



Pretreatment screening and counseling on prolonged erections for patients prescribed trazodone

Tejash Shah , Juhi Deolanker , Thaiphil Luu , Hossein Sadeghi-Nejad 

Department of Urology, Rutgers New Jersey Medical School, Newark, NJ, USA

Purpose: We examined whether patients are appropriately screened for previous prolonged erections or priapism and counseled about trazodone complications, specifically prolonged erections and priapism, prior to trazodone treatment.

Materials and Methods: We identified patients under the age of 50 on trazodone as of February 27, 2019 at the VA New Jersey Health Care System. Patients were asked about information provided to them prior to medication initiation, occurrence of prolonged erections/priapism, and reporting rate of side effects.

Results: Two hundred and twenty nine out of five hundred and twenty four male patients agreed to participate in the study. Forty three out of two hundred and twenty nine of patients were informed about the side effects of prolonged erections and 37/229 of patients were informed of risk of priapism prior to treatment. Only 17/229 of patients were asked if they had had any episodes of prolonged erection or priapism in the past. Eighteen patients developed prolonged erection while taking trazodone. Only 5/18 patients who had developed prolonged erections informed their physicians.

Conclusions: Only a fraction of patients were properly screened for previous prolonged erections or priapism and properly informed about the side effects of trazodone. Urologist should better educate trazodone prescribers, such as family medicine and psychiatric colleagues, regarding the side effects of trazodone. It is imperative that prescribing physicians appropriately screen and educate patients prior to trazodone initiation and instruct patients to report any treatment side effects to avoid potential long-term adverse outcomes.

Keywords: Antipsychotic agents; Drug-related side effects and adverse reactions; Priapism

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INTRODUCTION

Priapism is a urologic emergency defined as a prolonged, painful erection lasting greater than 4 hours, not usually initiated by sexual stimuli or desire. It has been established that there are a variety of risk factors for priapism, including the use of antipsychotics such as trazodone, and having

a history of prolonged erections. There are several reports in the literature of trazodone use leading to both prolonged erections and priapism, but patients are often not counseled on these well-known side effects [1]. If patients are not aware of such side effects, it is highly likely that they may delay seeking care for priapism/prolonged erections, which ultimately may lead to irreversible complications of ischemic

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Corresponding Author: Tejash Shah  <https://orcid.org/0000-0002-5301-8103>

Department of Urology, Rutgers New Jersey Medical School, 185 S Orange Ave, Newark, NJ 07103, USA
TEL: +1-917-804-6745, FAX: +1-973-972-3892, E-mail: shahtt@njms.rutgers.edu

penile fibrosis and subsequent erectile dysfunction.

Medications, including antidepressants, antihypertensives, anticoagulants, alpha-blockers and some psychoactive substances such as alcohol and cocaine, are responsible for the onset of 25% to 40% of cases of priapism. However, about 50% of all drugs related priapism is due to antipsychotics usage [2]. It is the prescribing physicians' duty to inform patients about all risks prior to initiating therapy, especially in this population who may be on an extensive pharmacologic regimen. It has been noted that all patients should be questioned about previous episodes of prolonged erections as a past significant history of delayed detumescence is present in approximately 50% of any subsequent cases of priapism [1]. Previous data also suggests that priapism is most likely to occur within the first 28 days of treatment initiation with a majority of the patients taking a dosage of 150 mg/day or less [3]. While medication side effects are never desired, if patients are aware of them, it is only intuitive that they can seek side effect management sooner and avoid long term consequences.

The veterans affairs (VA) system is the one of the largest health care systems in the United States, with almost over 8 million veterans enrolled and about 5 million receiving care. It is critical to investigate all adverse events related to antipsychotic medication use, particularly in view of studies indicating usage as high as 47.5% in the nursing home population and veteran affairs health care system [4]. Furthermore, off-label use of antipsychotic medications is extremely prevalent in the VA population, as almost 60% of patients had no record of a diagnosis for which these drugs were officially approved. The most common mental illnesses receiving antipsychotic prescriptions were post-traumatic stress disorder (41.8%), minor depression (39.5%), major depression (23.4%), and anxiety disorder (20.0%) [5]. Male veterans, especially those with suicidal ideation and psychiatric comorbidities, are more likely to receive antipsychotics than any other types of psychiatric medications [6]. With this high percentage of use, providers should be cautious when prescribing these medications.

In our clinical practice at the East Orange Veterans Affairs Hospital, we recently came across two patients with priapism in the emergency room that were on trazodone, but were never informed about the medication side effects. We therefore set out to evaluate whether the larger cohort of patients on trazodone were appropriately counseled about prolonged erections and priapism prior to starting the medication. We also sought to identify the incidence of prolonged erections in those taking trazodone, as well as the rate of patient reported events of prolonged erection to the prescribing

physicians.

MATERIALS AND METHODS

Institutional Board Review of VA New Jersey Health Care System approval was obtained (approval number: 00001450) and subsequently a pharmacy search was performed at the VA New Jersey Health Care System (VANJHS), to identify all male patients under the age of 50 currently taking trazodone as of February 27, 2019. Patients previously on trazodone or those who discontinued it prior to this date for any reason, including priapism, were not included. Patients were contacted via telephone, informed consent about study participation was obtained, and were asked about information provided prior to medication initiation, whether history of prolonged erection or priapism was elicited prior to medication initiation, occurrence of prolonged erections/priapism while on trazodone therapy, and communication with prescribing physicians in case these adverse events had been encountered. We defined prolonged erections as erections lasting anywhere from one to four hours.

RESULTS

Two hundred and twenty nine out of a total of 524 male patients on trazodone at the VANJHS participated in the study, with an average age of 38.57 ± 6.88 years. Indications for prescribing trazodone were insomnia, depression or post-traumatic stress disorder in all cases. Dosages of trazodone administered ranged from 50–100 mg, two to three times a day (Table 1). Prior to prescribing trazodone, only 43/229 (18.78%) of patients were informed about the side effects of prolonged erections. Even fewer numbers of patients were informed about the risk of priapism, 37/229 (16.16%).

Table 1. Patient demographics

Patient characteristic	Result (n=229)
Age (y)	38.57 (25–50)
Sex	
Male	229 (100.0)
Female	0 (0.0)
Trazodone dosage (mg)	
50	138 (60.3)
100	91 (39.7)
Indications	Insomnia; depression; PTSD

Values are presented as mean (range) or number (%). PTSD, post-traumatic stress disorder.

Table 2. Rates of screening, side effect counseling and side effect reporting

Asked about previous prolonged erection/priapism	Informed about risk of prolonged erection	Informed about risk of priapism	Incidence of prolonged erections	Incidence of priapism	Reporting rate to physician about side effect
17/229 (7.42)	43/229 (18.78)	37/229 (16.16)	18/229 (7.86)	0	5/18 (27.78)

Values are presented as number (%).

Only 17/229 (7.42%) of patients were asked if they previously had any episodes of prolonged erection. Similarly, only 17/229 (7.42%) of patients were asked if they ever had priapism in the past. After the initiation of trazodone therapy, 18/229 (7.86%) of patients developed prolonged erection and only 2/18 were informed about the risk of prolonged erections prior to initiation of therapy. Only 5/18 of those who developed prolonged erections told their physicians. Patients did not report these events to physicians due to embarrassment and/or lack of awareness that this side effect was possibly associated with trazodone. None of the patients who were actively taking trazodone had an episode of priapism requiring an emergency room visit while on the medication (Table 2).

DISCUSSION

Priapism is a true urologic emergency as a delay in care can lead to deleterious long-term consequences. There are a variety of risk factors for priapism, including the use of antipsychotics such as trazodone as there are several reports in the literature of trazodone use leading to both prolonged erections and priapism. Initially, priapism was only noted to be associated with the use of the more typical first generation antipsychotic medications and trazodone, but now there have been some reports of the newer atypical antipsychotics causing priapism as well [7]. Trazodone is U.S. Food and Drug Administration-approved for treating major depressive disorder, but it can also be used for off-label purposes such as insomnia, post-traumatic stress disorder, anxiety, Alzheimer’s, personality disorders, and cocaine/alcohol withdrawal. The medication can be orally dosed in 50, 100, 150, and 300 mg tablets with 300 mg/day being the maximum dosage for outpatient and 600 mg/day for inpatient usage. Priapism is considered as an adverse effect occurring in less than 1% of patients on trazodone. This is more likely to occur in male who have multiple myeloma, sickle cell anemia, leukemia, autonomic dysfunction, or those who have a penile anatomic variation such as cavernosal fibrosis, angulation, or Peyronie’s disease [8]. One study by Haria et al. [9] reported a priapism incidence rate of 1:1,000 to 1:10,000 for male on trazodone, while the incidence of priapism in

the general population has been reported to significantly lower at 1.5:10,000 [10]. Psychotropic-induced priapism is thought to be caused by the alpha1-adrenergic antagonism of these medications within the corpora cavernosa which inhibits detumescence [11,12]. It has been shown that during the rapid eye movement sleep period, during which spontaneous erectile activity usually occurs, the detumescence phase of erection which is under sympathetic control, was significantly prolonged 24 times by trazodone compared to placebo. *In vitro*, trazodone at similar concentrations to those that are achieved in plasma considerably affected corporeal smooth muscle contractions that were induced by electrical stimulation of adrenergic nerves and antagonized contractions caused by exogenous norepinephrine [13]. With all the studies performed to understand the mechanism of action of trazodone and other antipsychotics, the most widely accepted mechanism involves a decrease in local sympathetic tone with respect to the local parasympathetic tone [14]. In addition to the alpha1-adrenergic antagonism with which priapism is caused by, trazodone also inhibits the neuronal uptake of serotonin and is a histamine antagonist [15].

Multiple case reports have established a connection between the use of a combination of trazodone and other antipsychotics with priapism occurrence [16]. A particular case report of a military veteran receiving treatment for PTSD (post-traumatic stress disorder) with trazodone and three other antipsychotic medications notes the patient having recurrent priapism with the first episode being three months after initiation of treatment. At that time, he was instructed to stop trazodone. The second episode presented one month after discontinuation, at which he then discontinued prazosin, and after 6 weeks he did not experience recurrence [17]. Several cases with the use of other antipsychotics such as quetiapine, carbamazepine, olanzapine, and clozapine have also been reported, signifying the prevalence of priapism when on these medications. Olanzapine and quetiapine, specifically, have been implicated numerous times. A case report of an individual with schizoaffective disorder discusses recurrent priapism over a three year period, each time related to the ingestion of quetiapine [18]. More recently, a case series from the AMSP (Arzneimittelsicherheit in der Psychiatrie) database reviews 19 case reports of priapism

that are likely caused by typical and atypical antipsychotics, as well as trazodone. Common amongst the reports was the introduction of a psychotropic drug causing the immediate development of priapism and a shift in drug plasma concentration due to a change in drug dosage or due to co-administration of specific selective serotonin reuptake inhibitors [19]. Physicians should also be aware that there are reports of priapism occurring even in children under the age of 6 who are on trazodone [20].

Patients on trazodone or other antipsychotics should be made aware of such side effects prior to initiating treatment as the lack of awareness of the side effects may lead to a delay in patients seeking medical attention and thus leading to irreversible damage and poor erectile function. The prescribing physicians must inform patients about all risks prior to initiating therapy. When patients taking trazodone or other antipsychotics present with priapism, the treatment algorithm is the same as for ischemic, low flow priapism [21]. The main goals of medical therapy are decompression of the corporal bodies and restoration of arterial blood flow to reduce ischemia and the potential risk of tissue necrosis. Prompt treatment within 4 to 6 hours of onset has been shown to reduce long term effects and decrease the need for surgical intervention.

In the present study, patients were not appropriately counseled as only 43/229 (18.78%) of patients were informed about the side effects of prolonged erections and even fewer numbers of patients were informed about the risk of priapism, 37/229 (16.16%). It is also concerning that prior to trazodone initiation, only 17/229 (7.42%) of patients were asked if they previously had any episodes of prolonged erection and priapism. A change in the prescribing algorithm must be made to include clear disclosure of trazodone side effects. While medication side effects are never desired, if patients are aware of potential adverse effects, then they can get seek medical care and side effect management sooner to hopefully avoid long term consequences. Interestingly, in the past 2 years at various private and academic hospitals covered by Rutgers New Jersey Medical School urology residents, in addition to the two patients on trazodone who developed priapism at the VANJHS there have been three cases of patients with priapism on trazodone, all who were never counseled on this side effect. While anecdotal, this suggests that there is not proper discussion of trazodone side effects regarding prolonged erection and priapism in the community as well.

This study focuses on veteran patients, a population that has a high percentage of usage of trazodone and other antipsychotic medication. Given the patient population and

the complex psychotropic regimen, the study population may be at higher risk for priapism and prolonged erections. It is noteworthy that despite multiple episodes of prolonged erections, none of the patients in the study required an emergency room visit for priapism during the study. This is likely because patients who did have priapism while taking trazodone, the medication was discontinued and not captured in our study. Based on our findings, it is clear that patient education and counseling needs to be drastically improved prior to starting trazodone. Providing the proper information to patients can foster a more communicative and well-informed patient-doctor relationship that allows patients with complications to feel comfortable discussing adverse effects with their physician.

Limitations of the study include the study population as we only included patients who were on trazodone at the time of our study, and did not account for patients who may have discontinued trazodone for priapism or any other adverse effect. We defined prolonged erections as lasting between one to four hours but did not obtain more detailed information as to the specific length of each patients prolonged erections. Additionally, our study only looked at the practice patterns at one veterans affair system. Further investigation needs to be done regarding the true incidence of prolonged erections and priapism in patients in the general population taking trazodone, other antipsychotics, or a combination of antipsychotic medications.

CONCLUSIONS

Patients taking trazodone are known to have an increased risk of prolonged erections and priapism. Only a fraction of patients were properly screened for previous prolonged erections or priapism and properly informed about the side effects of trazodone treatment prior to receiving the medication. Urologist should better educate trazodone prescribers, such as family medicine and psychiatric colleagues, regarding the side effects of trazodone. It is imperative that physicians appropriately screen patients prior to trazodone initiation, educate patients about the risks of prolonged erections and priapism and instruct patients to report any treatment side effects.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

AUTHORS' CONTRIBUTIONS

Research conception and design: Thaiphi Luu and Hossein Sadeghi-Nejad. Data acquisition: Thaiphi Luu and Juhi Deolanker. Statistical analysis: Tejash Shah and Juhi Deolanker. Data analysis and interpretation: Tejash Shah. Drafting of the manuscript: Tejash Shah and Juhi Deolanker. Critical revision of the manuscript: Tejash Shah and Hossein Sadeghi-Nejad. Supervision: Hossein Sadeghi-Nejad. Approval of the final manuscript: Tejash Shah, Hossein Sadeghi-Nejad, and Juhi Deolanker.

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