

# Reboxetine Induced Painful Ejaculation: A Case Report

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## ÖZET:

Reboksetinle indüklenmiş ağrılı ejakülasyon: Bir olgu sunumu

Cinsel işlev bozuklukları antidepresan ilaçların önemli ve sık karşılaşılan yan etkilerinden olup bazen tedavinin erken bırakılmasına neden olabilir. Reboksetin önceleri cinsel yan etkisi olmayan bir ilaç olarak bilinmekteydi. Ancak, biz burada reboksetin tedavisine başladıktan kısa bir süre sonra ağrılı ejakülasyon geliştirmiş olan bir olguyu sunmaktayız. Kırk yaşındaki bu hastaya depresyonu nedeniyle reboksetin tedavisi başlanmıştı. Başlanan 4 mg/gün dozundaki reboksetin tedavisinden 3 hafta sonra hasta ağrılı ejakülasyondan şikayetçi olmaya başladı. Tedavinin kesilmesinden sonra hastanın ağrılı ejakülasyonu kendiliğinden düzeldi. Reboksetin ile erkek hastaların tedavisinde cinsel yan etkiler, özellikle de ağrılı ejakülasyon dahil ejakülasyon bozuklukları akılda bulundurulmalıdır.

**Anahtar sözcükler:** reboksetin, ağrılı ejakülasyon, cinsel işlev bozukluğu

*Journal of Mood Disorders* 2011;1(4):166-8

## ABSTRACT:

Reboxetine induced painful ejaculation: a case report

Sexual dysfunction is one of the important and common side effects of the antidepressant drugs. It can sometimes result in early discontinuation of the treatment. Reboxetine was previously not known to cause sexual side effects. However, we present here a case who developed painful ejaculation shortly after initiation of reboxetine treatment. The patient, a 40 years old male, was prescribed reboxetine treatment for his depression. Before the treatment he did not have any sexual dysfunction. Three weeks after initiation of reboxetine 4 mg/day treatment the patient started to complain about painful ejaculation. After cessation of the treatment his painful ejaculation spontaneously subsided. Sexual side effects particularly in terms of ejaculation disorders including painful ejaculation should be kept in mind when treating male patients with reboxetine.

**Key words:** reboxetine, painful ejaculation, sexual dysfunction

*Journal of Mood Disorders* 2011;1(4):166-8

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Kabul tarihi / Date of acceptance:  
18 Aralık 2011 / December 18, 2011

## Bağıntı beyanı:

M.A.A., O.D., Y.B.: Yazarlar bu makale ile ilgili olarak herhangi bir çıkar çatışması bildirmemişlerdir.

## Declaration of interest:

M.A.A., O.D., Y.B.: The authors reported no conflict of interest related to this article.

## INTRODUCTION

Antidepressant-induced sexual dysfunction sometimes may be an important reason for non-compliance with the medication (1,2). Sexual dysfunction associated with antidepressant use interferes with quality of life, self-esteem, mood, and relationship with partner (1,3). Sexual side-effects of the antidepressants are important aspects of these drugs to be considered when planning a treatment regimen. Decreased sexual arousal and libido, orgasm, and ejaculation problems are among the most common sexual side effects of the antidepressants (4). According to some studies in the literature, types of the sexual dysfunction varies across antidepressant classes. Tricyclic antidepressants (TCAs) may have negative impact on all phases of sexual behavior (5), whereas selective serotonin reuptake inhibitors (SSRIs)

are mainly associated with ejaculation and orgasm problems such as delay or inhibition of them (6). Additionally, selective noradrenalin reuptake inhibitors (sNARIs) occasionally cause erectile dysfunction (7).

Sexual side effects resulting from antidepressants may be mediated by a number of central and peripheral mechanisms. Serotonergic system plays a major role in etiology of sexual dysfunction during antidepressant treatment. Regarding to sexual side effect profile, TCAs provoke higher rates of sexual dysfunction than SSRIs and SNRIs, respectively. Bupropione, moclobemide, reboxetine, mirtazapine, nefazodone have more favorable sexual side effect profile compared to escitalopram, paroxetine, venlafaxine, sertraline, or fluoxetine (1,8). Several strategies have been employed for management of patients with sexual dysfunction associated with antidepressant treatment, including spontaneous resolve,

behavioral strategies to modify sexual technique, individual and couple psychotherapy, delaying the intake of antidepressants until after sexual activity, reduction in daily dosage, use of adjuvant treatments, and switching to a different antidepressant (9).

Reboxetine which mainly acts by binding to the norepinephrine transporter and blocking the reuptake of extracellular norepinephrine, is the first selective norepinephrine reuptake inhibitor used in depression treatment. It has been reported that reboxetine has no predominant sexual side effects (2,4). Here, we describe a patient with major depressive disorder, who experienced sexual dysfunction (i.e. painful ejaculation) associated with reboxetine treatment.

## CASE

A 40 year old man was referred to our outpatient clinic with depressive symptoms. He had been suffering from anergia, anhedonia, avolition, depressed mood, and pessimistic thoughts known as characteristic symptoms of depression without any sexual dysfunction. His Montgomery Asperg Depression Rating Scale (MADRS) score was 39 in his first visit. He was sexually active and reported 1 or 2 episodes of sexual intercourse per week. He was diagnosed with "Major Depressive Disorder" according to Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV). He reported neither previous psychiatric history nor use of any antidepressant drug. Reboxetine 4 mg/day was prescribed to the patient for his depression considering his predominant symptoms related with psychomotor retardation. After 3 weeks, during the second visit, he reported painful ejaculation that began concurrent with initiation of the treatment. Reboxetine treatment was stopped after his complaint of painful ejaculation. After cessation of reboxetine his ejaculatory complaints subsided spontaneously without any need for further medical interventions. After discussing alternative treatments with the patient, cognitive behavioral psychotherapy was planned for his depression. During the following 8 weeks the patient was provided psychotherapy as planned. At the end of the last session, his MADRS score was 14 (>50% reduction), which indicates significant clinical improvement. He reported neither ejaculation problem nor any other sexual dysfunction during this treatment period.

## DISCUSSION

It is widely accepted that antidepressant reboxetine has a considerably favorable sexual side effect profile. Its non-serotonergic mechanism makes it superior to other antidepressant agents. Reboxetine can be an alternative drug when sexual side effects are observed with the other antidepressant agents. Supporting this suggestion some previous studies reported that sexual function and satisfaction in depressed patients had improved greater during treatment with reboxetine than treatment with paroxetine or fluoxetine (2,10). However, it should be kept in mind that reboxetine is not totally free of sexual side effects. Reboxetine-induced prolonged orgasm of reduced intensity and seminal emission after defecation was reported by Haberfellner in 2002 (11). Both disorders were accompanied by pain and ceased within two days after discontinuation of the drug. The side effects of reboxetine may include painful ejaculation as emerged in this case. Painful ejaculation following the administration of reboxetine has been previously described in two patients by Demyttenaere and Huygens in 2002 (7). It has also been shown that tamsulosin, the selective  $\alpha$ 1A-adrenoceptor antagonist, rapidly and completely resolved the painful ejaculation and urinary hesitancy in these patients. Abnormal ejaculation (primarily painful ejaculation) was also reported as a side effect by 20% (11/56) of male patients receiving reboxetine by Clayton et al in 2003 (2). In addition to other ejaculation side effects, our case also provides modest evidence that painful ejaculation can also occur with reboxetine treatment. The mechanism of antidepressant induced painful ejaculation remains obscure. To explain it two possible mechanisms were proposed. First is the partial blockade of peripheral sympathetic adrenergic receptors similar to the one observed during TCA use. It is suggested that this action could interfere with coordinated contractions of the smooth muscles involved in semen transport and thus induce painful spasms (12). Second is that the noradrenaline potentiation could interfere with the ejaculatory mechanism, thereby inducing a painful spasticity. This hypothesis can indeed explain why painful ejaculation has predominantly been described both with TCAs (desipramine, imipramine, nortriptyline and clomipramine) and reboxetine. It could also explain why painful ejaculation has been reported with the dual uptake inhibitor venlafaxine (13).

## CONCLUSION

Sexual dysfunctions are common problems encountered during antidepressant treatment and should be assessed thoroughly during treatment, as well as during the course of psychiatric disorders. The data available about reboxetine suggest that sexual side effects with this drug are infrequent. Although reboxetine may be a good alternative for patients suffering from sexual side effects of other antidepressants, individual

vulnerabilities for such side effects should be considered. Sexual side effects particularly in terms of ejaculation disorders that include painful ejaculation should be taken into account prior to administration of reboxetine or while switching to reboxetine due to sexual side effects induced by other antidepressant agents. Clinicians should also consider to discuss alternative treatment strategies like psychotherapy with these patients who are vulnerable to some side effects of antidepressants including ejaculatory problems.

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