Original Research Article

Use of Prazosin for Post-traumatic Stress Disorder in Adolescents is Associated with Longer Inpatient Psychiatric Hospitalization

Abstract

Objectives: Prazosin has been shown to be effective in reducing PTSD-related nightmares in adolescents in outpatient studies with modest sample sizes. There are no data on the effects of prazosin on length of inpatient psychiatric hospitalization. Given prazosin's adverse effects, we hypothesize that prazosin initiation during inpatient psychiatric hospitalization is associated with prolonged length of stay.

Patients and Methods: Retrospective chart review identified 255 psychiatric admissions of adolescents with PTSD from 2012-2017 at an academic medical center. The treatment group comprised 101 admissions during which prazosin was initiated. Given a lack of rating scales, number of concurrent diagnoses and discharge medications were used to approximate overall illness severity.

Results: There were no statistical differences between the treatment and non-treatment (control) groups with respect to age, gender, number of diagnoses or discharge medications. The mean dose of prazosin was 1.5±0.7 mg nightly with mean duration of 7.6±6.1 days. Length of hospital stay was significantly longer for the prazosin group compared with controls (11.1±6.6 vs 9.5±5.8 days, p=0.04). There was no difference in rates of orthostatic hypotension between groups. Adverse reactions were observed in 41% of individuals taking prazosin with a discontinuation rate of 14% due to intolerable side effects, lack of efficacy or request to reduce polypharmacy.

Conclusions: Treatment with prazosin during inpatient psychiatric hospitalization may be associated with increased length of stay for adolescents with PTSD. Further studies are needed to validate these results.

Key word: PTSD, Prazosin, Psychiatric

Introduction

As many as 62% of U.S. youth have experienced at least one traumatic event in their lifetime[1] and about 16% of those go on to develop post-traumatic stress disorder (PTSD).[2] Prazosin, an alpha-1 adrenergic receptor antagonist, has been shown in placebo-controlled clinical trials to decrease the incidence of nightmares and improves overall functional status in adults.[3–5] Large trials of prazosin in adolescents are lacking. In a recent case series, eight outpatient adolescents with PTSD treated with prazosin experienced relief from nightmares in frequency, return of normal sleep latency, reduced hyperarousal and global clinical improvement.[6–9] A retrospective chart review of 34 adolescents treated with prazosin in the outpatient setting demonstrated 26% rate of adverse effects with dizziness and lightheadedness being a common cause for discontinuation.[10]

Treatment with prazosin in the inpatient adolescent setting has not been well studied.

Numerous studies have shown that psychiatric hospitalization can be a traumatic experience, especially for those with a history of trauma, and may lead to worsening of symptoms. [11–13] Additionally, psychiatric hospitalization is costly and increased length of stay places burden on patients and hospital resources. When safe and appropriate, efforts should be made to shorten length of hospitalization for youth with PTSD.

We sought to determine the association of prazosin initiation in adolescents with PTSD and length of psychiatric hospitalization. Given prazosin's side effect profile and potential need for monitoring, we hypothesize prazosin may prolong length of stay in adolescents hospitalized in inpatient psychiatric units.

Materials and Methods

We performed a single-center retrospective case-control study of adolescents, aged 12-17, who met DSM-5 criteria for PTSD with a psychiatric admission from 2012 through 2017, at which time the institution's electronic medical record changed. The treatment and control groups comprised of admissions in which prazosin was initiated (n=106) and those without (n=149). A total of 8 participants were excluded; seven subjects did not have a recorded length of stay, and one outlier with a length of stay of 90 days. A total of 247 subjects were included in the analysis (101 subjects in the prazosin group and 146 in the control group). Baseline demographics, orthostatic vital signs, length of hospital stay, and physician-recorded incidence of side effects were collected. Factors including age, gender, race, trauma type, length of stay, duration of prazosin therapy, concurrent psychiatric diagnoses, and number of psychiatric medications at discharge were collected for each group. Given that patients were not provided rating scales, concurrent psychiatric diagnoses and number of medications were used to approximate overall illness severity.

The primary outcome measure was length of hospital stay. Secondary measures included development of orthostasis as well as spontaneously reported or objective reports of adverse effects in the prazosin group. Orthostasis was evaluated on admission and at discharge in both groups by obtaining blood pressure readings (systolic and diastolic pressures) seated and then again standing after 5 minutes.

Orthostasis was defined as a decrease in systolic pressure of at least 20mmHg or diastolic pressure of at least 10mmHg. All progress notes and event notes for the prazosin group were reviewed for evidence of subjective and objective reports of adverse events, such as dizziness and falls, respectively.

Statistical Analysis

Categorical variables are summarized as frequencies and percentages, while continuous variables are summarized as mean ± standard deviation. Categorical variables between groups were compared using Fisher's exact test. Continuous variables were compared using an unpaired t-test. All tests were two-sided. A multiple linear regression comparing length of stay between the two groups was conducted with covariates of age, gender, race, trauma type, number of psychiatric diagnoses, and number of psychiatric medications (excluding prazosin). Findings were considered significant if $p \leq 0.05$. All analyses were conducted in GraphPad software (version 8.4.3).

Results

Demographic data are described in Table 1. There were no statistical differences in age, gender, race, or ethnicity between the treatment and control groups. Patients from both the prazosin and control group experienced either physical (33% vs 45%, p=0.08), sexual (83% vs 62%, p=0.0003), or verbal trauma (0% vs 4%), or a combination. Prazosin-treated patients had a significantly higher percentage of sexual trauma (83% vs. 62%, p=0.0003).

There was no significant difference in the number of psychotropic medications prescribed at discharge (prazosin excluded) between the treatment group and controls (2.17±1.0 vs 2.40±1.2, p=0.12). There was also no difference between the prazosin group compared to the control group in terms of psychotropic medication classes: selective serotonin reuptake inhibitors (81% vs. 75%), atypical antidepressants (15% vs. 13%), serotonin and norepinephrine reuptake inhibitors (5% vs 7%), anxiolytics (10% vs. 18%),

antihistamines (31% vs 23%), atypical antipsychotics (37% vs 45%), and mood stabilizers (6% vs 5%). Other psychotropic classes were present in less than 5% of each group.

Both groups had a similar number of diagnoses at discharge (2.96±0.88 vs. 3.07±0.91, p=0.35). There was no difference between specific diagnoses in the prazosin group compared to the control group: depressive disorders (78% vs 75%), anxiety disorders (15% vs 24%), substance-use disorder (32% vs 24%), eating disorders (11% vs 14%), and bipolar disorder (9% vs 3%). Other disorders were present in less than 5% of cases for each group. In the treatment group, the dose of prazosin was 1.5±0.7 (max: 5) mg nightly and the duration of treatment was 7.6±6.1 (max: 28) nights.

Length of hospital stay was significantly longer for the prazosin group compared with controls (11.1±6.6 vs 9.5±5.8, p=0.04). (Figure 1) Length of stays ranged from 2-36 days. Length of stay remained significantly longer in prazosin-treated patients after accounting for age (p=0.04), gender (p=0.05), race, as categorized by Hispanic vs. Non-Hispanic (0=0.047), number of diagnoses (p=0.03), and number of medications excluding prazosin (p=0.01). Length of stay also remained significantly longer in the prazosin treated group after accounting for the increased proportion of patients with a history of sexual trauma (p=0.02).

Adverse reactions were observed in 41 individuals (41%) taking prazosin, with dizziness/lightheadedness being the most common (n=26, 26%). One patient (1%) experienced a fall, while another (1%) had an episode of syncope. (Table 2) Of those reporting difficulties with tolerability, fourteen individuals (34%) experienced eventual symptom resolution. Prazosin was discontinued in thirteen patients (14%) due to intolerable side effects, lack of efficacy or request to reduce polypharmacy. Adverse event rates for the control group and discontinuation rates for other medications were not collected.

Orthostatic hypotension was collected on admission and at follow-up. On admission, 193 did not have orthostatic hypotension: 84 from the prazosin group and 109 from the control group. Thirteen patients

(15%) taking prazosin had newly developed orthostatic hypotension at follow-up compared to eight patients (7%) in the control group (p=0.1). (Table 2)

Discussion

In our retrospective review, prazosin administration to adolescents with PTSD during inpatient psychiatric hospitalization was associated with a lengthier hospital stay. This difference remained significant after accounting for potential confounding factors, including age, race, gender, type of trauma and approximations of overall illness severity including number of concurrent diagnoses and discharge medications. No validated measures of illness severity were performed, and it is unclear if illness severity may have been a factor in determining hospital stay.

The implication of longer hospital stays for adolescents with PTSD due to prazosin initiation is cause for concern. Several studies have shown that psychiatric hospitalization can be a traumatic experience, especially for those with a history of trauma. [11–13] Rosenberg et. al showed that females with a history of sexual abuse experienced worsening of PTSD symptoms during involuntary hospitalizations and with the use of restraints.[11] Assuming the patient can be safely discharged to a nontoxic and nonviolent location, efforts should be made to shorten the hospitalization course.

The cost burden of lengthier hospital stays is also worth noting. Estimates have shown that cost of psychiatric hospitalization is largely driven by length of stay. [15] Further, as inpatient beds remain full, newly admitted patients requiring hospitalization remain boarded in the emergency department. This in turn leads to longer hospital stays for those who wait for admission from the emergency department, along with increased cost burden for the health care system and worse outcomes for these patients who remain in the emergency department. [15]

The cause of increased length of stay is unclear. Polypharmacy has previously been shown to contribute to increased length of hospitalization. [14] Adverse effects from prazosin may have triggered a need for a longer stay to monitor the patient for resolution of symptoms. While there was no significant difference in

development of orthostasis between the groups, side effects were noted in a large proportion of those taking prazosin, consistent with previous studies evaluating the use of prazosin in adolescents.[5,10]

The following limitations are important to note. This was a retrospective chart review. Illness severity was inadequately measured, and it is unclear if longer hospital stays were associated with illness severity, which prompted the use of prazosin. Further, adverse events were based on spontaneous report and were not collected for patients in the control group. Lastly, socioeconomic factors were not adequately collected which may also have contributed to length of hospital stay.

Conclusion

Our findings suggest an association between initiation of prazosin for adolescents during inpatient psychiatric admission and lengthier hospital stays. Prospective randomized control trials are needed to validate these findings.

Ethical Approval:

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

Consent

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

COMPETING INTERESTS DISCLAIMER:

Authors have declared that they have no known competing financial interests OR non-financial interests OR personal relationships that could have appeared to influence the work reported in this paper.

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Table 1. Data statistics

Variable	Prazosin Group (101)	Control Group (146)	p-value
Age	15.34±1.30	15.12±1.47	0.24
Female	85 (84%)	110 (75%)	0.11
Race			
Caucasian	53 (52%)	94 (64%)	0.06
Hispanic	31 (31%)	33 (23%)	0.18
Other*	17 (17%)	18 (12%)	0.36
Diagnoses	2.96 ±0.88	3.07 ±0.91	0.35
Medications	2.17±0.98	2.40±1.21	0.11

**includes Asian, African American, and mixed race*

Table 2. Adverse Events

	Prazosin Group n (%)	**Control Group n (%)**	**P-value**
Adverse events reported while being administered prazosin *Dizziness* *Fall* *Syncope*	42 (42%) *26 (26%)* *1 (1%)* *1 (1%)*	N/A	
Prazosin discontinuation	13 (13%)	N/A	
Orthostatic hypotension at baseline	17 (17%)	37 (25%)	
Newly developed orthostatic hypotension	13 (15%)	8 (7%)	0.1

Figure 1.

Average Length of Stay (Days) In Adolescents Treated with Prazosin vs. Controls