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Case report
Olgu sunumu

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Auditory, visual and tactile hallucinations in a 16-year-old adolescent with high-dose duloxetine at one time

16 yaşındaki ergende tek seferde yüksek doz duloksetin kullanımı ortaya çıkan işitsel, görsel ve dokunsal halüsinasyonlar

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Abstract
Duloxetine is a dual-acting serotonin-noradrenaline reuptake inhibitor. It has FDA approval for the diagnosis of Major Depressive Disorder (MDD), Generalized Anxiety Disorder (GAD), Diabetic Neuropathic Pain, Fibromyalgia, Chronic Skeletal Muscle Pain in adults, and GAD in children and adolescents. This article presents a 16-year-old female patient referred to the emergency department with hallucinations starting after she took a total of 330 mg/day duloxetine for headaches. It is thought that her experienced hallucinations may be due to increased dopamine, as a result of inhibition of serotonergic system and noradrenaline transport system. It is thought that this article will contribute to the literature in terms of pharmacokinetic and pharmacodynamic effects of duloxetine in children and adolescents.
Keywords: Duloxetine, Hallucination, Adolescent

Öz
Duloksetin dual etkili serotonin-noradrenalin geri alım inhibitörüdür. Erişkinlerde Major Depresif Bozukluk (MDD), Yaygın Anksiyete Bozukluğu (GAD), Diyabetik Nöropatik Ağrı, Fibromiyalji, Kronik İskelet Kas Ağrısı tanılarında, çocuk ve ergenlerde GAD için FDA onayı vardır. Bu yazıda, baş ağrıları olduğu için toplam 330 mg/gün duloksetin içen sonrasında halüsinasyonları başladığı için acil servise başvuran 16 yaşındaki kadın hasta sunulacaktır. Halüsinasyonların serotonerjik sistem ve noradrenalin transport sisteminin inhibisyonu sonucunda dopamin artışına bağlı olabileceği düşünülmektedir. Bu yazı, duloksetinin, çocuk ve ergenlerdeki farmakokinetik ve farmakodinamik etkileri açısından literatüre katkı sağlayacağı düşünülmüştür.
Anahtar kelimeler: Duloksetin, Halüsinasyon, Ergen

Introduction

Duloxetine is a serotonin-noradrenaline reuptake inhibitor [1]. It has FDA approval for the diagnosis of Major Depressive Disorder, Generalized Anxiety Disorder, Diabetic Neuropathic Pain, Fibromyalgia, Chronic Skeletal Muscle Pain in adults, and GAD in children and adolescents older than 7 years old [2]. It has been reported that no dose adjustment is needed in children and adolescents, and that the dose is similar to that used with adults [3]. In a study conducted on the pharmacokinetics of duloxetine in children and adolescents, no clinically significant difference was found when compared with adults [4]. The most common side effects associated with duloxetine are nausea, dry mouth, dizziness, decreased appetite, constipation, and insomnia [5]. The most common psychiatric side effects are increased suicidal ideation, suicidal behavior, shift to mania, and hypomania [1]. In this article, a case with visual, auditory, and tactile hallucinations that occurred after 330 mg/day duloxetine use will be presented.

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Case presentation

A 16-year-old female patient was referred to our clinic from the emergency services for our evaluation. It was learned that no pathologies were found to explain hallucinations in cardiological, neurological examinations, blood (complete blood count, liver function tests, kidney function tests, electrolytes, glucose, blood lipids, thyroid function tests, and imaging tests (MR) before she was referred. The patient stated that she used one duloxetine 30 mg capsule (Cymbalta® 30 mg capsule), which her mother used for headaches; she then took 11 tablets in a row as one did not have any effect upon her. It was approved by her and her family that she had used a total of 330 mg. It was learned that she tried to sleep when it did not work; she woke up approximately five hours later and saw someone in the room. It was learned that her family waited, thinking that it would pass; however, a few hours later, she stated that the person she saw talked by touching her back. She communicated to her father by making a sign of a telephone with her hand, and was then referred to the emergency service with her family. The patient stated that, in addition to hallucinations, she had a tingling sensation in her feet and hands, a sense of flushing, difficulty in urinating, and feelings of palpitations. It was observed that the patient had difficulty sitting and following the speech content during the examination. She stated she was worried about hallucinations and that she saw the person she had seen before during the examination. She stated that she took the large quantity of drugs as she believed they would work if she took more. Although this situation suggests a suicide attempt, it was learned that there were no significant complaints from neither the patient's statements, nor the Beck Depression Scale and STAI-II scales she completed during the examination. At the same time, the history taken from her family revealed that she had no previous suicide attempts and self-injurious behavior. The fact that she did not have psychiatric complaints, depressive symptoms, suicidal thoughts, and active suicide plans, and that her hallucinations started all of a sudden after she took medication suggested that she did not have a psychiatric disease. The case was followed up without medication due to the uncommon hallucinations, their sudden onset and her good family functioning. With a close follow-up, it was observed that the hallucinations regressed after five days and that there were no active complaints. When psychopathologies were re-evaluated in the control appointment two weeks later, it was concluded that there was no active psychopathology.

When she was assessed with Naranjo Adverse Drug Reactions Probability Scale, she recorded six points, which suggested that the association of this adverse effect with duloxetine was “probable” [6]. It was thought that the hallucinations were an adverse effect of the high duloxetine. For this reason, considering the possible contribution to the literature, a case report was made upon the completion of a consent form from the patient and her family.

Discussion

Duloxetine, which is rarely used in Turkey since there is no reimbursement by insurance in children and adolescents, is thought to be safe in children and adolescents [7]. It is frequently preferred in the treatment of children and adolescents, as well as resistant MDD and GAD cases [8,9]. Although there are case reports in the literature that conclude duloxetine causes hallucinations [10–12], only one case report of hallucinations in children and adolescents was sourced [13]. It was reported that the case was followed up to observe any GADs, and that the hallucinations had started on the fifth day following when the duloxetine dosing commenced.

In case reports, there is no clear information in the literature about how duloxetine causes hallucinations. Since DAT is not very high in the prefrontal cortex, dopamine is removed from the synaptic space via NET [14]. It is thought that, increased dopamine in the synaptic range, alongside the NET inhibition of SNRIs, may cause hallucinations [15]. It is also emphasized that serotonin may cause hallucinations as a result of increased dopamine in the ventral striatum via 5HT2 and 5HT3 receptors, as a consequence of the inhibition reuptake [16–18]. It is also said that even if the SNRIs are weak, they can increase the dopamine level by inhibiting the dopamine reuptake pump (dopamine transporter) [14].

The presence of multiple drug use in some reports and the presence of an underlying psychopathology in some reports may be considered as a confusing factor in the relationship between hallucinations and duloxetine. In the present study’s case, the lack of underlying psychopathology provides an opportunity to say something more clearly about the relationship between hallucination and duloxetine. In addition, the fact that duloxetine was reportedly used within the appropriate dose range in cases in which it is reported to cause hallucinations, as well as that it was not within the appropriate dose range in our case suggests that this adverse effect is dose-independent.

Conclusions

Hallucinations occurring in the onset of treatment and in dose changes suggest that there is a need to be wary and conscious of hallucinations in every stage of the treatment in cases that use duloxetine.

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