

Acute Urinary Retention Associated with Increased Dose of Atomoxetine in a Child: A Case Report

Caner Mutlu¹, Ozgur Yorbik², Hamiyet Ipek¹, Ilhan Asya Tanju³

ABSTRACT:

Acute urinary retention associated with increased dose of atomoxetine in a child: a case report

Urinary side effects of atomoxetine are extremely rare, especially in children. We report the presentation of acute urinary retention in an 8-year-old boy with attention deficit hyperactivity disorder (ADHD). To the best of our knowledge, this is the first case of a school-aged child experiencing urinary retention due to an increased dose of atomoxetine. We propose that noradrenergic systems in the urinary tract, possibly precipitated by a higher than usual initial dose of atomoxetine, may have been over-activated. Moreover, it may be suggested that urethral smooth muscles become more sensitive to alpha-adrenergic receptor stimulation before puberty.

Keywords: atomoxetine, urinary retention, child

Klinik Psikofarmakoloji Bulteni - Bulletin of Clinical Psychopharmacology 2015;25(3):299-301



¹M.D., Bakirkoy Research and Training Hospital for Psychiatry, Neurology and Neurosurgery, Department of Child and Adolescent Psychiatry, Istanbul - Turkey
²Prof., Uskudar University, Faculty of Health Sciences, Department of Child Development, Division of Child and Adolescent Psychiatry, Istanbul Turkey
³M.D., Gulhane Military Medical School, Haydarpaşa Teaching Hospital, Department of Pediatrics, Istanbul - Turkey

Corresponding author:

Dr. Caner Mutlu,
Bakirkoy Ruh ve Sinir Hastaliklari Egitim ve Arastirma Hastanesi, Çocuk ve Ergen Ruh Sağlığı ve Hastaliklari Klinigi,
Istanbul - Türkiye

E-mail address:

canermutlu@yahoo.com

Date of submission:

January 03, 2014

Date of acceptance:

April 08, 2014

Declaration of interest:

C.M., O.Y., H.I., I.A.T.: The authors reported no conflict of interest related to this article.

INTRODUCTION

Attention deficit hyperactivity disorder (ADHD) is a commonly diagnosed childhood disorder¹ that occurs in 2.4-19.8% of school-aged children². The management of ADHD typically requires a multidisciplinary approach and may involve a number of different psychosocial interventions and pharmacological treatments. Drug therapy for ADHD has consisted of the stimulants and non-stimulant medications¹. Atomoxetine (ATX) is a specific noradrenergic reuptake inhibitor that was approved by the Food and Drug Administration

(FDA) as a non-stimulant for the treatment of ADHD in children over 6 years of age, adolescents, and adults^{2,3}. Although ATX is generally well tolerated, it is associated with many common side effects including headache, abdominal pain, nausea, vomiting, decreased appetite, weight loss, irritability, insomnia, and sedation. Elevated liver enzymes and motor tics are also significant, but less common, side effects. In addition, urinary retention, erectile dysfunction, dysmenorrhea, and decreased libido have been reported in adults³.

Drug-induced side effects reduce the quality of

life of the patients and may result in discontinuation of the treatment. It is therefore important to understand the side effects of ATX in terms of treatment management. Urinary side effects, such as urinary retention, are rarely seen but have been reported especially in adults³ and in one adolescent case⁴ taking ATX. No cases of this rare acute urinary difficulty has been reported in children. To the best of our knowledge, we report here the first case of urinary retention due to ATX in a school-aged child with ADHD.

CASE

An 8-year-old boy presented to our child and adolescent psychiatry outpatient clinic with hyperactivity, difficulty sustaining attention, losing school materials, avoiding schoolwork, getting easily bored, forgetfulness, talking excessively, intruding on colleagues, and swearing, all of which had contributed to his moderate academic performance. In addition, he was unable to pass urine. Before admission to our clinic, he had been diagnosed with ADHD in the children's psychiatry outpatient clinic of a private psychiatric hospital. A child psychiatrist had prescribed him oral ATX, 40 mg/day, for a body weight of 48 kg. Approximately one month after starting ATX treatment, he had lost 5 kg in weight. The child psychiatrist subsequently increased the ATX dose to 60 mg/day. The patient's inability to pass urine had begun upon taking the first 60 mg ATX capsule. He had no history of trauma to the spine, fecal incontinence or constipation, burning sensations during micturition, colicky pain, or urinary incontinence. Despite frequently forcing continence, he had often not been able to pass urine throughout the day and was only able to produce a very small amount of urine if he strained hard. At this point, he was admitted to our outpatient clinic with the same symptoms and upon evaluation was advised by a pediatrician to discontinue ATX. His bladder was mildly tender and palpable, but did not require catheterization. An emergency ultrasonography of the lower abdomen was unremarkable. The

next day he did not complain of any further symptoms. Except for being circumcised three months ago based on family's muslim religious tradition his medical history was normal, and there was no family history of medical or mental illness. He was evaluated in our outpatient clinic again, and osmotic-release oral system methylphenidate hydrochloride (OROS-MPH) was initiated at a dose of 27 mg/day, suitable for a body weight of 43 kg. A clinical improvement in ADHD symptoms was observed with OROS-MPH of 36 mg/day. For the treatment of behavioral symptoms, risperidone was included at 0.5 mg/day. The patient still receives 36 mg/day of OROS-MPH and 0.5 mg/day of risperidone, with no reported side effects.

DISCUSSION

Acute urinary retention (AUR) is an uncomfortable condition characterized by a sudden inability to pass urine and completely empty the bladder. In this case, obstructive, neurogenic, pharmacologic, and psychogenic causes of AUR were excluded because of normal physical examination and laboratory test results and a lack of history of potential other causes. Moreover, the sudden onset with the increasing dose of ATX, and subsequent disappearance after discontinuation of the medication, strongly suggested a causal link.

Bladder storage and urine elimination are predominantly regulated by the balance between parasympathetic and sympathetic pathways. Tonically active sympathetic mechanisms facilitate bladder filling via beta adrenoreceptors in the bladder and inhibit urination via alpha adrenoreceptors, particularly alpha-1, in the urethra⁵. During urination, parasympathetic pathways facilitate voiding while the sympathetic pathways are suppressed. If sympathetic pathways are overactivated, they may suppress the parasympathetic pathways leading to retention of urine⁶. Also, the properties of adrenoreceptors in the urinary tract change with age, and the response to noradrenergic agents may differ with

aging^{5,7}. In an animal study, it was shown that age-related increase of alpha-1 adrenoreceptor responsiveness occurred in the proximal urethra⁷. During puberty, hormones such as estrogens may increase the urethral smooth muscle sensitivity to alpha-adrenergic receptor stimulation⁵. These age-related findings may indicate the possibility of a lower response to noradrenergic agents and lower rate of urinary retention in children compared to adults. However, Camporeale et al.⁸ reported that the rates of genitourinary adverse events, including urinary hesitation, were generally similar between adult and adolescent male patients taking ATX. It is known that ATX has no anticholinergic effects. Although the pathophysiology of urinary retention due to ATX can be complex and its causal mechanisms have not been precisely established, peripheral noradrenergic mechanisms of action, especially by

alpha-1A receptor agonism, are suggested as being responsible for urinary retention⁹.

In our case, a higher than usual initial dose of ATX may have precipitated the noradrenergic system, and the increasing dose may have dysregulated the balance between the sympathetic and parasympathetic systems. The overactive sympathetic system could then have inhibited urination, leading to AUR. Our case may also suggest that urethral smooth muscles become more sensitive to alpha-adrenergic receptor stimulation before puberty. This case suggests that AUR may occur in children as the dosage of ATX is increasing, and this side effect quickly responds to discontinuation of the drug and, if necessary, common clinical intervention for the condition (i.e. catheterization). We should consider starting ATX at lower doses and carefully monitor for side effects when ATX doses are increased.

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