



● PERSPECTIVE

Prazosin: a potential new management tool for iatrogenic autonomic dysreflexia in individuals with spinal cord injury?

Spinal cord injury (SCI) is a devastating condition that not only results in a loss of motor functions but also severe autonomic dysfunctions (Krassioukov and Claydon, 2006). Autonomic dysreflexia (AD) is a life threatening episode of transient hypertension that occurs up to 30x/day (11x/day on average) in those with cervical or high thoracic SCI (Hubli et al., 2015). Most common triggers of AD are from stimuli such as a full bowel and/or bladder, or sexual arousal (Teasell et al., 2000). Penile vibrostimulation (PVS) is a clinical procedure for sperm retrieval used for the purpose of family planning or fertility assessment that unfortunately iatrogenically induces episodes of AD (Elliott, 2006). Recently, we published a clinical trial highlighting that prazosin may be a viable option for treating AD secondary to PVS (Phillips et al., 2014).

Currently, the most commonly used medication to mitigate the severity of AD episodes during PVS is nifedipine (Adalat), an immediate-release calcium channel blocker (Krassioukov et al., 2009). However, individuals with SCI experience persistently low resting blood pressure (BP) as well as orthostatic hypotension (Krassioukov and Claydon, 2006). While nifedipine is effective at significantly reducing the severity of BP increases secondary to AD, it unfortunately has the tendency to lower resting BP for up to 5 hours. Also, SCI patients with persistent hypotension may experience dizziness, fatigue, and weakness after being administered nifedipine (Krassioukov et al., 2009). Together, these factors contribute to the need to explore alternative therapies for mitigating AD severity in the SCI population.

Nifedipine lowers BP by blocking both the renin-angiotension (RAS) pathway and the α -adrenergic receptors.

Prazosin (Minipress), on the other hand, is a selective α -adrenergic blocker that preserves the vasoactive actions of the RAS pathways (Jaillon, 1980; Krassioukov and Claydon, 2006). Consequently, prazosin exudes a less abrupt suppressive effect on resting BP (Jaillon, 1980). A previous clinical study suggests that prazosin may be a feasible prophylactic treatment of AD, as it has shown a reduced incidence and severity of AD episodes in hospitalized SCI patients due to urogenic complications or other causes (Krum et al., 1992).

We recently conducted a clinical trial to examine the efficacy of prazosin at reducing AD severity in SCI outpatients undergoing PVS who regularly experienced severe iatrogenically-induced episodes of AD. Six patients with complete chronic SCI (> 2 years) were tested in a placebo controlled trial using a 1 mg tablet of prazosin at home the night before testing (loading dose), followed by a second 1 mg tablet 2 hours prior to the PVS procedure. Participants acted as their own controls. Hemodynamic assessments took place for 10 minutes prior to and during the procedure. The resting BP was calculated from minutes 3–8 of the 10 minute recording before the procedure, after both doses of prazosin were administered. All six participants experienced AD episodes following ejaculation from PVS after taking either placebo or prazosin. We noted two major findings: 1) patients experienced a significantly smaller increase in SBP after ejaculation after being administered prazosin compared to placebo (97 ± 34 mmHg vs. 141 ± 46 mmHg, $P = 0.02$), 2) no difference in resting BP between prazosin and placebo trials (Figure 1). The results suggest that like nifedipine, prazosin is effective at reducing the severity of iatrogenically-induced AD due to PVS. However, prazosin did not result in a decrease in resting BP, suggesting it may be a viable alternative for mitigating AD severity, with particular benefit in patients suffering from persistent hypotension.

One critical consideration when administering prazosin to manage AD symptoms in SCI is the risk of eliciting what is referred to as a “first-dose phenomenon”; where patients experience a severe drop in BP the first time it is administered (Graham et al., 1976). It is recommended that if administering as prophylactic, the first dose (*i.e.*, “loading dose”) should be ingested before night-time sleep (when patient is

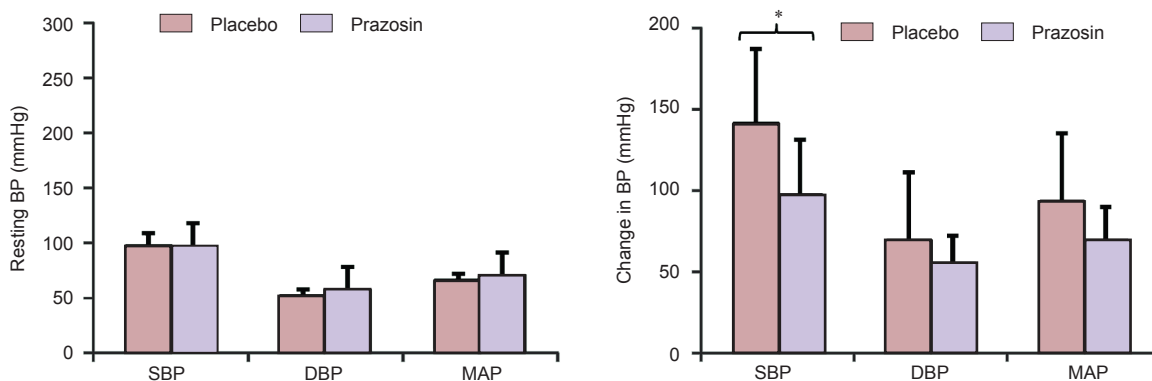


Figure 1 Comparing systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) at baseline (figure on left) to development of autonomic dysreflexia during ejaculation with penile vibrostimulation (figure on right), after either placebo or prazosin was administered.

The increase in SBP was mitigated during ejaculation when prazosin was administered compared to placebo ($*P = 0.02$), as shown with two-way repeated measures ANOVA; however, resting blood pressure was not different between the two trials.



in supine position) to mitigate the risk of severe orthostatic hypotension. This phenomenon does not occur on subsequent days of administration. Larger clinical trials should be conducted in the future, using more sophisticated BP measurements (*i.e.*, 15 minute interval 24 hour ambulatory BP monitoring), to further establish the use of prazosin as a prophylactic management of AD. This would allow for more powerful and generalizable results.

In conclusion, we have shown for the first time that 1 mg prazosin (administered orally once the night before, and once 2 hours prior to ejaculation) is effective at reducing the severity of iatrogenically-induced AD in those with SCI during PVS. Importantly, low resting BP was not exacerbated by prazosin in SCI patients.

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