

Spontaneous ejaculation; caused by venlafaxine, reverted by mirtazapine

Mehmet Akif Camkurt

Department of Psychiatry, Afsin State Hospital, Kahramanmaraş, Turkey

ABSTRACT

Spontaneous ejaculation is a rare side effect of antidepressants. SSRIs, SNRIs, and reboxetine are reported to cause spontaneous ejaculation. Previous reports suggest to stop or change medication in the presence of this side effect, and less is known how to manage patients who want to continue the medication with this side effect. Mirtazapine is a noradrenergic and specific serotonergic antidepressant, mostly used for the treatment of depression. It is recommended as an add-on pharmacotherapy to relieve sexual side effects. Here, we demonstrate a case of spontaneous ejaculation, caused by venlafaxine, and reverted by mirtazapine.

Eur Res J 2015;1(3):157-159

Keywords: Spontaneous ejaculation; management; venlafaxine; mirtazapine

Introduction

Venlafaxine is a dual reuptake inhibitor of serotonin and noradrenaline. It is widely used to treat depressive and anxiety disorders [1]. The frequency of sexual side effects with antidepressants are reported to be about 58-73% [2] and 36% of psychiatrists prefer to change medication when sexual side effects occur [3]. Spontaneous ejaculation is a rare sexual side effect of antidepressants, mostly reported by serotonergic and noradrenergic reuptake inhibitors [4, 5]. According to previous reports antidepressant switch is suggested to manage spontaneous ejaculation

[6]. We have limited information about pharmacological management of spontaneous ejaculation.

Mirtazapine is a noradrenergic and specific serotonergic antidepressant, mostly used for treatment of depression. As far as we know, mirtazapine cause fewer sexual side effects and recommended as an add on treatment for antidepressant induced sexual side effects [7-9]. Here, we present a case report of spontaneous ejaculation, caused by venlafaxine and reverted by mirtazapine.

Address for correspondence:

Mehmet Akif Camkurt, MD, Department of Psychiatry, Medicine, Afsin State Hospital, Kahramanmaraş, Turkey

Email: Dr.akif@gmail.com

Received: 23.06.2015; Accepted: 17.09.2015; Published Online: 04.11.2015

Case Presentation

A 29-year-old male patient, admitted to our clinic to prescribe his drugs. During the psychiatric interview, he stated he was on venlafaxine 75 mg/d treatment for 1 year, his symptoms were headache and neck ache, spasm in shoulders, feeling anxious and being worried about all fields of life at the beginning of his illness. Patient said that he was feeling well with venlafaxine, his symptoms were mostly gone, but he was experiencing loss of sexual desire and spontaneous ejaculation following micturition and defecation 3 weeks after initiation of venlafaxine. Urological consultation and total urine examination didn't explain this condition. We offered patient to stop medication, because we thought it was related to venlafaxine. Patient refused to stop venlafaxine because of its' beneficial effects on his symptoms, so we started mirtazapine 30 mg/d. Because to the best of our knowledge, mirtazapine is beneficial for management of loss of sexual desire caused by antidepressants and also has fewer sexual side effects. At the visit 2 weeks after starting mirtazapine, patient stated frequency of spontaneous ejaculation decreased apparently. At the visit after 6 weeks, spontaneous ejaculations ended up and loss of sexual desire relieved. At the visit after 3 months patient was still stable and free of spontaneous ejaculation.

Discussion

Spontaneous ejaculation is a rare side effect of antidepressants. There are several reports of spontaneous ejaculation with noradrenergic drugs. Three cases of spontaneous ejaculation due to noradrenergic drugs was reported by Oosterhuis *et al.* [10]. First case was a 40-year-old man taking atomoxetine, second one a 25-year-old man using methylphenidate and third case was a 60-year-old man whom was started venlafaxine. In addition, two cases were reported with a specific noradrenergic reuptake inhibitor reboxetine [4, 11]. nefazodone, milnacipran and zotepine are other noradrenergic drugs that caused spontaneous ejaculation [12-14]. In our case, although

venlafaxine is a dual reuptake inhibitor of serotonin and noradrenaline, thus we think potential mechanism related with spontaneous ejaculation is serotonergic mechanism, because patient was taking venlafaxine 75 mg per/day.

Belli *et al.* [6] reported spontaneous ejaculation and erectile dysfunction with escitalopram. They switched to fluvoxamine to manage this side effect. Virit and Savas [15] described a 27-year-old man who experienced spontaneous ejaculation after initiation of citalopram and they changed citalopram with paroxetine to stop spontaneous ejaculation. Although some SSRIs are reported to cause spontaneous ejaculation, however it is a fact that they are used effectively for treatment of premature ejaculation [6, 15, 16]. Taking into account both SSRIs cause spontaneous ejaculations rarely and ejaculation inhibition frequently, we interpret that spontaneous ejaculation is a unique and patient specific side effect due to antidepressants. Owing to diverse effects of SSRIs on ejaculation, it is not easy to explain exact mechanisms of ejaculation and spontaneous ejaculation.

Mechanisms of ejaculation depends on central and peripheral interaction of multiple systems. These systems could be sorted as parasympathic, sympathetic, dopaminergic and adrenergic systems. In the rat models, suppressor effects of serotonin have been demonstrated on ejaculation. However various serotonin receptors may effect ejaculation in different ways [17]. Somatodendritic 5HT_{1A} stimulation shortens ejaculatory latency time, conversely postsynaptic 5HT_{2c} stimulation causes ejaculation inhibition. selective alpha 1 receptor antagonists like tamsulosin and alfuzosin are responsible from decreased ejaculate volume [18].

Mirtazapine is a noradrenergic and specific serotonergic antidepressant. It has a unique receptor binding profile, differentiating from other antidepressants. Mirtazapine increases serotonergic and noradrenergic stimulation, regardless of reuptake inhibition. Alpha 2 auto receptor plays a crucial role in acting mechanism of mirtazapine and its' antagonism causes disinhibition of serotonergic and noradrenergic transmission. Likewise, mirtazapine blocks 5HT_{2c} and 5HT₃ [19].

To date, in most cases changing or stopping medication recommended to manage spontaneous

ejaculations. To the best of our knowledge, almost all antidepressants are related with this side effect, also less is known about how to manage spontaneous ejaculation if patient refuses to change medication with this side effect. Our case is important in terms of demonstrating mirtazapine combination as an option to manage spontaneous ejaculation. Mirtazapine was chosen in this patient for two reasons. First, combination of mirtazapine with antidepressants is suggested by previous studies, to relieve sexual side effects and second mirtazapine itself has fewer sexual side effects [7]. Furthermore, alpha 2 agonistic and 5HT_{2c} and 5HT₃ antagonistic properties of mirtazapine are believed to relieve diminished sexuality in depression and sexual side effects of antidepressants [9]. In this context, alpha 2 agonism and 5HT_{2c} and 5HT₃ antagonism of mirtazapine could be the potential regulatory mechanisms that stopped spontaneous ejaculation in our case.

Conclusion

Management of spontaneous ejaculation with mirtazapine hasn't been reported before. It is the first case report suggests combination of mirtazapine as a novel option to treat spontaneous ejaculation caused by antidepressants.

Informed Consent

Written informed consent was obtained from the patient for the publication of this case report.

Competing interests

The authors declare that they have no competing interests with respect to the authorship and/or publication of this article.

References

- [1] Clerc GE, Ruimy P, Verdeau-Pailles J. A double-blind comparison of venlafaxine and fluoxetine in patients hospitalized for major depression and melancholia. *Int Clin Psychopharmacol.* 1994 Sep;9(3):139-43.
- [2] Montejo AL, Llorca G, Izquierdo JA, Rico-Villademoros F. Incidence of sexual dysfunction associated with antidepressant agents: a prospective multicenter study of 1022 outpatients. Spanish Working Group for the Study of Psychotropic-Related Sexual Dysfunction. *J Clin Psychiatry.* 2001;62(Suppl 3):10-21.
- [3] Dording CM, Mischoulon D, Petersen TJ, Kornbluh R, Gordon J, Nierenberg AA, et al. The pharmacologic management of SSRI-induced side effects: a survey of psychiatrists. *Ann Clin Psychiatry.* 2002 Sep;14(3):143-7.
- [4] Sivrioglu EY, Topaloglu VC, Sarandol A, Akkaya C, Eker SS, Kirli S. Reboxetine induced erectile dysfunction and spontaneous ejaculation during defecation and micturition. *Prog Neuro-Psychopharmacology Biol Psychiatry.* 2007 Mar 30;31(2):548-50.
- [5] Yanik M. Spontaneous orgasm started with venlafaxine and continued with citalopram. *Can J Psychiatry.* 2004 Nov;49(11):786.
- [6] Belli H, Aslaner D, Ural C, Vardar MK, Yesilyurt S, Gul ES. Escitalopram related erectile dysfunction and spontaneous ejaculation during micturition. *West Indian Med J.* 2010 Dec;59(6):715-6.
- [7] Gelenberg AJ, Laukes C, McGahuey C, Okayli G, Moreno F, Zentner L, et al. Mirtazapine substitution in SSRI-induced sexual dysfunction. *J Clin Psychiatry.* 2000 May;61(5):356-60.
- [8] Shimojo M, Imai Y, Nakajima K, Mizushima S, Uemura A, Kohsaka S. Interleukin-2 enhances the viability of primary cultured rat neocortical neurons. *Neurosci Lett.* 1993 Mar 19;151(2):170-3.
- [9] Boyarsky BK, Haque W, Rouleau MR, Hirschfeld R. Sexual functioning in depressed outpatients taking mirtazapine. *Depress Anxiety.* 1999;9(4):175-9.
- [10] Oosterhuis I, Heijting L, van Puijenbroek E. Spontaneous ejaculation with the use of noradrenergic reuptake inhibitors. *Eur J Clin Pharmacol.* 2012 Oct;68(10):1461-2.
- [11] O'Flynn R, Michael A. Reboxetine-induced spontaneous ejaculation. *Br J Psychiatry.* 2000 Dec;177:567-8.
- [12] Micheal A, Ramana R. Nefazodone-induced spontaneous ejaculation. *Br J Psychiatry.* 1996 Nov;169(5):672-3.
- [13] Wang PW, Wang SY, Huang CJ. Zotepine-induced spontaneous ejaculation. *Int J Clin Pharmacol Ther.* 2008 Nov;46(11):571-3.
- [14] Yoshida K, Higuchi H, Takahashi H, Shimizu T. Ejaculation after defecation without orgasm induced by milnacipran. *J Neuropsychiatry Clin Neurosci.* 2004 Fall;16(4):544.
- [15] Virit O, Savas HA. Citalopram-associated spontaneous ejaculations. *J Clin Psychopharmacol.* 2008 Jun;28(3):360-1.
- [16] Safarinejad MR. Safety and efficacy of escitalopram in the treatment of premature ejaculation: a double-blind, placebo-controlled, fixed-dose, randomized study. *J Clin Psychopharmacol.* 2007 Oct;27(5):444-50.
- [17] Giuliano F, Clément P. Physiology of ejaculation: emphasis on serotonergic control. *Eur Urol.* 2005 Sep;48(3):408-17.
- [18] Hellstrom WJG, Sikka SC. Effects of acute treatment with tamsulosin versus alfuzosin on ejaculatory function in normal volunteers. *J Urol.* 2006 Oct;176(4 Pt 1):1529-33.
- [19] Stahl SM. Stahl's essential psychopharmacology: neuroscientific basis and practical applications. Cambridge University Press; 2013.