

Priapism due to a Single Dose of Quetiapine: A Case Report



Fuat TORUN¹, Elif YILMAZ¹, Eyüp GÜMÜŞ²

SUMMARY

Priapism is characterized by a prolonged and painful erection in the absence of sexual desire and arousal. Priapism is a rare and serious side effect of psychotropic drugs, and is thought to be attributable to blockage of alpha-1 adrenergic receptors in the corpus cavernosum. Although priapism is commonly associated with typical antipsychotics, there are some (but not many) case reports of priapism due to atypical antipsychotics. This side effect has been reported in patients taking ziprasidone, risperidone, clozapine, quetiapine, aripiprazole, and olanzapine. Not all antipsychotics bind to alpha-1 adrenergic receptors with the same intensity; as compared to other antipsychotics, quetiapine has an intermediate affinity. Priapism could be considered an idiosyncratic reaction, because it is correlated neither with the dose nor duration of psychotropic drug use. Herein we present a case of priapism caused by a single 300-mg dose of quetiapine, and a brief review priapism in the light of this case.

Key Words: Priapism, quetiapine, atypical antipsychotic

INTRODUCTION

Priapism is characterized by a prolonged and painful erection in the absence of sexual desire and arousal (Compton and Miller 2001). Priapism is a rare and serious side effect of psychotropic drugs, and is thought to be attributable to blockage of alpha-1 adrenergic receptors in the corpus cavernosum (Segraves 1989). Thirty percent of priapism cases are caused by a drug, and more than 50% of these cases are attributable to antipsychotic drugs (Brichart et al. 2008). Most psychiatric patients encounter cases of priapism after the use of conventional antipsychotics and trazodone. Although priapism is commonly associated with typical antipsychotics, there are some (but not many) case reports of priapism due to atypical antipsychotics, such as clozapine, quetiapine, risperidone, olanzapine, ziprasidone, and aripiprazole (Rosen and Hanno 1992; Seftel et al. 1992; Emes and Milson 1994; Tekel and 1995; Diermenjian et al. 1998; Sood et al. 2008).

The literature contains several case reports of priapism occurring after the use of quetiapine. In the first case report 675 mg of quetiapine caused priapism (Pais and Ayzavian 2001); subsequent case reports highlighted that a daily standardized dose of quetiapine might also lead to priapism, and that priapism is correlated neither with the dose nor duration of psychotropic drug use (Daval and Rukstalis 2005). Herein we present a case of priapism caused by a single 300-mg dose of quetiapine, and a brief review of priapism associated with atypical antipsychotics in the light of this case.

CASE

YU was a 50-year-old male that had been imprisoned because of drug abuse for 4 months. His history of drug abuse for the previous 4 months was negative. He presented to our psychiatry outpatient clinic with complaints of insomnia, irritability, intolerance against people in the ward, and restlessness. He was

Received: 08.11.2010 - **Accepted:** 10.01.2011

We thank Fethah Tosun, MD for his help during the emergency room treatment of the presented case.

¹MD, Psych., Department of Psychiatry, ²MD, Assoc. Prof., Department of Urology, Umraniye Training and Research Hospital, İstanbul
Fuat Torun MD., e-mail: fuatorun@hotmail.com

TABLE 1. Atypical antipsychotic affinity for alpha-1 adrenergic receptors.

Antipsychotic	Affinity for alpha-1 adrenergic receptors*
Ziprasidone	38.5
Risperidone	37.0
Clozapine	14.7
Quetiapine	12.0
Paliperidone	9.9
Aripiprazole	3.9
Olanzapine	1.9

*[107*M -1]. Higher values indicate higher affinity (Andersohn et al. 2010).

well groomed, and his speech was coherent and appropriate (normal rate, volume, and rhythm). His affect was restricted and sad. He described his mood as depressed. His thought on the content of the thought had not to deserve to be in prison. He denied having hallucinations. The patient did not report any psychiatric disorders, except for drug abuse. Based on his psychiatric evaluation, he was diagnosed with substance abuse-early full remission, according to DSM-IV.

As he had a history of drug abuse, it was recommended that he take quetiapine 300 mg o.p.d. in the evening. Quetiapine is preferred due to relapse prevention of substance abuse, affective symptoms, anger controlling, and insomnia (Croissant et al. 2006). He presented to an emergency room due to a painful penile erection (priapism) a few hours after taking the drug; the painful erection continued for 28 h. The emergency room examination by a urologist and subsequent investigations suggested no pathology that could explain priapism, and it was therefore attributed to the use of quetiapine. He had taken no drug other than quetiapine before presenting to the emergency room.

He had no physical disease, perineal trauma, or history of priapism. Whole blood count and urine analysis were normal. He was immediately hospitalized in the department of urology and underwent a bilateral cavernosal intervention for the administration of adrenalin combined with drainage, but his erection returned. Despite cavernosal drainage being performed 4 times, his erection returned even though it almost fully regressed. His priapism was thought to be due to quetiapine, and a psychiatric consultation was ordered. Considering that an antipsychotic may have caused the patient's priapism, treatment with antidepressants and anxiolytics was initiated. During the subsequent follow-up visits he reported that he had no re-occurrence of priapism

DISCUSSION

A search of the PubMed and EBSCOHost databases showed that only 9 cases of priapism had been published (Pais and Ayvazian 2001; du Toit et al. 2004; Davol and Rukstalis 2005;

TABLE 2. Conditions associated with priapism.

Physical obstruction	Decreased blood flow	Drugs
Trauma	Sickle cell disease	Anti-psychotics
Tumors	Leukemia	Anti-depressants
Spinal-cord injuries	Multiple myeloma	Anti-coagulants
Stroke	Nephrotic syndrome	Anti-hypertensives
	Hyper viscosity states	Anxiolytics

(Hosseini and Polonowita 2009)

Harrison et al. 2006a,b; Prado and Formoso 2006; Casiano et al. 2007; Birnbaum and Pinzone 2008; Geraci et al. 2010); the presented case is the 10th. The presented case is interesting because of the absence an accompanying physical disease and he did not use any other medicine except quetiapine, as well as the occurrence of priapism after a single 300-mg dose of quetiapine.

It is important to know the risk factors, etiology, mechanism, and relationship of dosage and duration of treatment in priapism cases. Priapism is caused by blockage of venous drainage in the corpora cavernosa. Physical obstruction of the venous system, blood dyscrasias, stasis of blood flow in the venous system, and alpha-1 adrenergic receptor blockage can lead to priapism. Dysregulation of smooth muscle cell tone in the penile vascular tissue, leading to hypoxia and ischemia, has been proposed as the most probable pathway of drug-induced priapism (Yuan 2008). One of the pharmacological mechanisms that can cause penile vascular dysregulation is blockade of alpha-1 adrenergic receptors, which might also play a crucial role in priapism associated with antipsychotics (Sood et al. 2008).

Atypical antipsychotics differ in affinity to adrenergic receptors. Among the atypical antipsychotics, ziprasidone and risperidone have the highest affinity, with clozapine and quetiapine having moderate affinity, and paliperidone, aripiprazole, and olanzapine having the lowest affinity (Table 1) (Andersohn et al. 2010). Priapism is a specific (idiosyncratic) condition that may occur during any stage of antipsychotic treatment, independent of dose and duration of use (Thompson et al. 1990). As priapism occurred in the presented case following a 300-mg dose of quetiapine, we wonder if priapism would occur if we would start with lower doses of quetiapine and titrate up slowly.

In patients treated with psychotropic drugs a prolonged and painless erection lasting 15-30 min in the absence of sexual activity, may be an indicator of priapism. In such cases it will be sufficient to stop the medicine the patient is using. We stopped antipsychotic medication in the presented case due to symptoms of anxiety. Then, escitalopram and alprazolam were started, and the patient's treatment continued with these drugs. In such cases, an incomplete history taking such as substance abuse, sickle cell anemia, which can cause priapism or neglect of these situations may cause an irreversible impo-

tence. It is important to inform patients treated with antipsychotics about the possible side effects and to monitor them. The presented case did not have any medical conditions known to be associated with priapism. Clinicians should assess the likelihood of developing priapism before starting medications known to be associated with priapism (Table 2).

The literature contains a number of case reports of priapism occurring with concomitant use of quetiapine. A case report was about with the use of quetiapine at the dose of 675 mg for a suicidal purpose (Pais and Ayyazian 2001). In another case report a patient taking risperidone and trazodone developed priapism. His treatment was then changed to quetiapine 600 mg d⁻¹ and he again developed priapism 24 d later. Then, he was treated with olanzapine and 53 d later he developed priapism again. Finally, loxapine were chosen because it is associated minimal alpha-1 adrenoceptor blockade, and the patient had no additional episodes of priapism (du Toit et al. 2004). Another patient experienced priapism with the use of quetiapine 600 mg d⁻¹ (Daval and Rukstalis 2005). Neither of these 2 patients had a concomitant disease or was treated with another drug that could cause priapism. It was reported that an HIV-positive gay patient developed priapism after the use of quetiapine concurrently with an amphetamine, and it was recommended that drug abuse should be take into consideration in such cases (Harrison et al. 2006b). In another patient aged 77 years with Alzheimer's dementia quetiapine was initiated in order to prevent irritability and aggression; after the dose was increased to 175 mg d⁻¹ the patient developed priapism (Harrison et al. 2006a).

Priapism was reported in a patient taking quetiapine, clozapine, and haloperidol (Casiano 2007), and in a patient taking antiretroviral treatment and perphenazine (Geraci et al. 2010). A patient with the sickle cell trait that was abusing alcohol and other substances attempted suicide by ingesting 7-9 quetiapine tablets, and subsequently developed priapism. Medications used prior to presentation included quetiapine, amlodipine, atorvastatin, quinapril, glipizide, duloxetine, and divalproex sodium, though he was not taking them regularly (Birnbaum and Pinzone 2008). Based on these reports we think that multiple drug use is a risk factor for priapism.

The literature includes several reports of priapism following the use of atypical antipsychotics other than quetiapine. Clozapine is an atypical antipsychotic that has been used for years, the first reported case of priapism caused by an atypical antipsychotic was associated with clozapine. Of those patients, who has been reported to develop priapism because of a treatment with clozapine at a high dose, also low doses of clozapine use can cause priapism (Sood et al. 2008).

Risperidone has a high affinity for alpha-1 adrenergic receptors (Richelson 1999). The literature contains reports of the use of risperidone alone, and combined with paroxetine (Yang and Tsai 2004), citalopram (Freudenreich 2002), olanzapine and

fluvoxamine (Seger and Lamberti 2001) leading to priapism. One case report described a patient that was taking quetiapine and trazodone that developed priapism twice, and after switching to risperidone priapism recurred (Rosenberg et al. 2009). The dose of olanzapine associated with priapism ranges from 5-100 mg (Sood et al. 2008). A single dose of olanzapine inducing priapism has been described (Hosseini and Polonowita 2009). The risk of priapism increases in cases of multiple medication use due to any medical conditions or combined use of psychotropic drugs. Although there is no study showing that lithium alone causes priapism, it has been reported that addition of lithium to olanzapine treatment (Jagadheesan et al. 2004), or addition of olanzapine and lithium to risperidone treatment (Owley et al. 2001) leads to priapism. Moreover, of all the atypical antipsychotics olanzapine is the only agent reported to cause clitoral priapism (Medina 2002).

Although ziprasidone is the atypical antipsychotic that causes alpha-1 adrenergic blockage most frequently, only 3 cases of priapism have been attributed to the use of ziprasidone (Sood et al. 2008), which is probably due to the fact that ziprasidone is not commonly use at present. In the first priapism case associated with aripiprazole it was reported that priapism occurred 6 h after a single dose (Mago et al. 2006). In this patient priapism developed within 7 days despite discontinuation of aripiprazole treatment, and recurred 2 times. It was reported that the patient had diabetes mellitus, hypertension, and hyperlipidemia, in addition to a psychological disorder, and used atorvastatin and metformin together with aripiprazole. In another case priapism occurred due to a combination of lithium and oxcarbazepine used concomitantly with aripiprazole, although it could not be determined which drug caused priapism (Negin and Murphy 2005).

To date, the literature does not contain any reports on the relationship between priapism and the use of such atypical antipsychotics as paliperidone, sertindole, zotepine, amisulpride, bifeprunox, or melperone.

CONCLUSION

Clinical use of atypical antipsychotics is increasing. As increased clinical use will lead to an increase in the incidence of sexual side effects such as priapism, clinicians must be aware of these side effects. Priapism can occur during every stage of treatment due to use of psychotropic drugs in addition to an antipsychotic. It is impossible to predict which patients will develop priapism. When treating patients with a history of priapism, drug abuse, or sickle cell anemia (conditions that increase the risk of priapism) clinicians should be careful and always inquire about sexual side effects during follow-up visits. If a patient complains of painless and frequent erections, priapism should be considered a likely outcome and the currently used antipsychotic should be changed, if necessary.

REFERENCES

- Andersohn F, Schmedt N, Weinmann S et al. (2010) Priapism associated with antipsychotics: role of alpha1 adrenoceptor affinity. *J Clin Psychopharmacol*, 30:68-71.
- Andres Prado MJ, Vidal Formoso V. (2006) Priapism associated with quetiapine in an elderly patient. *Actas Esp Psiquiatr*, 34:209-10.
- Birnbaum BF, Pinzone JJ. (2008) Sickle cell trait and priapism: a case report and review of the literature. *Cases J*, 30:429.
- Brichart N, Delavierre D, Peneau M et al. (2008) Priapism associated with antipsychotic medications: a series of four patients. *Prog Urol*, 18: 669-73.
- Casiano H, Globerman D, Enns MW. (2007) Recurrent priapism during treatment with clozapine, quetiapine and haloperidol. *J Psychopharmacol*, 21:898-9.
- Compton MT, Miller A. (2001) Priapism associated with conventional and atypical antipsychotic medication. *J Clin Psychiatry*, 62: 362-366.
- Croissant B, Klein O, Gehrlein L et al. (2006) Quetiapine in relapse prevention in alcoholics suffering from craving and affective symptoms: a case series. *Eur Psychiatry*, 21: 570-573.
- Davol P, Rukstalis D. (2005) Priapism associated with routine use of quetiapine: case report and review of the literature. *Urology*, 66: 880.
- Diermenjian JM, Erhart SM, Wirshing D A. (1998) Olanzapine-induced reversible priapism: a case report. *J Clin Psychopharmacol*, 18; 351-353.
- du Toit RM, Millson RC, Heaton JP et al. (2004) Priapism. *Can J Psychiatry*, 49: 868-869.
- Emes CE, Millson RC. (1994) Risperidone-induced priapism. *Can J Psychiatry*, 39: 315-316.
- Ereshfsky L, Riesenman C, Lam YW. (1995) Antidepressant drug interactions and the cytochrome P 450 system. *Clin Pharmacokinet*, 29 (Suppl 1): 10-18.
- Freudenreich O. (2002) Exacerbation of idiopathic priapism with risperidone/citalopram combination. *J Clin Psychiatry*, 63:249-250.
- Geraci MJ, McCoy SL, Crum PM. (2010) Antipsychotic-induced priapism in an HIV patient: a cytochrome P450-mediated drug interaction. *Int J Emerg Med*, 26:81-4.
- Harrison G, Dilley JW, Loeb L et al. (2006a) Priapism and quetiapine: a case report. *Psychopharmacol Bull*, 39: 117-9.
- Harrison G, Dilley JW, Loeb L et al. (2006b) Priapism and quetiapine in an HIV-positive male. *J Clin Psychopharmacol*, 26:100-1.
- Hosseini SH, Polonowita AK (2009). Priapism associated with olanzapine. *Pak J Biol Sci*, 12:198-200.
- Jagadheesan K, Thakur A, Akhtar S. (2004) Irreversible priapism during olanzapine and lithium therapy. *Aust N Z J Psychiatry*, 38:381.
- Mago R, Anolik R, Johnson RA et al (2006) Recurrent priapism associated with use of aripiprazole. *J Clin Psychiatry*, 67:1471-1472.
- Medina CA. (2002) Clitoral priapism: a rare condition presenting as a cause of vulvar pain. *Obstet Gynecol*, 100:1089-1091.
- Negin B, Murphy TK. (2005) Priapism associated with oxcarbazepine, aripiprazole and lithium. *Am Acad Child Adolesc Psychiatry*, 44:1223-1224.
- Owley T, Levenathal B, Cook Eh Jr. (2001) Risperidone-induced prolonged erections following the addition of lithium. *J Child Adolesc Psychopharmacol*, 11:441-442.
- Pais VM, Ayvazian PJ. (2001) Priapism from quetiapine overdose: first report and proposal of mechanism. *Urology*, 58:462.
- Richelson E. (1999) Receptor pharmacology of neuroleptics: relation to clinical effects. *J Clin Psychiatry*, 60 (Suppl 10):5-14.
- Rosen SI, Hanno PM. (1992) Clozapine-induced priapism. *J Urol*, 148: 876-877.
- Rosenberg I, Aniskin D, Bernay L. (2009) Psychiatric treatment of patients predisposed to priapism induced by quetiapine, trazadone and risperidone: a case report. *Gen Hosp Psychiatry*, 31: 98.
- Seftel AD, Saenz de Tejada I, Szetela B. (1992) Clozapine-associated priapism: a case report. *J Urol*, 147; 146-148.
- Seeger A, Lamberti JS. (2001) Priapism associated with polypharmacy. *J Clin Psychiatry*, 62:128.
- Segraves RT. (1989) Effects of psychotropic drugs on human erection and ejaculation. *Arch Gen Psychiatry*, 46: 275-284.
- Sood S, James W, Bailon MJ. (2008) Priapism associated with atypical antipsychotic medications: a review. *Int Clin Psychopharmacol*, 23:9-17
- Tekell JI, Smith EA, Silva JA. (1995) Prolonged erection associated with risperidone treatment (letter). *Am J Psychiatry*, 152:1097.
- Thompson JL, Ware EA, Blashfield R. (1990) Psychotropic medication and priapism: a comprehensive review. *J Clin Psychiatry*, 51: 430-433.
- Yang P, Tsai J. (2004) Occurrence of priapism with risperidone-paroxetine combination in an autistic child. *J Child and Adolesc Psychopharmacol*, 14:342-343.
- Yuan J, Desouza R, Westney OL et al. (2008) Insights of priapism mechanism and rationale treatment for recurrent priapism. *Asian J Androl*, 10:88-101.