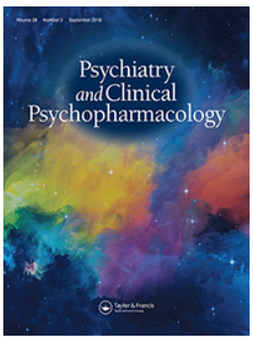

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Kemal Utku Yazici & Ipek Percinel Yazici

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CASE REPORT

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Visual hallucination induced by duloxetine use: a male case diagnosed with generalized anxiety disorder

Kemal Utku Yazici and Ipek Percinel Yazici

Department of Child and Adolescent Psychiatry, Firat University Medical Faculty, Elazig, Turkey

ABSTRACT

Duloxetine is a serotonin-noradrenaline reuptake inhibitor. It has been increasingly used in child and adolescent psychiatric practice in recent years. In this paper, we presented a 16-year-old male patient diagnosed with generalized anxiety disorder who had developed visual hallucinations after treatment with duloxetine. The visual hallucinations resolved after duloxetine were stopped. To the best of our knowledge, this is the first reported case from the adolescent age group who described visual hallucinations during duloxetine treatment.

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Adolescent; duloxetine; generalized anxiety disorder; visual hallucination

Introduction

Duloxetine is a serotonin-noradrenaline reuptake inhibitor (SNRI). A review of the literature shows that duloxetine is used with increasing frequency for treatment of many psychiatric disorders of the childhood and adolescent periods including major depressive disorder, generalized anxiety disorder (GAD), attention deficit hyperactivity disorder, somatoform disorders, and overactive bladder [1–5]. Common side effects observed with duloxetine use include nausea, vomiting, abdominal pain, dry mouth, loss of appetite, headache, dizziness, fatigue, somnolence, and sedation [6].

In this paper, we discuss a male case receiving duloxetine treatment for GAD who experienced visual hallucinations during the treatment that were thought to be associated with duloxetine use.

Case presentation

Sixteen-year-old male case had been followed-up in a child and adolescent psychiatry outpatient clinic in an external centre for 3 years with a diagnosis of GAD. During that time, the patient had received sertraline, fluoxetine, citalopram, venlafaxine, clomipramine, lorazepam, alprazolam, mirtazapine, hydroxyzine, and propranolol treatments, either alone or in combination, with adequate duration and proper dosage. Additionally, the patient had received 12 sessions of cognitive-behavioral therapy. The case presented to our clinic because he did not see benefit from previous treatments. At the time of presentation, he had intense anxieties, believing that something bad would happen to himself or his loved ones, and that he would fail in his exams. His extremely perfectionistic and meticulous personality was prominent. He was fidgety. He stated that he could not control his thoughts, could not get his anxieties out of his mind, and therefore, had difficulty in falling asleep and could not sleep adequately. His anxieties had adverse effects on school performance and his relationships with friends and his family. Upon evaluation, the case was diagnosed with GAD. Additionally, he had moderate depressive symptoms. In consideration of his previous medication history, it was decided to start duloxetine treatment. Laboratory tests performed prior to treatment (complete blood count, liver function tests, kidney function tests, electrolytes, glucose, blood lipids, and thyroid function tests), vital signs, and cardiovascular system examination did not show any abnormalities. The case had not been using any medications during the 2 months prior to his presentation to our clinic. He did not experience any serious adverse drug reactions associated with the psychotropic medications that he had been using before. Duloxetine 30 mg/day was initiated. On the fifth day of treatment, the case, together with his family, presented to our outpatient clinic as an emergency. The case stated that he saw strange visions since the night before, sometimes a white cat and sometimes a black dog was passing near, and the cat and the dog were looking at him as if they were going to attack. He told that these visions persisted for the whole night, so he could not sleep comfortably. It was learned that the case did not use any other medications during this time. The case was consulted with paediatric neurology, but no organic aetiology that could explain the visual hallucinations

CONTACT Ipek Percinel Yazici ipek.pr@hotmail.com

was found. Two days after discontinuing duloxetine treatment, his visions disappeared completely. Naranjo Drug Adverse Reaction Scale was applied [7], and the case had a score of 6. This score indicated that the visual hallucination was "probably" due to duloxetine. Based on all these findings, it was considered that the visual hallucination could be an adverse effect associated with duloxetine use.

Discussion

Duloxetine is an SNRI that has been increasingly used in child and adolescent psychiatry practice in recent years. Its effects/side effects in paediatric and adolescent cases are not clearly known yet. However, some studies propose that duloxetine can be used in paediatric population without any need for dose adjustment, at the same doses as adults, and that it is well tolerated [6]. A 2015 randomized placebo-controlled trial found that duloxetine was more effective than placebo in treatment of GAD in paediatric and adolescent age groups, and that it could be used safely [4]. In consideration of the previous treatment history of our case, it was decided to initiate duloxetine treatment. However, the case developed visual hallucinations on the fifth day of duloxetine treatment (30 mg/day dose) that were considered to be due to duloxetine treatment. During the period when visual hallucinations occurred, the case was only receiving duloxetine. Additionally, he did not describe any drug or substance use prior to duloxetine treatment. He had discontinued his previous psychiatric medications approximately 2 months before. In addition to all these features in his medical history, our assumption that his visual hallucinations were due to duloxetine treatment was further supported by the fact that his visual hallucinations disappeared completely 2 days after discontinuing duloxetine treatment.

In the literature, visual hallucinations that are thought to be associated with duloxetine use have been previously reported in three adult cases [8–10]. To our knowledge, there is no previous report of a paediatric or adolescent case on this subject. It is not clear how duloxetine induces visual hallucination. Increased dopamine release that is thought to result from inhibition of noradrenaline transporters in the prefrontal cortex, or increased dopamine as a result of inhibition of serotonin reuptake may be the reason for such adverse effects [10–12].

There are several reports of hallucinations induced by selective serotonin reuptake inhibitors (SSRI) in the literature [13,14]. This suggests that inhibition of serotonin reuptake, which is a main mechanism of action of duloxetine, may be the cause of hallucinations in our case. Serotonin reuptake inhibition (SSRI/SNRI) can lead to psychotic symptoms either by directly inhibiting dopamine reuptake or by increasing dopamine levels, particularly in the ventral striatum, via 5HT2 and 5HT3 receptors [13,15,16]. Furthermore, another important mechanism of action of SNRIs is inhibition of norepinephrine transporters (NETs). In the prefrontal cortex, NETs do not only transport norepinephrine. Dopamine is also carried by NETs in this part of the brain. Indeed, NETs present in the prefrontal cortex show higher affinity towards dopamine compared to norepinephrine. Thus, inhibition of NETs by SNRIs results in an increased amount of dopamine in the prefrontal cortex [17]. There are reports of hallucinations caused by venlafaxine, which is another NSRI, observed both in adolescent and in adult cases [18,19].

In our case, we thought the visual hallucinations occurred as a result of increased dopamine, either as a result of inhibition of serotonin reuptake, or inhibition of NET. However, our case did not experience visual hallucinations during his previous treatments including SSRIs (sertraline, fluoxetine, and citalopram) and venlafaxine. This suggests that the possible responsible mechanism was inhibition of NET rather than the inhibition of serotonin reuptake. Additionally, although the case did not develop visual hallucinations with venlafaxine in the past, it is known that venlafaxine shows a primarily serotonergic effect at low doses with increasing noradrenergic effect as the dose is increased, and in a general sense, inhibition of serotonin reuptake is more prominent than inhibition of norepinephrine [17]. This may explain why our case did not develop visual hallucinations during venlafaxine treatment.

To our knowledge, this is the first reported case from the adolescent age group who described visual hallucinations during duloxetine treatment. It is important for clinicians to be aware of such possible adverse effects during treatment with duloxetine, which has been increasingly commonly used in child and adolescent psychiatric practice. We believe our report has significance in this context. This subject should be elaborated with future studies.

Disclosure statement

No potential conflict of interest was reported by the authors.

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