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Case Report
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Noradrenergic Modulation of Appetite and Impulse Control: Reboxetine in a Treatment-Resistant Case of Bulimia Nervosa

Berkay Tayşi, Mahmut Cem Tarakçıoğlu

Department of Child and Adolescent Psychiatry, Istanbul University - Cerrahpaşa Faculty of Medicine, İstanbul, Türkiye

ABSTRACT

Bulimia nervosa (BN) is a severe eating disorder often linked to impulsivity and emotional dysregulation. Despite selective serotonin reuptake inhibitors (SSRIs) being the primary pharmacological intervention, a portion of patients continues to exhibit treatment resistance. We present the case of a 17-year-old female diagnosed with BN who demonstrated enduring binge-purge behaviors and diminished motivation, despite undergoing treatment with fluoxetine and sertraline, both administered alongside low-dose aripiprazole. The introduction of reboxetine, a selective norepinephrine reuptake inhibitor (NRI), resulted in prompt and enduring decreases in binge eating, termination of laxative use, and significant enhancements in motivation, mood, and social functioning. The combination of reboxetine and aripiprazole was well tolerated, with no adverse effects reported. This case report highlights the potential clinical impact of noradrenergic modulation in adolescents with treatment-resistant BN. Reboxetine may ameliorate core symptoms by enhancing impulse control and motivational drive, and its adjunctive use with aripiprazole may further support emotional regulation. These findings suggest that reboxetine, particularly when combined with aripiprazole, could serve as a promising pharmacological alternative for similar cases, warranting further clinical investigation. Reboxetine, particularly when combined with aripiprazole, may serve as a promising pharmacological alternative for treatment-resistant BN, necessitating additional clinical research.

Keywords: Bulimia nervosa, reboxetine, binge-eating

Corresponding author:
Berkay Tayşi

E-mail:
drberkaytaysi@gmail.com

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INTRODUCTION

Bulimia nervosa (BN) is an eating disorder marked by recurrent binge-eating episodes followed by inappropriate compensatory behaviors, including self-induced vomiting, excessive exercise, or laxative misuse, to prevent weight gain.[1] In recent findings, lifetime Diagnostic and Statistical Manual of Mental Disorders, 5th ed. (DSM-5) BN diagnosis is reported as 0.8-2.6% in young women in Western countries, with similar prevalence rates in other regions of the world.[2] There is a growing body of literature examining the pharmacotherapies for BN. Most of them reduced the frequency of binge-eating and vomiting episodes, body weight, and depressive symptoms in patients with BN; however, the efficacy was not statistically significant. The efficacy of each drug varies, addressing distinct aspects and symptoms to enhance the clinical outcomes for BN patients.[3] The sole medication presently approved by the U.S. Food and Drug Administration (FDA) for the treatment of BN is fluoxetine,

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a selective serotonin reuptake inhibitor (SSRI), which has proven effective in diminishing binge-purge episodes and improving related mood symptoms. However, despite its advantages, a considerable proportion of patients do not attain complete remission with fluoxetine alone, requiring the exploration of supplementary pharmacological approaches.[4] One option, the second-generation antipsychotic aripiprazole, has demonstrated efficacy in mitigating symptoms of bulimic eating behaviors owing to its distinctive pharmacological characteristics related to dopamine and serotonin receptor modulation.[5] Another option, although rarely employed in BN, is reboxetine, a selective norepinephrine reuptake inhibitor (NRI), which could provide therapeutic benefits by regulating appetite control and impulsive behaviors linked to binge eating.[6]

While reboxetine is infrequently initiated for BN treatment, a few studies and case reports indicate its potential efficacy in diminishing binge eating episodes and improving impulse control. These reports suggest that reboxetine's noradrenergic effects may play a role in appetite regulation and the diminishment of compulsive behaviors, positioning it as a potentially beneficial alternative or supplementary therapy in treatment-resistant scenarios.[6,7]

This case report demonstrates the clinical progression of a female adolescent diagnosed with BN according to DSM-5-TR version and comorbid major depressive disorder (MDD) as determined through a structured clinical interview using the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL), who exhibited partial resistance to standard SSRI therapy. It demonstrates the potential therapeutic advantages of integrating atypical pharmacological agents—namely reboxetine and aripiprazole—into the treatment protocol, leading to significant clinical improvement.

The study was conducted in accordance with the principles of the Declaration of Helsinki. Ethical approval was not required for this case report. Written informed consent was obtained from the patient and her legal guardians for participation and publication of this case report.

CASE PRESENTATION

A 17-year-old female patient with a 4-year history of disordered eating attitudes, starting after the coronavirus disease-2019 (COVID-19) pandemic, was referred to our outpatient clinic with symptoms of binge eating, purging, and the utilization of laxatives. Her body mass index was 20.2 kg/m^2, and her weight had increased by 17 kg over a period of 6 months.

She reported experiencing considerable anergia and anhedonia, characterized by a loss of interest and pleasure in activities she formerly enjoyed, including hobbies, socializing with friends, and participating in family events. Furthermore, she experienced significant anergia, characterized by enduring physical and mental fatigue that made even her daily tasks exhausting. She exited her conventional school environment, stating an incapacity to handle the academic and social pressures, and transitioned to remote education to better manage her condition in a less stressful environment. She also reported difficulties in attention-related tasks. She isolated herself from her friends and family, staying in her room for days. Her everyday existence revolved around thinking about her weight, accompanied by chronic depressed symptoms and diminished functioning. She was diagnosed with BN according to the DSM-5, text rev.

The initial treatment consisted of fluoxetine at a dosage of 20 mg/day, with an additional dose of aripiprazole at a dosage of 5 mg/day. In addition to pharmacological treatment, the patient received dietary interventions conducted by a dietitian who has experience working with eating disorder diagnosed patients; however, she didn't receive any psychotherapy. In the subsequent month, the dosage of fluoxetine was increased to a maximum of 60 mg/day. Despite the increase in dosage, after 3 months, binge-eating/purging episodes continued to occur (5-7 times for binge-eating and 10-12 times for purging per week), and the commitment to diet was inconsistent.

A gradual decrease in the dosage of fluoxetine was implemented, and sertraline was started at 50 mg/day and gradually increased to 200 mg/day within a month. Two months into the treatment with sertraline 200 mg/day and aripiprazole 5 mg/day, the patient continued to experience episodes of binge eating as well as ongoing thoughts about her weight and the amount of food she consumed.

Both fluoxetine and sertraline provided limited improvement in mood, binge-eating, and purging behaviors. No notable SSRI-related adverse effects were observed. This partial efficacy contextualized the clinical decision to transition to reboxetine.

Following the administration of reboxetine at a dosage of 4 mg twice daily, sertraline was gradually decreased. Within 3 weeks, despite her concerns about her body image, she experienced a reduction in the number of binge/purge episodes to 0-1 per week, an improvement in her hunger and irregular meal patterns, and she stopped using laxatives.

Over the course of 2 months, both anergia and anhedonia markedly resolved; she progressively returned to her academic endeavors, re-engaging with her coursework and demonstrating improved concentration, motivation, and task completion relative to her prior condition. Alongside her academic recovery, she reengaged in social activities, including meeting with friends, attending family gatherings, and partaking in recreational hobbies. These all indicate her social functioning and emotional well-being have been recovered. Throughout this phase of improvement, she stated that she did not encounter any adverse effects from her treatment protocol. Furthermore, she and her caregivers noted a substantial improvement in her overall quality of life. Follow-up and treatment have been ongoing through monthly visits for the past 5 months.

DISCUSSION

This case report suggests evidence that reboxetine medication, with adjunct aripiprazole, may be an effective treatment for BN, particularly in situations where SSRIs have been unsuccessful in treating the condition. The improvement in functionality, appetite management, and the frequency of binge eating may be due to this treatment protocol. In contrast to SSRIs, which target the serotonin pathways associated with mood and satisfaction, reboxetine acts on norepinephrine, which may be the reason for its beneficial effects. There is a connection between norepinephrine and impulsivity, as well as motivation and appetite.[8]

Several brief studies and small case series have indicated the potential advantages of NRIs in the treatment of BN.[6,7] These studies and series have been executed in a restricted number of instances. These reports suggest that NRIs may improve impulse control and regulate appetite pathways, consequently decreasing the incidence of

binge-purge episodes. Moreover, the activating properties of these substances may mitigate comorbid symptoms, such as anergia and diminished motivation, commonly seen in individuals with eating disorders. The preliminary findings underscore the necessity for additional research on the efficacy and safety of NRIs as an alternative or adjunctive treatment for BN, given the current limitations of available evidence.

The aripiprazole treatment adjunct to the reboxetine was maintained throughout treatment and is still ongoing. The concurrent use of aripiprazole may have contributed to the clinical improvement due to its partial agonist activity at dopamine D2 receptors and effects on serotonergic modulation.[9] The concomitant use of both reboxetine and aripiprazole may have contributed positively to the patient's clinical improvement. However, because both agents were administered simultaneously, it is difficult to determine the independent effect of each medication. This limits the ability to attribute the observed therapeutic benefits solely to reboxetine or aripiprazole. Future studies should consider evaluating each agent separately to clarify their individual contributions.

Another NRI, atomoxetine, approved for attention-deficit/hyperactivity disorder (ADHD), has small open-label studies and preliminary trials suggesting reductions in binge/purge frequency and improvements in impulsivity and attention, particularly at standard ADHD doses (e.g., 40-100 mg/day), though data remain limited and heterogeneous.[10-12] Mechanistically, both primarily inhibit the norepinephrine transporter (NET) and secondarily elevate prefrontal dopamine through NET blockade; atomoxetine's clinical profile is more thoroughly delineated in adolescents, whereas reboxetine's pediatric data are limited. Atomoxetine often causes a loss of appetite, upset stomach, and trouble sleeping.[12]

Even though there were no negative effects in this case, reboxetine can cause several side effects, such as insomnia, dry mouth, constipation, urinary hesitancy or retention, a faster heart rate, anxiety or agitation, and too much sweating. There have also been reports of orthostatic hypotension and high blood pressure.[13] During treatment, it is important to regularly check vital signs, sleep patterns, and any changes in behavior that may be occurring.

Adverse events were monitored only during the short-term treatment period; therefore, the long-term safety and tolerability of reboxetine, alone or in combination with aripiprazole, remain unknown and should be considered a limitation of this case report.

Even though aripiprazole and reboxetine were used concomitantly, reboxetine may still be associated with the improvement of behavioral and social abilities of the patient without causing any adverse effects. These findings may suggest that it could be safe and beneficial for adolescents with BN who are under close supervision.

CONCLUSION

For adolescents who are unresponsive to SSRIs for the treatment of BN, there may be a possibility that reboxetine could be an effective alternative treatment option, and it may be useful in reducing binge eating and the symptoms that are associated with it due to the noradrenergic effect that it possesses. When it comes to the pharmacological treatment of eating disorders, additional research, particularly randomized controlled trials, is required to show its function.

Learning Points

• Reboxetine, while prescribed infrequently in BN, may provide therapeutic advantages for patients exhibiting partial response to SSRI treatment by improving impulse control and energy levels.

• Aripiprazole, when used as an adjunct to the standard pharmacotherapy, may mitigate binge-purge behaviors and facilitate emotional stabilization in patients with bulimia.

• The combination of unconventional pharmacological agents may be an effective approach in treatment-resistant instances of BN, especially when affective symptoms and motivational deficits are evident.

Data Availability Statement: The data that support the findings of this study are available on request from the corresponding author.

Ethics Committee Approval: The study was conducted in accordance with the principles of the Declaration of Helsinki. Ethical approval was not required for this case report.

Informed Consent: Written informed consent was obtained from the patient and her legal guardians for participation and publication of this case report.

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