic range, as evaluated through reports from parents and teachers and the clinic's assessment. The Naranjo Adverse Drug Reaction Probability Scale assigned a total score of 9, indicating a definite adverse drug reaction to MPH causing hyperhidrosis (3). Our case experienced no sweating at 27 mg/day, mild sweating at 36 mg/day, and excessive sweating at 54 mg/day. The decrease in sweating at 36 mg/day suggests a dose-dependent side effect. The literature stated that insomnia and loss of appetite were related to the dose. However, other side effects did not seem to be dose-related (4). To our knowledge, the dose-related hyperhidrosis has not been mentioned before.

The exact mechanism of MPH-associated hyperhidrosis is unclear. Midbrain dopaminergic neurons in the ventral tegmental area and noradrenergic neurons in the locus coeruleus (LC) are major sources of dopamine (DA) and norepinephrine (NE) to the prefrontal cortex (5). Methylphenidate non-competitively blocks the reuptake of DA and NE into the terminal by blocking the dopamine transporter (DAT) and the noradrenaline transporter (NAT), thereby increasing the presence of these neurotransmitters. It activates the noradrenergic pathway projecting from the locus coeruleus and the dopaminergic pathway projecting from the ventral tegmental area. The activation of the LC results in a well-defined set of autonomic changes: in tissues receiving predominantly sympathetic innervation (e.g., arterioles and sweat glands), there is an increase in activity, whereas in those receiving predominantly parasympathetic innervation (e.g., salivary glands), there is a decrease in activity (6). Thus, MPH-induced hyperhidrosis was most likely caused by LC activation.

Untreated hyperhidrosis can lead to skin infections. Moreover, hyperhidrosis may lead to social embarrassment, lowered self-confidence, and emotional stress. Adverse effects can cause nonadherence and discontinuation of medications. Reducing these side effects may improve adherence and outcomes. For this reason, clinicians should recognize this side effect. This report suggests that hyperhidrosis may be a dose-dependent side effect of OROS-MPH. Clinicians should also be aware that it may be related to the dose.

Conflict of Interest: The authors declare that they have no conflict of interest.

Informed Consent: Informed consents were obtained from both the patient and his parents.

Use of AI for Writing Assistance: Not declared.

Financial Disclosure: The authors declare that they have no financial support.

Peer-review: Externally peer-reviewed.

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