



Atomoxetine Induced Separation Anxiety; A Case Report

Atomoksetin Tedavisine Bağlı Ayrılma Anksiyetesi; Olgu Sunumu

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ABSTRACT

Atomoxetine, a selective norepinephrine (NE) inhibitor, is introduced as a safe non-stimulant alternative treatment of children and adolescents with attention deficit hyperactivity disorder (ADHD), especially co-morbid ADHD and anxiety disorder and/or Tourette syndrome. Generally known side effects were including weight loss, decrease appetite, nausea and somnolence, exacerbation of tics. In this paper, we want to present an adolescent case with ADHD-inattention type who developed separation anxiety during Atomoxetine treatment. It will be discussed in light of current knowledge about possible neurotransmitter systems associated with side effects of Atomoxetine. Consequently, atomoxetine treatment may trigger anxiety or obsessional thoughts although without any premorbid psychopathology. However, it is unclear whether effects of genetic, gender or adolescence period are associated with this.

Key Words: Atomoxetine, ADHD, Separation Anxiety

ÖZET

Atomoxetine, DEHB, (Dikkat Eksikliği Hiperaktivite Bozukluğu) tedavisinde, özellikle eş tanı olarak anksiyete bozukluğu ve Tourette bozukluğunun olduğu durumlarda uyarıcı olmayan, güvenilir bir alternatif tedavi olarak bilinen seçici norepinefrin geri alım inhibitörüdür. Çoğunlukla bilinen yan etkileri kilo kaybı, iştahta azalma, bulantı, uykuya eğilim ve tiklerde alevlenmedir. Bu yazıda Atomoksetin tedavisi sırasında ayrılma anksiyetesi geliştiren DEHB-dikkat eksikliği tanılı bir ergen olgu sunulacaktır. Güncel bilgiler ışığında Atomoksetin yan etkileri ile ilişkili muhtemel nörotransmitter sistemleri tartışılacaktır. Sonuç olarak Atomoksetin tedavisi premorbid psikopatoloji olmamasına rağmen anksiyeteyi ve obsesyonel düşünceleri tetikleyebilir. Ancak bu reaksiyonun cinsiyet, ergenlik ve genetik etkenlerle ilişkilendirilip ilişkilendirilemeyeceği kesin değildir.

Anahtar Kelimeler: Atomoksetin, DEHB, Ayrılma Kaygısı

INTRODUCTION

Attention Deficit/Hyperactivity Disorder (ADHD) is a common behavioral disorder found in 3–7% of school age children¹. ADHD is characterized by levels of increased motor activity, impulsiveness, distractibility, restlessness and inattention that is maladaptive and inconsistent with the child's developmental level. Three subtypes have been identified: inattentive, hyperactive/impulsive and combined (inattentive/hyperactive/impulsive)¹. Dysfunction in

the transmission of dopamine and norepinephrine has been defined in this disorder and medications that target the catecholaminergic system have been used as efficacious for treatment².

Atomoxetine, a selective norepinephrine (NE) inhibitor³, is introduced as a safe non-stimulant treatment of children and adolescents with attention deficit hyperactivity disorder (ADHD), especially for co-morbid ADHD and anxiety disorder and/or tourette syndrome⁴⁻⁵. It was approved by the US Food and Drug Administration

(FDA) in November 2002 for the treatment of ADHD in children⁶. The most frequently reported side effects are weight loss, decrease appetite, nausea and somnolence and arising of tics⁵⁻⁷. However, we did not find any anxiety reactions associated with atomoxetine to date. In this paper, we want to present a case with ADHD-inattention type who developed separation anxiety during atomoxetine treatment.

CASE REPORT

A was a female adolescent, at the age of 15. According to her family and teachers, she had inattention symptoms since then early childhood and without any prior history of anxiety disorder and/or symptoms. ADHD-inattention type was diagnosed according to DSM-IV classification.¹ Her mental motor development was normal range, and no family history for any psychiatric disorder. There was no previous treatment history for ADHD. She was 56 kg; atomoxetine 25 mg/day was given once day (morning) through two weeks and then 40 mg/day titrated up to the target dose as 60 mg/day. At the second week of this treatment (40 mg/day), obsessive and ruminative thoughts were observed such as my "parents do not like me", "I would not succeed my exam", and "I am a very stupid girl", excessively checking of appearance own body image. State and Trait Anxiety Inventory-State (STAI-state) and State and Trait Anxiety- Trait (STAI-trait) scales were given. STAI-state score was 49, STAI-trait score was 37. At the same time, sleep difficulties, fear of losing parents, crying through all day, not to sleep alone, fear of going crazy were reported and she weight loss 2 kg through second week and total blood count, renal functions, hepatic functions, thyroid functions, fasting blood glucose, Anti Streptolysin-O (ASO), Electrocardiogram (ECG) were normal. At the end of third week, during 40 mg/day atomoxetine treatment, all anxiety symptoms continued and she began refuse to go to school because of fear to separation from her parents.

She had diagnosed "Separation Anxiety Disorder" according to DSM-IV criteria¹.

Atomoxetine treatment was stopped, another medication or therapeutic attempt was not applied, and her symptoms resolved totally at sixth day and STAI-state scores reduced to 28 and STAI-trait scores reduced to 19. Currently she has not any anxiety symptoms four weekly and drug free.

DISCUSSION

To our knowledge, only one report was described about atomoxetine use and mood dysregulation including irritability, anxiety and hypomanic state in ten years old a male patient⁸.

This paper is first anxiety reaction associated with atomoxetine use anxiety in adolescent age group. It can be explained by possible norepinephrine transmitter system that triggered anxiety. Norepinephrine is involved with modulating attention, working memory, behavioral inhibition, planning alertness, arousal, and vigilance⁹. Atomoxetine is preferred for co-morbid ADHD and anxiety disorder because of its noradrenergic blocker effect in clinically. Increased concentrations of dopamine levels may also trigger anxiety reactions¹⁰. Similar to dopamine, low to moderate levels concentrations of NE can be beneficial in improving prefrontal cortex function although it's extremely high concentrations can be induced stress and anxiety symptoms like this case¹¹.

In this case, psychogenic stress or another physiological factor might be also triggered to anxiety symptoms. On the other hand, there is not a history that referred a psychological or physiologic factor such as premenstrual period, anemia, hypoglycemia. All laboratory tests were normal; negative life events or psychogenic stresses were not reported by her and her family. Especially, it is supported the idea of atomoxetine related side effect that her all anxiety symptoms improve at the sixth day of drug free period without any medical intervention. Adolescence period, female gender or other biological factors may

precipitate this side effect. Consequently, there is need for long term follow-up studies to prove association of anxiety and non stimulant treatment regimens.

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