

Atomoxetine for encopresis in children with autism spectrum disorder: Report of 4 cases

Sumeyra Firat & Sabri Hergüner

Child and Adolescent Psychiatrist, Private Clinic Doctor

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INTRODUCTION

Autism Spectrum Disorder (ASD) is a neurodevelopmental condition characterized by deficits in social communication and interaction, alongside restricted and repetitive behaviors (American Psychiatric Association, 2013). In addition to these core symptoms, children with ASD often present with a range of comorbidities, including hyperactivity, inattention, mood dysregulation, and anxiety (Niemczyk et al. 2018). These psychiatric issues may further complicate the clinical picture of children with ASD, affecting their overall functioning and quality of life. These comorbidities often exacerbate their need for overall support (Stankovic et al., 2022)

In particular, incontinence, including fecal incontinence, has been identified as a significant concern in children with ASD. A systematic review reveals that the prevalence of fecal incontinence is notably higher in children with ASD compared to typically developing children. The association rate between ASD and encopresis in these studies varies, ranging from 2% to 12.5% (Niemczyk et al., 2018). However, there is a study indicating that the association of encopresis and ASD is 40% (Gubbiotti et al., 2019). Moreover, it has been suggested that neurodevelopmental deficits and behavioral differences common in ASD may contribute to the increased rate of fecal incontinence observed in these children (Niemczyk et al., 2018). Psychiatric comorbidity also appears to play a moderating role, with both children with ASD and typically developing children with fecal incontinence showing higher levels of psychopathological symptoms (Gubbiotti et al., 2019).

The management of encopresis in children with ASD requires a comprehensive, multidisciplinary approach that integrates both medical and behavioral interventions. Medical treatments aim to address physical factors

such as constipation, while behavioral therapies focus on helping children develop appropriate toileting habits and learn the defecation process. The combination of these two strategies is essential for effective management (Montgomery & Navarro, 2008).

However, in children with developmental disabilities such as ASD, the implementation of these treatment strategies can be particularly challenging. Cognitive and behavioral difficulties often make it difficult for children to engage in the necessary behavioral interventions, such as learning toileting routines or adjusting dietary habits. Furthermore, children with ASD may be particularly susceptible to issues such as food selectivity, which can limit fiber intake and exacerbate constipation, further complicating treatment (Call et al., 2017; Ustinova et al., 2019). Despite these challenges, there have been a limited number of case studies and randomized trials that report success with multidisciplinary approaches to the treatment of encopresis in children with ASD (Axelrod et al., 2016; Call et al., 2017; Mevers et al., 2020). These studies have demonstrated that, while successful, long-term interventions, consistent toileting schedules, and parent training are often required.

Atomoxetine, a selective norepinephrine reuptake inhibitor (SNRI), is primarily approved for the treatment of Attention-Deficit/Hyperactivity Disorder (ADHD) in children. Several case reports have highlighted the potential of atomoxetine in alleviating encopresis in children, both with and without ADHD (Şahin & Bozkurt, 2016; Yucel et al., 2015; Hergüner & Hergüner, 2012; Türkoğlu et al., 2015). In this study, we present a case series of four individuals with co-occurring ASD and ADHD to explore the potential effects of atomoxetine on encopresis. Our aim is to assess whether atomoxetine can improve encopresis symptoms in children with both ASD and ADHD, and to contribute to a better understanding of treatment options for this complex comorbidity.

CASES

Informed consent was obtained from all cases.

Case 1: An 8-year-old boy with a diagnosis of ASD referred to our clinic for encopresis and complaints of attention problems in lessons, couldn't reading and writing. In his history, it was learned that he was diagnosed with autism at the age of 4 and received special education support for autism for about 4 years. His intelligence level was within normal limits according to psychiatric examination and tests using the Wechsler Intelligence Scale for Children-Revised. He was diagnosed with ADHD/Inattentive type and encopresis with constipation and overflow according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM- 5). Atomoxetine 10 mg/day was initiated, and the dose was titrated up to 18 mg/day. In the examination 1 month after it was increased to the appropriate dose, the problem of encopresis was resolved. He has been using atomoxetine for 2 years, during this time, the encopresis did not recur, and he is still under follow-up.

Case 2: A 6-year-old non-verbal boy with a diagnosis of ASD referred to our clinic for encopresis and complaints of hyperactivity, aggression, screaming, and crying. He had been receiving special education support for autism since he was 3 years old. He had no history of psychiatric medication use. He was diagnosed as ASD, ADHD/Combined type and encopresis according to the DSM- 5. Atomoxetine 10 mg/day was initiated, and the dose was titrated up to 25 mg/day. During the treatment period, his encopresis decreased to once a week. In the summer, they stopped atomoxetine, encopresis repeated, and then atomoxetine was initiated again. Encopresis resolved. He has been followed for 4 years and is still using atomoxetine.

Case 3: A 7-year-old boy with a diagnosis of ASD referred to our clinic for encopresis and complaints of hyperactivity, impulsivity, and attention problems. He was verbal and going to the normal school. In the psychiatric assessment, he was diagnosed with ASD, ADHD/ Combined type and encopresis without constipation and overflow according to the DSM-5. Atomoxetine 10 mg/day was initiated, and the dose was titrated up to 20 mg/day. Encopresis was resolved in the examination 1 month after. In addition, his concentration and attention span were also improved, and academic success increased. He used atomoxetine for 1 year and then his family wanted to stop the drug. Encopresis did not recur after the drug was discontinued. He is still under follow-up

Case 4: A 7-year-old non-verbal boy with a diagnosis of ASD referred to our clinic for encopresis, inattention problems. He had been receiving special education

support since he was 3 years old. In his psychiatric assessment, he was diagnosed with ASD, ADHD/Inattentive type and encopresis with constipation and overflow according to the DSM- 5. Atomoxetine 10 mg/day was initiated, and the dose was titrated up to 20 mg/day. His encopresis improved, and it had beneficial effects on attention. During the summer break, the family stopped using atomoxetine and complained of encopresis restarted. Afterwards, atomoxetine was reinitiated, and encopresis resolved. He has been using atomoxetine for 4 years.

DISCUSSION

Encopresis is defined as the repeated passage of feces into inappropriate places, with a prevalence ranging from 1% to 3% in the pediatric population (Franco et al., 2015). It is classified into two subtypes: "with constipation and overflow incontinence" and "without constipation and overflow incontinence" (American Psychiatric Association, 2013). Children with encopresis often experience a range of challenges, including decreased organizational skills, attention difficulties, social problems, disruptive behaviors, and poor school performance (Cox et al., 2002; Johnston & Wright, 1993). These difficulties are compounded by the complex nature of encopresis and its impact on the child's daily functioning.

The regulation of bowel movements involves intricate physiological mechanisms, including both long- and short-acting reflexes, peptides, and neurotransmitters (Chatoor & Emmanuel, 2009). Additionally, individual variations in the tonic and phasic responses of the autonomic nervous system—responsible for maintaining continence—become evident early in childhood (Wass et al., 2015). These physiological factors contribute to the complexities of treating encopresis, particularly in children with co-occurring developmental disorders such as ASD.

Currently, there is no FDA-approved medication specifically indicated for the treatment of encopresis. However, various medications used to manage comorbid conditions have been shown to improve encopresis symptoms. For example, risperidone, when combined with non-pharmacological interventions, has demonstrated benefits in treating fecal incontinence in pediatric patients with psychiatric comorbidities. Its antagonistic effect on dopamine is believed to contribute to improvements in retention-type fecal incontinence (Zahed et al., 2024). Similarly, imipramine, a tricyclic antidepressant commonly used in ADHD treatment, has been found to help manage encopresis through its anticholinergic effects, which reduce gastrointestinal motility and increase sphincter tone

(Connell, 1972). Moreover, a study conducted on rats showed that amphetamine slowed gastric emptying and intestinal transit through its effects on the dopaminergic system (via D1 and D2 receptors) and, to a lesser extent, adrenergic receptors (Huang & Chien, 2012). There are case studies reporting that methylphenidate, with a mechanism similar to that of amphetamine, is also effective in treating encopresis (Yılmaz & Akça, 2013).

Several case studies have demonstrated the beneficial effects of atomoxetine in the treatment of encopresis. Sahin and Bozkurt reported a case of a 10-year-old child with ADHD, constipation, and overflow incontinence, in which atomoxetine treatment resulted in significant improvement in encopretic symptoms (Sahin & Bozkurt 2016). Similarly, Hergüner and Hergüner described two cases of children diagnosed with ADHD, aged 8 and 10, who presented with encopresis, constipation, and overflow incontinence. In both cases, atomoxetine led to symptomatic relief (Hergüner & Hergüner 2012). Furthermore, Türkoğlu et al. presented four cases of children with encopresis, two of whom had coexisting ADHD. In all cases, encopretic symptoms resolved following atomoxetine treatment, regardless of the type of encopresis (primary/secondary or retentive/non-retentive) (Türkoğlu et al. 2015). Yücel et al. reported that atomoxetine treatment resulted in the resolution of encopresis in a 7-year-old case with ADHD, combined type, as well as encopresis with constipation and overflow incontinence (Yücel et al. 2015). It has been suggested that the effects of ADHD medications on encopresis in individuals with ADHD may be related to their direct impact on executive functions, self-regulation skills, and impulse control, which enable children to recognize and respond to internal cues for defecation (Golubchik et al. 2009). In cases of encopresis accompanied by ADHD, Cox et al. suggested that due to the short attention span and lack of selective attention, the child could not notice the rectal stretching and could delay going to the toilet, and when he sat on the toilet he did not sit up to empty his stool completely due to his impulsivity (Cox et al. 2002). Some authors, however, have proposed that the effects of ADHD medications on encopresis may arise secondary to the resolution of child-parent relationship conflicts and improvements in poor social and academic functioning (Bilgiç 2011). These findings suggest that atomoxetine may have a positive impact on encopresis in children, particularly in those with ADHD, and support its potential as a therapeutic option for managing this challenging condition. In the study by Türkoğlu et al., the beneficial effects of atomoxetine on encopresis were observed in two patients who did not exhibit ADHD symptoms. It was suggested

that these effects may be mediated through atomoxetine's impact on peripheral gastrointestinal adrenergic receptors. Atomoxetine increases synaptic noradrenaline levels, which is a primary neurotransmitter of the sympathetic nervous system. Noradrenaline relaxes the internal anal sphincter through sympathetic efferent activity (Akervall et al., 1988). This relaxation may particularly contribute to the improvement of encopresis associated with constipation and overflow incontinence, where the internal anal sphincter is tightly strained. On the other hand, there is also a case study reporting an increase in the frequency of encopresis following atomoxetine treatment. The authors suggested that the elevation of norepinephrine by atomoxetine may have further exacerbated encopresis by affecting the tonic and phasic activity of the autonomic nervous system (Yektas et al., 2016).

In our case series, all four cases had ADHD co-occurring with ASD and encopresis. Following atomoxetine treatment, both ADHD symptoms and encopresis symptoms improved in these cases. Therefore, it remains unclear whether the improvement in encopresis was due to the enhancement of executive functions or through atomoxetine's effects on peripheral gastrointestinal adrenergic receptors. Given the challenges in treating encopresis, especially in individuals with ASD, atomoxetine may be considered a potential option for the treatment of encopresis in the presence of ADHD.

CONCLUSION

Encopresis associated with autism spectrum disorder is very difficult for children and families. Treatment options for encopresis in ASD are limited. With this case report, we found that atomoxetine may also be beneficial for encopresis by improving executive function in the presence of ADHD symptoms associated with ASD.

Ethical Considerations: Does this study include human subjects? YES

Authors confirmed the compliance with all relevant ethical regulations.

Conflict of interest: No conflict of interest

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Correspondence:

Sumeyra Firat,
Şehreküstü Mah. Mevlana Sk. No:7 Ladik/Samsun
Turkey
e-mail: drsumeyrafirat@gmail.com

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