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Original Research Article

A Prospective Randomized Clinical Study for Evaluation of Adding Desmopressin to Alpha Blockers in Treatment of Nocturia in Cases of Benign Prostatic Hyperplasia

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Conflict of interest: Nil

Abstract:

Background: One of the most distressing symptoms of the lower urinary tract in males with benign prostatic hyperplasia (BPH) is nocturia. A good way to relieve bladder outlet obstruction is using alpha-blockers. The purpose of the current study was to offer BPH patients the best medical care currently available for nocturia.

Methods: 44 male participants who complained of nocturia and lower urinary tract symptoms (LUTS) of BPH were included in this prospective, randomized study for a period of 12 weeks (from March 2022 to May 2022). They were split into two groups at random, each with 22 patients. Group A: The patient received once-daily oral tamsulosin with desmopressin. The patient in Group B received oral tamsulosin every day.

Results: Patients in group A had an average blood sodium level of 142.35. Before therapy, there was no discernible difference between the groups, but after 12 weeks of treatment, group A mean sodium level was significantly lower than group B and declined from before to after treatment (mean of Na=137.68±2.033). As group A had a substantially lower nocturnal void and nocturnal volume than the other groups, and as both groups had greatly improved from before to after treatment, there was no discernible difference between the groups in either of these measurements. When comparing the total International Prostate Symptom Score (IPSS) before and after treatment, no significant differences were identified (6.36±2.59 in group A and 10.55±4.13 in group B), although group A had a considerably lower total IPSS after treatment.

Conclusion: Desmopressin supplementation is an active treatment for BPH-afflicted males who experience nocturia and is preferred to α-blocker therapy alone.

Keywords: Alpha Blockers, BPH, Desmopressin, Nocturia.

Introduction

Nocturnal polyuria (NP), which is defined as a portion of the 24-hour urine volume that is voiding at night that is >20-33%, is defined as a 24-hour urine volume of >40 mL/kg body weight. In the majority of individuals receiving treatment for benign prostatic hyperplasia (BPH), NP is the most likely reason for chronic nocturia [1]. The degree of severity and increasing annoyance are positively correlated, making nocturia one of the lower urinary tract symptoms (LUTS) that bothers men with benign prostatic hyperplasia (BPH) the most [2]. Vasopressin also slightly affects urea reabsorption in the medullary collecting tubule and systemic vascular resistance. It has historically been used to treat central diabetes insipidus, bleeding diseases such Von Willebrand disease, and primary nocturnal enuresis [3]. It is currently the drug that is most commonly studied for the treatment of nocturia specifically. Desmopressin, a synthetic counterpart of arginine vasopressin, exhibits antidiuretic properties and significantly reduces both the amount of nocturia episodes and nocturnal urine production in nocturnal polyuria [4]. It is debatable if oral desmopressin should be frequently added to alpha blocker therapy to lessen patients' bothersome symptoms. By assessing the results (safety and efficacy) of oral desmopressin in the treatment of nocturia in patients with BPH, this study aims to give the best medical care currently available for nocturia in BPH patients.

Material and Methods

The Urology Department at Narayana Medical College and Hospital conducted this prospective study. For a period of 12 weeks (from March 2022 to May 2022), Sasaram, Bihar, 44 male patients

complaining of lower urinary tract symptoms (LUTS) of BPH with nocturia were included. All of them comprised male patients with BPH who were having nocturia frequency twice or more each night. The following cases were not included in the study: diabetes insipidus, diabetes mellitus (uncontrolled), polydipsia, congestive heart failure, use of diuretics, and impaired renal function. Using computer randomization software, patients were split into two parallel groups at random. In the first group (Group A), patients received alpha blockers (oral tamsulosin 0.4 mg at bedtime) together with desmopressin for 12 weeks. Patients in the second group (Group B) only took oral tamsulosin 0.4 mg at bedtime for 12 weeks. Desmopressin is typically started at 0.1 mg and taken orally at bedtime for 12 weeks. Patient response to a maximum desmopressin dose of 0.4 mg and a minimum dose of 0.05 mg was taken into account when deciding whether to increase or reduce the dose at 1-week intervals [6].

A detailed history of the problem was required for all patients, especially history of LUTS with focus on nocturnal polyuria by using:

- The IPSS which consist of an 8-item questionnaire, consisting of seven symptom questions and one Quality of life (QOL) question, which is (IPSS question 8): "If you were to spend the rest of your life with your urinary condition the way it is now, how would you feel about that?" with a score of 0 (delighted) to 6 (terrible).
- Bladder diary {Frequency voiding chart (FVC) was done for all cases. Patients were asked to complete 3-day FV charts. They were taught how to precisely complete the FV charts by the urologist and were asked not to alter their usual fluid intake and voiding habits during the study.

Following laboratory assessment done for included cases:

- **Urine analysis:** Urinalysis (dipstick or sediment) was included in the primary evaluation of any patient presenting with LUTS to determine conditions such as diabetes mellitus**.**
- **Serum electrolytes:** At the time of treatment initiation or dose change, older men with normal values of serum sodium (Na) were monitored by Na measurement at day three and day seven of treatment, and one month later. If Na concentration remained normal, no dose adjustment was intended. Patients were informed about the symptoms of hyponatremia (headache, nausea or insomnia)**.**
- **Renal function test (RFT):** renal function was assessed by serum creatinine.

Radiological assessment was also done for included cases which consisted of:

- Abdominal and pelvic ultrasound (US); used to evaluate both kidneys, urinary bladder and prostate with lower cost, lower radiation dose and less side effects.
- Post-void residue; Post-void residual (PVR) urine was assessed by transabdominal US, bladder scan or catheterisation. PVR is not necessarily associated with bladder outlet obstruction (BOO), since high volumes can be a consequence of obstruction and/or detrusor function (detrusor underactivity).

Data were recorded using Microsoft Excel software. Data were then imported into Statistical Package for the Social Sciences (SPSS version 20.0) software for analysis. Data were represented by mean ± standard deviation (SD) and compared by t test. P value was set at <0.05 for significant results and <0.001 for high significant result.

Results

Demographic data of the patients are shown in table 1.

Table 1: Demographic data of studied groups

	Group A(N=22) (Mean±SD)	Group B(N=22) (Mean±SD)	p-value
Age (year)	59.64±3.76	61.05±2.91	0.166
BMI	27.29±1.84	27.23±1.43	0.913
Duration(Weeks)	12.05±2.72	12.00±2.5	0.954

SD: Standard deviation, BMI=body mass index. The mean serum Na of patients at group A was significantly lowers than group B after 4 and 12 weeks. It was also significantly decreased from before to after treatment in group A (Table 2).

Table 2: Comparison of serum sodium (Na) levelsbefore and after treatment (12 weeks) between the studied groups

	Group A (Mean±SD)	Group B (Mean±SD)	p-value
Na (meq/l)/before	141.85±2.152	142.18±1.91	0.557
Na/ after 4weeks	139.86±2.12	141.86±1.88	0.002*
Na (meq/l)/after treatment	137.68±2.033	141.32±2.05	<0.001
p-value	0.003	0.098	

SD: Standard deviation. There was no significant difference between groups in both nocturnal void and nocturnal volume before treatment and after treatment group A was significantly lower than group B and both groups significantly changed and improved from before to after treatment (Table 3).

Table 3: Comparison of nocturnal voids and volume in bladder diary before and after treatmentbetween studied groups

	Group A (Mean±SD)	Group B (Mean±SD)	p-value
Nocturnal voids/beforetreatment	3.64±0.64	3.58±0.65	0.759
Nocturnal void after 4 weeks	2.32±0.64	2.86±0.64	0.008
Nocturnalvoids/after treatment	1.23±0.74	2.09±0.75	<0.001
P1	<0.01	<0.01	
Nocturnal volume/before treatment	38.86±12.9	37.73±11.82	0.762
Nocturnal volume/after 4 weeks	23.41±9.17	30.91±8.40	0.007
Nocturnal volume/after treatment	14.01±6.3	23.18±8.2	<0.001
P 2	<0.01	<0.01	

SD: Standard deviation. P1= P value of Nocturnal voids/before and after 4 weeks treatment, P2= P value of Nocturnal volume/before and after 12weeks treatment. Group A was significantly lower than group B asregard total IPSS after 12 weeks of treatment. Total IPSS in each group significantly decreased after 12 weeks of treatment (Table 4).

Table 4: Comparison of total IPSS before andafter treatment between the studied groups

	Group A (Mean±SD)	Group B (Mean±SD)	p-value
Total IPSS/beforetreatment	23.82±2.4	23.09±2.6	0.353
Total IPSS/after 4 weeks	14.18±3.30	15.82±3.78	0.134
Total IPSS/after 12 weeks of treatment	6.36±2.59	10.55±4.13	<0.001
P	<0.01	<0.01	

IPSS: International Prostate Symptom Score, SD: Standard deviation. Group A was significantly lower than group B asregard total IPSS-QOL after 4 and 12 weeks treatment. Total IPSS-QOL in each group significantly decreased from before to after 12 weeks of treatment (Table 5).

Table 5: Comparison of IPSS-QOL before andafter treatment between groups

	Group A (Mean±SD)	Group B (Mean±SD)	p-value
IPSS-QOL /before treatment	4.41±0.73	4.50±0.74	0.685
IPSS-QOL /after 4 weeks of treatment	2.23±0.92	3.45±0.96	<0.001
IPSS-QOL/after 12 weeks of treatment	1.14±1.08	2.68±0.94	<0.001
P	<0.01	0.003	

SD: Standard deviation. Group A was significantly lower than group B asregard ICIQ-N after 4 and 12 weeks treatment. ICIQ-Nin each group significantly decreased after 12 weeks oftreatment (Table 6).

Table 6: Comparison of ICIQ-N before and aftertreatment between the studied groups

	Group A (Mean±SD)	Group B (Mean±SD)	P
ICIQ-N/before treatment	6.86±1.20	6.82±1.22	0.902
ICIQ-N/after 4weeks of treatment	3.82±1.25	4.73±1.20	0.019
ICIQ-N/after 12weeks of treatment	1.77±0.86	3.0±1.02	<0.001
P	<0.01	0.002	

SD: Standard deviation

Discussion

Nocturia is the complaint which involves one or more night time awakening to void [7]. Most persons who have less than two voids every night have little discomfort, but when this number increases to more than two, nocturia is thought to be clinically relevant [8]. There are numerous individual or combined urological and non-urological causes of nocturia [9]. The hours of uninterrupted sleep (the period between going to sleep and the first time you wake up to urinate) were not significantly affected by tamsulosin (α-blocker) (p = 0.198), increasing from baseline by 81 minutes as opposed to 60 minutes for the placebo. Similar to this, nocturia was reduced by one nocturnal void with tamsulosin alone (p = 0.099) compared to 0.7 with placebo. Therefore, tamsulosin didn't seem to have any noticeable impacts [10]. Given that nocturnal polyuria accounts for up to 70% of instances of nocturia, the objective differences are discouraging [11]. Desmopressin is grade A recommended for the treatment of nocturia caused by NP and has level 1 evidence [12]. The FDA in the USA has approved desmopressin acetate nasal spray for the treatment of nocturia caused by NP in adults [13].

In our investigation, there was no discernible difference between the groups in terms of mean

age, BMI, or duration. These findings are in line with those of Mohammed and Al-Hakeem [14] who divided 51 patients into two groups: those who continued taking α-blocker (n = 22) and those who got oral desmopressin 0.2 mg add-on therapy along with β-blocker (n = 29). With no statistically significant difference (P-value=0.607), the mean age of patients using β-blockers alone was (63.95±10.15) years, compared to (62.43±10.72) years for patients receiving desmopressin as an addition.

In our investigation, patients in group A had a mean serum Na of 142.35. There was no discernible difference before therapy, but after four weeks and twelve weeks of treatment, group A had dramatically decreased from before to after. These findings are in agreement with those of Chen et al. [15], who measured the serum sodium level at 1, 4, and 12 weeks following the start of desmopressin therapy. In the non-NP group, the mean (SD) drop in serum sodium levels was 3.89 (1.22) mmol/L (P <0.001), while in the NP group, it was 4.69 (3.5) mmol/L (P <0.001). Additionally, Delfanian and Zawada [16] revealed some potential concerns for the development of hyponatremia after desmopressin treatment in a research comprising more than 250000 individuals. These included liver illness, an elevated desmopressin dose, and an excessive amount of fluid consumption. They came to the conclusion that hyponatremia may be avoided by avoiding low sodium liquids and closely monitoring serum electrolytes.

According to the level of discomfort, 2 voids per night are required to be considered clinically severe nocturia [17]. Additionally, according to Oelke et al. [8], only 5% of men had nocturia as their only symptom while 20.5% of men had nocturia concurrent with other storage and/or voiding LUTS. In our investigation, there was a significant difference between the groups' nocturnal void and nocturnal volume following therapy, with group A having a much lower difference between before and after treatment. These findings concur with those of Koca et al. [18], who examined desmopressin alone and found that it considerably reduced the number of nocturnal voids for 3 days at the 24-week visit from a baseline mean of 7.0 to 5.7 occurrences.

In our investigation, there was no significant difference between the groups before and after the 12-week treatment period in terms of total IPSS, although Group A saw a substantial decline in total IPSS that was greater than that of the other groups. These findings support those of Taha et al. [1] who examined the combined tamsulosin and desmopressin treatment, which was more successful in curing nocturia but caused a more substantial change in IPSS in the group taking solely □-blockers.

In our study, the mean of the IPSS-QOL before treatment showed no significant difference, but in group A it considerably reduced after 4 and 12 weeks of therapy, and in both groups it significantly decreased from before to after 12 weeks of treatment, but more in group A. According to Weiss et al. [19], males with nocturia who received low dose desmopressin medication experienced significant gains in health-related QOL when compared to placebo.

In our study, there was no statistically significant difference in the mean of the International Consultation on Incontinence Modular Questionnaire-Nocturia (ICIQ-N) before treatment, but in Group A it was significantly decreased after treatment, and in both groups, it was significantly decreased from before to after treatment (12 weeks), but more in Group A. These findings support Mohammed and Al-Hakeem's [14] claim that desmopressin considerably enhanced ICIQ-N when compared to the group who did not use it. These findings suggest the use of oral desmopressin (0.2 mg) as a supplement to □-blockers for the treatment of refractory nocturia in men with BPH/LUTS.

Conclusion

For males with BPH and nocturia, desmopressin addition to β-blockers is an active therapy that is preferable above β-blocker therapy alone.

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