Effect of α-blockers on Handgrip Test Response of Diastolic Blood Pressure in Hypertensive, Benign Hypertrophy of Prostate Patients in a Therapeutics Clinic, Kolkata: A Cross-sectional Study

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ABSTRACT

Background: The isometric handgrip (IHG) test is commonly used to detect sympathetic autonomic dysfunction. Tamsulosin, approved for the management of symptomatic benign prostatic hyperplasia (BPH), acts as an antagonist for α1-adrenergic receptors (α1-AR), whereas prazosin, an α1 receptor blocker, being less selective than tamsulosin, is used as an antihypertensive agent clinically. Our objective was to investigate if there is a distinction in blood pressure (BP) increase during IHG exercise between individuals with essential hypertension taking tamsulosin compared to those taking prazosin.

Materials and methods: A cross-sectional observational study was performed on 50 subjects receiving tablet prazosin and 47 subjects receiving tamsulosin, who were asked to undergo an IHG test. Pre- and posttest BP was recorded for both the groups, and the difference in diastolic BP (delta DBP) was compared between the groups and to their respective baseline values.

Results: Post-IHG test, mean DBP was found to be 93.98 ± 9.13 mm Hg in the prazosin group and 101.00 ± 12.05 mm Hg in the tamsulosin group, respectively. The change of delta DBP in the tamsulosin group was significant, but the prazosin group showed an insignificant rise in DBP.

Conclusion: Prazosin, being less selective than tamsulosin in terms of α1 receptor antagonism, showed suppression of BP during IHG. Tamsulosin demonstrates high selectivity for prostatic receptors while showing minimal affinity for vascular receptors. As a result, its impact on BP is expected to be minimal.

INTRODUCTION

Benign prostatic hyperplasia (BPH) denotes the nonmalignant enlargement of the prostate gland, commonly observed in men during the latter stages of their lives. The actual hyperplasia of the prostate gland, constituting BPH, arises primarily as a consequence of aging and is prevalent in nearly all men, typically beginning around the ages of 40–45. Various autopsy studies conducted worldwide have examined the histologic prevalence of BPH, revealing approximately 10% of men in their 30s affected, increasing to 20% in their 40s and reaching levels of 50–60% in their 60s.1 Clinically, BPH presents with lower urinary tract symptoms, which include irritative symptoms such as urgency, frequency, and nocturia, along with obstructive symptoms like hesitancy, 1 weak and interrupted urinary stream, difficulty initiating urination, and a sense of incomplete bladder emptying.2 α-adrenergic blockers are a commonly used class of drugs to relieve the symptoms associated with it. The rationale behind the utilization of α-adrenergic blockers stems from the action of noradrenaline on α1-adrenergic receptors (α1-AR) located in the neck and sphincter of the urinary bladder, which promotes contraction and urinary retention. Additionally, noradrenaline regulates the smooth muscles in the prostate capsule and prostate urethra.3 Prazosin was the pioneer selective α1-AR antagonist explored for the treatment of BPH. It features a piperazinyl quinazoline nucleus and acts as a selective α1-adrenergic antagonist, with an affinity 1000-fold higher than that for α2-receptors. Tamsulosin, the third uroselective α1-AR antagonist, exhibits 10-fold greater selectivity for the α1A-receptor subtype compared to the α1B-receptor subtype and has been approved for treating symptomatic BPH. Notably, a considerable decrease in urinary flow has been noted following the administration of a single dose (0.4 or 0.8 mg) of tamsulosin in comparison to placebo.4 As an α1-receptor antagonist, prazosin has the potential to competitively interact with α1-receptor autoantibodies. Its primary function is to selectively inhibit the α1-receptor on the postsynaptic membrane of vascular smooth muscle, inducing relaxation in small arteries and veins. This action reduces peripheral resistance, consequently lowering BP. This is the reason why prazosin is clinically widely used in the management of hypertension, especially in those with chronic kidney disease.5 Handgrip strength is good.

Tool to evaluate an individual’s autonomic function, precisely the sympathetic function, and when reduced, is associated with adverse health consequences. Few studies have described the association between conditions like diabetes and commonly prescribed antihypertensive drugs and diminished handgrip test response. Thus, in our study, we tried to evaluate the effect of the α-blocker class of agents on the result of the handgrip test.

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Materials and Methods

A total of 97 male subjects of essential hypertension with radiologically and clinically diagnosed benign prostatic hyperplasia aged between 50 and 70 years, attending the clinical pharmacology outpatient department, were part of this cross-sectional study. Informed consent was obtained from each participant prior to the initiation of the study. Subjects with diagnosed autonomic neuropathy, or any condition like diabetes mellitus that can have an impact on their autonomic nervous system or taking any drug that can alter autonomic neuronal function, were excluded from the study. Subjects were on angiotensin receptor blockers (ARB) for at least the last 1 year. Around 50 subjects were receiving tablet prazosin in optimum dosage according to their body weight and clinical status as an add-on therapy to ARB for hypertension and/or BPH for at least the last 6 months but not >2 years. Around 47 subjects were on tablet tamsulosin in optimum dosage as a part of their treatment for BPH. We evaluated the BP of all the subjects prior to doing the isometric handgrip (IHG) test at the baseline. All the subjects in both the prazosin and tamsulosin groups underwent an isometric exercise test in the form of a handgrip test for 3 minutes. IHG was conducted at 30% of the maximum voluntary contraction of the right hand, maintained for a duration of 3 minutes. Participants were directed to exert their maximum brief compressive force with their right hand on three separate occasions to establish their maximal voluntary contraction. The greatest tension reached during these trials was recorded as the maximal force at the end of the test; that is, after 3 minutes, the BP of all the subjects was recorded using an Omron HEM-7600T BP monitor. After completion of the test, the BP of all the subjects in both the prazosin and tamsulosin groups was measured, the mean BP was compared with the mean baseline BP value, and changes were recorded. The change in mean DBP was measured and compared between the prazosin and tamsulosin groups.

Results

The mean age of the study population was 70 years, with a standard deviation of 4.19. The mean body mass index (BMI) was 24.71. The DBP value (mean) was 83.71 ± 9.41 mm Hg at the baseline (Table 1). Subjects on the prazosin arm had a baseline mean DBP of 83.62 ± 9.01 mm Hg, whereas in the tamsulosin group, it was 83.81 ± 9.91 mm Hg at the baseline. After completion of the IHG test, the mean DBP was found to be 93.98 ± 9.13 in the prazosin group (p-value of 0.92), and 101.00 ± 12.05 was in the tamsulosin group (p < 0.001) (Table 2). Post-IHG, four subjects in the prazosin group showed an increment of DBP >16 mm Hg, whereas Figure 1 was 16 in the tamsulosin group. A 10–15 mm Hg rise in DBP was observed in 26 and 10 subjects in the prazosin and tamsulosin groups, respectively (Table 3).

Discussion

The involvement of catecholamine neurotransmitters in circulatory regulation, both in the brain and the periphery, occurs through specific receptors. Ahlquist was the first to propose categorizing catecholamine receptors into α and β subtypes in the late 1940s. The mechanisms of both α₁ and α₂ receptors play roles in regulating circulation and maintaining BP, exerting cardiovascular control at various peripheral and central locations. In the peripheral nervous system, α₁ receptors, or classic postsynaptic α receptors, are found on smooth muscle, mediate responses to noradrenaline released by neurons at vascular neuroeffector junctions and likely contribute to responses to circulating catecholamines as well. Several classes of drugs influence BP regulation through their interactions with peripheral α₁ receptors. The haloalkylamine α-adrenergic receptor antagonists were initially investigated during the 1940s. Prazosin was later examined as a potential therapy for BPH in numerous placebo-controlled clinical trials. It demonstrated better effectiveness compared to placebo and exhibited a reduced occurrence of unwanted α blockade side effects when compared to older drugs such as phenoxybenzamine. This suggests that α₁ selectivity provides advantages in terms of clinical tolerability. Three subtypes of the α₁-adrenoceptor (α₁a, α₁b, and α₁d) have been cloned and thoroughly characterized pharmacologically. Lepor et al. demonstrated that α₁a is the predominant subtype of α₁-adrenoceptor in the human prostate. Recently, α₁-blockers that exhibit a preference for acting on the prostate region rather than vascular smooth muscle, such as alfuzosin and tamsulosin, have been developed. Both medications are exclusively marketed for the treatment of BPH. Their efficacy is comparable to that observed with other α₁-blockers, and they are associated with a lower incidence of adverse events, particularly postural symptoms.

Numerous studies have indicated that individuals with a family history of hypertension are at an increased risk of developing hypertension. Additionally, there is a significant increase in systolic, diastolic, and mean BP observed during isometric exercise in individuals with hypertension, finding consistent with our own observations. Typically, during exercise, there is a rise in the concentrations of metabolites such as lactic acid and adenosine, which are detected by metabolite-sensitive nerve endings within the skeletal muscle interstitium. These substances stimulate the discharge of group IV (metaboreceptor) afferent fibers, thereby

![Image](https://example.com/image.png)

Table 1: Basic demographics

<table>
<thead>
<tr>
<th>Observed values (mean ± SD (range))</th>
<th>Prazosin arm (n = 50)</th>
<th>Tamsulosin arm (n = 47)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (years)</td>
<td>70.03 ± 4.19 (61–80)</td>
<td>72.01 ± 4.20 (65–80)</td>
</tr>
<tr>
<td>Mean BMI (kg/m²)</td>
<td>24.71 ± 3.01 (18.3–26.1)</td>
<td>24.85 ± 3.05 (18.5–26.5)</td>
</tr>
<tr>
<td>Mean baseline SBP (mm Hg)</td>
<td>136.32 ± 10.73 (116–156)</td>
<td>137.25 ± 10.89 (118–158)</td>
</tr>
<tr>
<td>Mean baseline DBP (mm Hg)</td>
<td>83.71 ± 9.41 (60–94)</td>
<td>83.80 ± 9.40 (60–93)</td>
</tr>
<tr>
<td>p-values</td>
<td>0.92</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Table 2: Changes post handgrip test

<table>
<thead>
<tr>
<th>Changes in DBP (n (%))</th>
<th>Prazosin arm (n = 50)</th>
<th>Tamsulosin arm (n = 47)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;10 mm Hg</td>
<td>20 (20.62)</td>
<td>14 (29.79)</td>
</tr>
<tr>
<td>10–15 mm Hg</td>
<td>26 (26.80)</td>
<td>22 (46.81)</td>
</tr>
<tr>
<td>&gt;16 mm Hg</td>
<td>4 (4.12)</td>
<td>1 (2.13)</td>
</tr>
</tbody>
</table>

p-value < 0.00001

Fig. 1: Changes in DBP in prazosin and tamsulosin group

![Graph](https://example.com/graph.png)
initiating a potent reflex that augments sympathetic nerve activity. This ultimately leads to vasoconstriction, contributing to an elevation in BP. Our findings were consistent with these results.

A study conducted in Japan showed a greater increment in DBP after conducting the IHG test was observed among subjects with essential hypertension compared to normotensive subjects. The study also showed that BP changes during IHG were significantly less in subjects taking prazosin than in subjects with no treatment. They further suggested BP elevation with prazosin was markedly suppressed due to the blockade of postjunctional α adrenoreceptor by the drug. Such a response is less likely with tamsulosin because it is a more selective α1a receptor blocker, which is predominantly present in prostatic tissue. It is also proposed that due to its higher selectivity, tamsulosin is expected to minimally affect BP and is unlikely to enhance the antihypertensive effects of other agents.

**CONCLUSION**

Tamsulosin exhibits high selectivity for prostatic receptors and has minimal affinity for vascular receptors. Consequently, it is expected to have minimal impact on BP and is unlikely to enhance the antihypertensive effects of other agents.

**REFERENCES**