

COMPLICATED CASE HISTORIES

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Atomoxetine Induced Hypothermia: A Case Report

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ABSTRACT ~ Adverse drug reactions are common in drugs used during childhood and adolescence. Atomoxetine, a selective reuptake inhibitor, was introduced as a safe non-stimulant alternative treatment for attention deficit hyperactivity disorder. Described common side effects of atomoxetine include: headache, abdominal pain, decreased appetite, fatigue, nausea, vomiting and dizziness. In our case, we present an adolescent male who developed hypothermia under atomoxetine treatment. To our knowledge, this is the first report of a causal connection between atomoxetine intake and hypothermia. Because hypothermia is a life-threatening condition and can be treated when interfered immediately, clinicians should be aware of this adverse effect of atomoxetine. *Psychopharmacology Bulletin*. 2011;44(2):88–90.

INTRODUCTION

Attention-deficit-hyperactivity disorder (ADHD) is a common, chronic neuropsychiatric disorder that impairs social, academic, and occupational functioning in children, adolescents, and adults. The prevalence of this disorder in the United States is 6–9% in youth (i.e., children and adolescents) and 3–5% in adults.¹ As a highly selective noradrenaline reuptake inhibitor, atomoxetine hydrochloride, is the first non-stimulant drug that has been indicated for the treatment of ADHD. According to the data collected from clinical trials, atomoxetine hydrochloride is considered to be safe, effective and associated with relatively few adverse drug reactions: dyspepsia, nausea, vomiting, fatigue, rash, irritability, headache, somnolence, dizziness, decreased appetite and weight loss.² Hypothermia, a condition in which core body temperature drops below 35.0°C, is a rarely seen side effect of stimulant drug use. Here we would like to present an 11-year-old treatment-naïve and healthy adolescent who developed hypothermia after treatment of ADHD with atomoxetine.

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CASE REPORT

An 11-year-old male adolescent was referred to our outpatient clinic due to his poor attention, having difficulties in finishing work and poor academic performance. He was diagnosed with ADHD, predominantly inattentive type, according to the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) criteria.³ He had normal physical examination and no history of significant medical illness. He was started on atomoxetine 10 mg per day. After taking the drug, his mother noticed that his face and his hands were cold, but they disregarded. On the second day of the treatment, he felt "cold" and a little tired. His temperature was found 34.0°C at home and upon his admittance to the hospital his rectal temperature was 34.2°C. Complete blood count and biochemical analysis revealed no abnormality. Passive external rewarming techniques (blanket and a heating lamp) were applied. His body temperature rose to 35.2°C an hour later and was gradually normalized (36.3°C) in 3 hours, under close monitoring of his body temperature every 30 min. The medication was discontinued and no other adverse effect was seen during the following two weeks. The patient has provided permission to publish these features of his case, and the identity of the patient has been protected.

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DISCUSSION

Stimulant drugs used in the treatment of ADHD can influence thermoregulation and hypothermia in patients using stimulants is a serious and unpredictable adverse effect that may result in hospitalization. Nocturnal enuresis, seizure disorder, debilitating physical illness, and mental retardation are determined as conditions to increase the risk of hypothermia in psychiatric patients. Drugs used in psychiatry such as antipsychotics, beta-adrenergic antagonists, benzodiazepines, and other sedatives might have an additional effect on the risk of hypothermia.⁴ The mechanism of action of atomoxetine is thought to be related to its selective inhibition of presynaptic norepinephrine reuptake in the prefrontal cortex. It has a high affinity and selectivity for norepinephrine transporters, but little or no affinity for other various neurotransmitter receptors.⁵ The mechanism of hypothermia induced by atomoxetine is not clear. Besides, it was emphasized that, in rats, intraperitoneally administrated atomoxetine significantly increases extracellular norepinephrine and dopamine levels in the prefrontal cortex by up to 290% and 323% of basal levels; while serotonin levels did not significantly differ from baseline.⁶ It is mentioned that under normal condition, dopamine tends to act to reduce body temperature, while serotonin elevates body temperature.⁷ In our case, elevated levels of dopamine, particularly in the mesolimbic area, might have resulted in hypothermia.

CONCLUSION

To our best knowledge, this is the first report in the literature of an adolescent with ADHD who developed hypothermia after administration of atomoxetine. Our case suggests that clinicians should be aware of the development of thermoregulatory changes when prescribing atomoxetine for patients with ADHD. ❀

CENTERS PARTICIPATED IN THIS REPORT

This case report is presenting a patient that is under treatment at the outpatient service of the Department of Child and Adolescent Psychiatry, Faculty of Medicine, İstanbul University.

DISCLOSURE

The work described in the above manuscript was done as part of our employment with the ministry of health and is therefore in the public domain. The authors warrants that the material contained in the manuscript represents original work, has not been published elsewhere, and is not under consideration for publication elsewhere.

CONFLICT OF INTEREST

Dr. Abali and Dr. Yilmaz report no biomedical financial interests or potential conflicts of interest.

REFERENCES

1. Katragadda S, Schubiner H. ADHD in children, adolescents, and adults. *Prim Care*. 2007 Jun;34(2):317–341.
2. Caballero J, Nahata MC. Atomoxetine hydrochloride for the treatment of attention-deficit/hyperactivity disorder. *Clin Ther*. 2003;25:3065–3083.
3. American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, 4th ed. Washington, DC, American Psychiatric Association, 1994.
4. Young DM. Risk factors for hypothermia in psychiatric patients. *Ann Clin Psychiatry*. 1996 Jun;8(2):93–97.
5. Barton J. Atomoxetine: a new pharmacotherapeutic approach in the management of attention deficit/hyperactivity disorder. *Arch Dis Child*. 2005 Feb;90(1 Suppl.):126–129.
6. Bymaster FP, Katner JS, Nelson DL, et al. Atomoxetine increases extracellular levels of norepinephrine and dopamine in prefrontal cortex of rat: a potential mechanism for efficacy in attention deficit/hyperactivity disorder. *Neuropsychopharmacology*. 2002 Nov;27(5):699–711.
7. Yamawaki S, Lai H, Horita A. Dopaminergic and serotonergic mechanisms of thermoregulation: mediation of thermal effects of apomorphine and dopamine. *J Pharmacol Exp Ther*. 227 (1983):383–388.