

## CASE REPORT

# Painful Ejaculation with Cyclobenzaprine: A Case Report and Literature Review

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### ABSTRACT

**Introduction.** Sexual dysfunction is a well-known side effect of antidepressants. Painful ejaculation is a rare side effect that has been reported with the use of some psychiatric drugs such as tricyclic antidepressants. Cyclobenzaprine is a muscle relaxant that is structurally similar to tricyclic antidepressants. It is the most commonly prescribed muscle relaxant in the United States and accounts for 18% of all prescriptions written for chronic back pain.

**Methods.** A 55-year-old man was referred to our pain medicine clinic for evaluation and treatment of pain with ejaculation.

**Main outcome Measure.** The main outcome measure was to review the current published literature and case reports on painful ejaculation from medication use, in particular tricyclic antidepressants.

**Results.** After discontinuation of cyclobenzaprine, our patient's sexual dysfunction resolved. This result was consistent with the literature reviewed on the topic.

**Conclusion.** Painful ejaculation is likely an underreported side effect of tricyclic antidepressants and cyclobenzaprine use. Fortunately, these symptoms are reversible and discontinuation of these medications is typically an effective cure. **Kraus MB, Wie CS, Gorlin AW, Wisenbaugh ES, and Rosenfeld DM. Painful ejaculation with cyclobenzaprine: A case report and literature review. Sex Med 2015;3:343–345.**

**Key Words.** Cyclobenzaprine; Orgasmic Disorder; Sexual Dysfunction; Ejaculation

### Introduction

Sexual dysfunction is a well-known side effect of antidepressants. Painful ejaculation, also referred to as post-orgasmic pain, dysorgasmia, or orgasmalgia, is a rare side effect that has been reported with the use of tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, as well as antipsychotic drugs [1–8]. Cyclobenzaprine is a commonly prescribed muscle relaxant that is structurally similar to TCAs. We present a case of painful ejaculation secondary to cyclobenzaprine

use, discuss proposed mechanisms, and offer a literature review of this side effect with other related drugs.

### Case Report

A 55-year-old man was referred to our pain medicine clinic for evaluation and treatment of pain with ejaculation. Two years prior, he underwent hip surgery that was complicated by retroperitoneal and inguinal hematoma. Postoperatively, he complained of muscle spasms and was prescribed

cyclobenzaprine 10 mg daily. A few weeks after the initiation of cyclobenzaprine, he began to have pain on ejaculation located in the right groin region.

Over the course of 2 years, he noticed worsening pain on ejaculation escalating to 10/10 on the visual analog scale. He described the pain as a sharp, stabbing pain located in the groin area, predominantly on the right. The pain would maintain that intensity for a few minutes before slowly improving and ultimately resolving after 10 minutes. The pain was only on ejaculation, he denied symptoms during erection, arousal, or intercourse. In addition, he occasionally had a small volume of ejaculate. He denied any dysuria or difficulty urinating. He had no history of sexual or urologic dysfunction. This significantly affected his quality of life and resulted in reduced sexual activity. He was referred to our clinic by a urologist. The urologist did a thorough physical exam, including a full genitourinary and prostate exam that was unremarkable. He also sent urine analysis, culture, and prostate-specific antigen, which were normal. After evaluation in our clinic, he was advised to discontinue cyclobenzaprine. He returned for reevaluation 6 weeks later to report complete resolution of his pain. He stated that he saw notable improvement 2 weeks after stopping cyclobenzaprine. Subsequently, he started methocarbamol for muscle spasms in his lumbar and hip regions without any significant side effects. He remained symptom free at 3 months.

## Discussion

The estimated prevalence of ejaculatory pain is between 1% and 6.7% among the general population [1]. Mainly located in the penis, pain usually lasts less than 5 minutes. Patients may also experience pain in the testes, rectum, and abdomen [9,10]. It is associated with prostatitis, ejaculatory duct obstruction, benign prostatic hyperplasia, chronic pelvic pain syndrome, and radical

prostatectomy. Treatment options include physical therapy, alpha-blockers, pudendal nerve blocks and surgical procedures [1,11].

Painful ejaculation is a known side effect of various medications. Sixteen cases were identified in eight case reports and research studies with painful ejaculation related to antidepressant and antipsychotic use. Three case reports and one experimental study were identified describing ten cases of painful ejaculation related to TCA use (see Table 1). No reports or articles were identified related to cyclobenzaprine or muscle relaxant use and sexual dysfunction.

Male erection, ejaculation, and orgasm are complex mechanisms. The arousal phase, which leads to an erection in men, is mediated largely by parasympathetic fibers from S2, S3, and S4 spinal segments. The orgasmic phase is directed largely by the sympathetic fibers. Emission is an adrenergic function while ejaculation involved the tonic-clonic contraction of the bulbocavernosus and ischiocavernosus muscles under some degree of parasympathetic control [13]. Ejaculation is comprised of contraction of the seminal vesicals and ejaculating ducts with simultaneous closure of the internal sphincter of the urethra. Ejaculation is mediated by peripheral sympathetic alpha 1A-adrenoreceptors.

Two hypothetical mechanisms have been proposed to cause painful ejaculation with the use of TCAs. The first proposes that a partial blockade of peripheral sympathetic adrenergic receptors could interfere with coordinated contractions of smooth muscles involved in semen transport and thus induce painful spasms or retrograde ejaculation [3,13]. Problems with this theory include the striking differences in the incidence of this side effect among drugs that have comparable alpha1-adrenoceptor inhibition, and with drugs that have very low alpha blockade such as venlafaxine. Also, there is a reported case of painful ejaculation with fluoxetine, which does not have significant alpha-

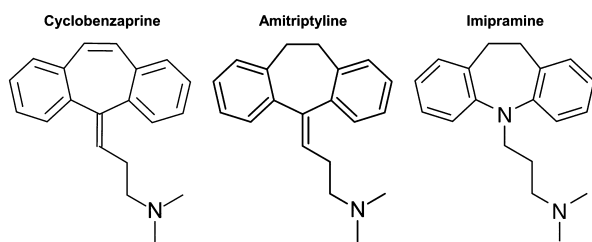
**Table 1** Case reports and experimental studies which identified painful ejaculation related to TCA use

First author	Drug(s)	Dose	Drug class	Symptoms	Urinary symptoms?	Outcome
Kulik [3]	Amoxaprine	75 mg daily	TCA	Pain radiating to testicles, decreased ejaculate	No	Resolved when discontinued
Aizenberg [2]	Imipramine Clomipramine	125 mg daily 150 mg daily	TCA	Painful ejaculation	No	Resolved when discontinued
Monteiro [12]	Clomipramine	NA	TCA	Pain at orgasm	Yes	NA
Simpson [4]	Desmethylimipramine	225 mg daily	TCA	Painful orgasm	Yes	NA

NA = not applicable; TCA = tricyclic antidepressant.

adrenergic receptor affinity [1]. The second explanation states that noradrenaline potentiation could interfere with the ejaculatory mechanism thereby inducing a painful spasticity. This is also supported by the successful use of tamsulosin for the treatment of painful ejaculation. Tamsulosin is a prostate-specific alpha-adrenergic receptor blocker. It acts via smooth muscle relaxation of the bladder neck and prostate resulting in reduced bladder outlet obstruction. Demyttenaere treated two men who complained of urinary hesitancy and painful ejaculation after reboxetine treatment with tamsulosin. One week later, both symptoms resolved [5]. Barnas and colleagues published a prospective study of 98 patients with orgasmic pain given tamsulosin. Overall improvement was 77% with complete resolution in 13% of patients [9].

Cyclobenzaprine is the most commonly prescribed muscle relaxant in the United States and accounts for 18% of all prescriptions written for chronic back pain [14]. In addition to its antihistamine, anticholinergic, and sedative properties, cyclobenzaprine is a weak inhibitor of norepinephrine and serotonin reuptake. It was developed as an antidepressant, but had more adverse side effects and less antidepressant effects than other drugs. It is structurally quite similar to TCAs. (Figure 1) Although its mechanism as a muscle relaxant has not been fully elucidated, cyclobenzaprine is thought to act on the brain stem inhibiting both gamma and alpha motor systems [15]. Common side effects of cyclobenzaprine include fatigue, drowsiness, headache, nausea, constipation, and confusion. To our knowledge, this is the first formal report of this painful ejaculation secondary to cyclobenzaprine use in the literature. We propose that the mechanism of cyclobenzaprine-induced painful ejaculation is similar to TCAs given their structural similarities.



**Figure 1** The chemical structures of cyclobenzaprine, amitriptyline, and imipramine, highlighting the similarities.

## Conclusion

Painful ejaculation is likely an underreported side effect of TCAs and possibly cyclobenzaprine [12]. This side effect is likely more prevalent than the literature suggests because patients may not report sexual dysfunction [4]. Awareness of these effects may lead to anticipatory reassurance or discontinuation of cyclobenzaprine and the initiation of an alternative muscle relaxant. Fortunately, painful ejaculation because of a medication use is reversible. In our case, as with others reported, discontinuation of the causative medication led to resolution of symptoms. In summary, cyclobenzaprine is a commonly prescribed muscle relaxant associated with possible sexual side effects.

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## References

- 1 Ilie CP, Mischianu DL, Pemberton RJ. Painful ejaculation. *BJU Int* 2007;99:1335–9.
- 2 Aizenberg D, Zemishlany Z, Hermesh H, Karp L, Weizman A. Painful ejaculation associated with antidepressants in four patients. *J Clin Psychiatry* 1991;52:461–3.
- 3 Kulik FA, Wilbur R. Case report of painful ejaculation as a side effect of amoxapine. *Am J Psychiatry* 1982;139:234–5.
- 4 Simpson GM, Blair JH, Amuso D. Effects of anti-depressants on genito-urinary function. *Dis Nerv Syst* 1965;26:787–9.
- 5 Demyttenaere K, Huygens R. Painful ejaculation and urinary hesitancy in association with antidepressant therapy: Relief with tamsulosin. *Eur Neuropsychopharmacol* 2002;12:337–41.
- 6 Hsu JH, Shen WW. Male sexual side effects associated with antidepressants: A descriptive clinical study of 32 patients. *Int J Psychiatry Med* 1995;25:191–201.
- 7 Michael A. Venlafaxine-induced painful ejaculation. *Br J Psychiatry* 2000;177:282–283.
- 8 Kotin J, Wilbert DE, Verburg D, Soldering SM. Thioridazine and sexual dysfunction. *Am J Psychiatry* 1976;133:82–5.
- 9 Barnas J, Parker M, Guhring P, Mulhall JP. The utility of tamsulosin in the management of orgasm-associated pain: A pilot analysis. *Eur Urol* 2005;47:361–5, discussion 365.
- 10 Barnas JL, Pierpaoli S, Ladd P, Valenzuela R, Aviv N, Parker M, Waters WB, Flanigan RC, Mulhall JP. The prevalence and nature of orgasmic dysfunction after radical prostatectomy. *BJU Int* 2004;94:603–5.
- 11 Delavierre D, Sibert L, Rigaud J, Labat JJ. Painful ejaculation. *Prog Urol* 2014;24:414–20.
- 12 Monteiro WO, Noshirvani HF, Marks IM, Lelliott PT. Anorgasmia from clomipramine in obsessive-compulsive disorder. A controlled trial. *Br J Psychiatry* 1987;151:107–12.
- 13 Petrie WM. Sexual effects of antidepressants and psychomotor stimulant drugs. *Mod Probl Pharmacopsychiatry* 1980;15:77–90.
- 14 Luo X, Pietrobon R, Curtis LH, Hey LA. Prescription of nonsteroidal anti-inflammatory drugs and muscle relaxants for back pain in the United States. *Spine* 2004;29:E531–7.
- 15 Biggs JT, Spiker DG, Petit JM, Ziegler VE. Tricyclic antidepressant overdose: Incidence of symptoms. *JAMA* 1977;238:135–8.