

Diplopia; an Adverse Effect of Citalopram

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Abstract

Citalopram, a selective serotonin reuptake inhibitor (SSRI), was approved by the Food and Drug Administration in 1998 as a safe and well-tolerated antidepressant; the use of it may result in rare and sometimes dangerous side effects. Diplopia is a rare adverse effect of citalopram that comes with double vision and disrupts daily living. Currently, only two cases of citalopram-related diplopia have been internationally reported. The current paper presents a third reported case of diplopia following citalopram use in a healthy subject. A 47-year-old man involved in an accident was subsequently affected by serious depression. Following 6 months of a 40-mg daily dose of citalopram, the patient complained of itchy irritated eyes and double vision symptomatic of diplopia. He was referred to an eye specialist, who confirmed no apparent problems following an examination of the eye. After a decrease in the dose of citalopram, the eye symptoms steadily decreased and eventually disappeared. The rapid disappearance of diplopia subsequent to the discontinuing use of citalopram suggests an association between the adverse reaction and the medicine. As a result, it is recommended that physicians inform patients of the possibility of induction of diplopia related to the use of citalopram and other SSRIs. In the future, the prescription of SSRIs at higher doses may be ordered with and on the recommendation of patients, who have been aware of the risks of the drug.

Keywords: Diplopia, Double vision, Adverse effect, Citalopram

Introduction

Eye movement is controlled by extraocular muscles that are innervated from oculomotor nerves and the supranuclear centrum. Diplopia can occur because of damage or injury to these structures, making it impossible for both eyes to look in the same direction. Diplopia is defined and more commonly known as "double vision". Binocular diplopia is a type of double vision that is eliminated when either eye is occluded (1).

Citalopram is an antidepressant that affects serotonergic neurotransmission through the potent and selective inhibition of serotonin reuptake. Neuroendocrine studies suggest a decrease in serotonergic responsiveness in patients with major depression. Citalopram is more effective than a placebo in treating depression; like tricyclic and tetracyclic antidepressants and other SSRIs, therapeutic doses up to 60 mg/d are safe and well-tolerated (2). A study investigating 3107 patients from 24 clinical trials revealed mild to moderately severe side effects of citalopram, including nausea, dry mouth, somnolence, increased sweating, tremors, diarrhea, and ejaculation failure with significant frequency (3).

Although citalopram has been reported to be a safe and well-tolerated SSRI antidepressant, rare phenomena and dangerous adverse reactions may occur. Diplopia is an unusual phenomenon that may occur after citalopram ingestion (4). A review based on reports from the Food and Drug Administration and social media between 1999 and 2012 revealed that out of 25938 people, who experienced side effects when taking Celexa, only 109 people (0.42%) experienced double vision. Celexa contains the active ingredients of citalopram hydrobromide (5).

To the best of our knowledge, there have been just two cases of diplopia associated with citalopram (4, 6). One report presented a case of a person with HIV and hepatitis C co-infection, who developed diplopia while being treated with citalopram (6); thus, it cannot be firmly concluded that diplopia was associated with citalopram use because diplopia was also reported, following interferon treatment (7). Although the patient was on interferon treatment for 1 year, she had no diplopia since citalopram was discontinued (6). Therefore, diplopia induced by citalopram has remained controversial.

Herein, we report diplopia, following citalopram medication in a healthy subject.

Case report: While driving a car, a 47-year-old man was involved in rollover accidents, but he did not suffer a concussion or a loss of consciousness. However, he did subsequently suffer from severe depression, premature fatigue, hopelessness, loss of energy, forgetfulness, lack of desire and motivation, and also decreased libido. He did not show any indications of post-traumatic stress disorder or neurological symptoms. This patient was referred to our clinic 2 years after the onset of his symptoms without any history of depression, psychiatric illness, or a family history of mood disorders. Furthermore, the patient was not preoccupied with the accident and did not show any symptoms of delusions, hallucinations, or obsessions. According to the Diagnostic and Statistical Manual of Mental Disorders, after a clinical interview, the patient was diagnosed with depression. The patient started taking 25 mg of sertraline and gradually increased the dosage to 100 mg. After 2 weeks, the sertraline was discontinued because of dizziness and intolerance.

A new dosage of 10 mg of citalopram was ordered and was increased to 40 mg during three weeks. The patient's symptoms were reduced by approximately 30%–40% as indicated by the Visual Analog Scale (VAS). To increase the treatment's efficacy, 150 mg of bupropion was added daily and discontinued after two weeks due to the patient's tinnitus and headaches. The patient was instructed to continue his treatment with citalopram. After six months of taking citalopram, the patient returned with complaints of itchy eyes related to diplopia. He was referred to a neurologist and an ophthalmologist, neither found any problems during their examinations. The patient was instructed to reduce the daily dosage of citalopram and then to stop taking it after three weeks. As a result, the patient's eye symptoms gradually decreased and disappeared spontaneously. To offset the patient's sensitivity to SSRIs, 40 mg of duloxetine was administered daily, divided into multiple smaller doses. After three months, the patient's symptoms of depression improved significantly.

Discussion

Here we report the case of a man, who developed diplopia as the result of citalopram therapy. According to the neurological and ophthalmological examinations and the lack of medical reasons for the observation of diplopia, which resolved after citalopram withdrawal, there likely is a link between this adverse event and citalopram.

Although the *Physicians' Desk Reference* mentions diplopia as an adverse effect of sertraline treatment, 2 clinical cases of citalopram-induced diplopia have been identified in the literature. The basic etiology of this phenomenon is unknown and may be related to the eye's interneuronal serotonergic fibers (8). The cases of diplopia have been reported following psychotropic treatment with drugs such as topiramate, lamotrigine, and oxcarbazepine (9). In these cases, diplopia can be associated with ciliary spasm, the effusion of the ciliary body and peripheral uveal, interneuronal serotonergic fibers of the eye, or anticholinergic activity (9). Two clinical cases of acute

myopia and diplopia, which are attributable to the use of aripiprazole, have also been reported (10, 11). In these cases, diplopia was not associated with anticholinergic mechanisms because aripiprazole lacks anticholinergic activity (12). Moreover, patients showed no anticholinergic symptoms, and there was insufficient evidence of other mechanisms to clarify the reason for diplopia (10, 11). As diplopia has been reported after the high doses of antidepressants, such as citalopram and sertraline, the role of ocular interneuronal serotonergic fibers is more believed to have led to diplopia.

Here, we report a case of diplopia related to citalopram. Notably, this is the third report, while two of them are from Iran (6). Although the diagnosis will likely remain controversial, further evidence of the cause-effect and the possible etiology relation may be found in a large number of patients. However, physicians are made aware of the possible risk of diplopia induced by SSRIs and the prescription should be ordered on the recommendation of physicians.

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Authors' Contributions

Hamzeh Hosseini visited and followed the patient, gathered the data, and revised the final draft of the manuscript. Amirhossein Ahmadi analyzed the data, wrote the first draft, and revised the final draft of the manuscript.

Conflict of Interests

The authors declare no conflict of interest.

References

1. Rhee D, Pyfer M. *The Wills Eye Manual*. 3rd ed. Philadelphia, PA: Lippincott Williams and Wilkins; 1999:2–3.
2. Keller MB, Citalopram therapy for depression: a review of 10 years of European experience and data from U.S. clinical trials. *J Clin Psychiatry* 2000; 61:896–908.
3. Wang SM, Han C, Bahk WM, Lee SJ, Patkar AA, Masand PS, et al. Addressing the side effects of contemporary antidepressant drugs: a comprehensive review. *Chonnam Med J* 2018; 54:101–12.
4. Dorell K, Cohen MA, Huprikar SS, Gorman JM, Jones M. Citalopram-induced diplopia. *Psychosomatics* 2005; 46:91–3.
5. Review: Will Celexa cause Double vision?. (*eHealthMe*, Jan2019).
6. Mowla A, Ghanizadeh A, Ashkani H. Diplopia with citalopram: a case report. *J Clin Psychopharmacol* 2005; 25:623–4.
7. Riedel RR, Schmitt A, Hartmann A. Ocular pseudo-myasthenic reaction induced by interferon in an AIDS patient. *Klin Wochenschr* 1999; 69:930–931.
8. Sener EC, Kiratli H. Presumed sertraline maculopathy. *Acta Ophthalmol Scand* 2001; 79:428–30.
9. Laurence Brunton, Bruce Chabner, Bjorn Knollman. *Goodman and Gillman's The Pharmacological Basis of Therapeutics*. 12th ed. NewYork: McGraham-Hill Companies; 2011. p.583–607.
10. Selvi Y, Atli A, Aydin A, Yener H. Aripiprazole-related acute transient myopia and diplopia: a case report. *J Clin Psychopharmacol* 2011; 31:249–50.
11. Atli A, Yildiz A, Kaya MC. Aripiprazole-induced diplopia: a case report. *Bulletin of Clinical Psychopharmacology* 2013; 23:353–6.
12. Chew ML, Mulsant BH, Pollock BG, Lehman ME, Greenspan A, Kirshner MA, et al. A model of anticholinergic activity of atypical antipsychotic medications. *Schizophr Res* 2006; 88:63–72.