Original Research Paper

Volume - 10 | Issue - 6 | June - 2020 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

General Surgery

ROLE OF DESMOPRESSIN IN NOCTURIA OF ADULTS

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ABSTRACT **OBJECTIVE-**To study the dose, effectiveness and the side effects of oral desmopressin in control or improvement of nocturia in adults more than 40 years old(40-80 years).

METHOD- Out of the total 50 patients, two groups were divided of 25 patients each.25 patients received placebo while the other half received optimal dose of oral desmopressin after undergoing a dose titration phase which determined the optimal dose.All patients kept a 3-day frequency-volume charts (FVC). The efficacy assessments was based on data from the patients' FVC after the 4-week treatment period. The safety of oral desmopressin was evaluated based on the collected adverse events.

RESULTS- Mean nocturnal void and mean nocturnal volume as per the FVC decreased in the patients treated with desmopressin..

CONCLUSION - Desmopressin was effective in nocturia with 0.2 mg being the most optimal dose and with the least side effects.

KEYWORDS : Desmopressin, Nocturia, Urology, Surgery.

INTRODUCTION

Nocturia is currently defined by the international continence society as the complaint that an individual has to wake at night one or more times to void.[1]

Evidence suggests that most people with <2voids/night generally have only minimal bother from the condition. Only when ≥2 voids/night occurs on a regular basis is nocturia likely to have more serious consequences for the patient.[2]

For example, patients with LUTS, which encompass voiding, post-voiding, and storage symptoms (including nocturia), report that nocturia of ≥2 voids/night is one of their most bothersome symptoms. A recent population-based study of LUTs in Finland suggested that moderate or major bother are only reported by those with ≥3 voids/night.[3]

Nocturia is an underreported, understudied, and infrequently recognized problem in adults.[4]

Desmopressin (DDAVP) is the synthetic analogue of the antidiuretic hormone vasopressin. It acts on the renal collecting ducts to increase water resorption, thereby reducing urine production.

Other drugs that are often used to treat nocturia include oxybutynin, tolterodine, solifenacin, and other antimuscarinic agents. These drugs are especially used in patients who suffer from nocturia due to an overactive bladder and urgency incontinence because they help bladder contractility.

Other modalities of treatment include behavioral modifications such as Restriction of Fluid Intake, Afternoon Naps, Elevation of Legs and Compression Stockings.

Transurethral prostatectomy/transurethral incision of the prostate may be appropriate when obstruction related to the prostate is believed to be a significant causative factor of nocturia. Surgical correction of pelvic organ prolapse, sacral nerve neuromodulation, detrusor myectomy, and clam cystoplasty are options for the treatment of patients with intractable nocturia associated with overactive bladder (OAB).

MATERIAL AND METHODS

Patients of lower urinary tract symptoms with nocturia as the chief complaint in OPD of S.N. Medical College, Agra with required eligibility criteria were considered in this study conducted from January 2018 to June 2019.

This prospective study was conducted in the department of surgery of s.n. medical college, Agra.

ELIGIBILITY CRITERIA

Based on detailed history, thorough clinical examination and relevant investigations of patients were done.

A detailed pro forma was used to collect this information.

Total 50 cases with the following inclusion and exclusion criteria were selected for the study.

INCLUSION CRITERIA

Adults with age group 40-80 years were considered.
The patients who were thoroughly cooperative were included.

EXCLUSION CRITERIA

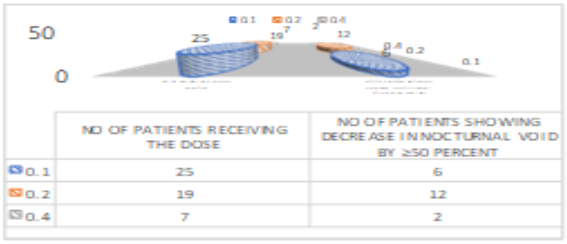
The patients having diabetes mellitus, cognitive impairment, bladder outlet obstruction, CVA, spinal disorders, dyselectrolytemia and lower urinary tract infection were excluded.

After an initial 1 week of screening total 50 patients were selected. Two groups were divided of 25 patients each.25 patients received placebo as the treating drug while the other half received optimal dose of oral desmopressin after a dose titration (1-2 weeks) phase to select an optimal dose of desmopressin. The patients' optimum oral desmopressin dose (0.1, 0.2, 0.4 mg) was determined as the dose that decreased the number of nocturnal voids by ≥50%.m. One group received placebo while the other group was treated with the determined optimum oral desmopressin for 4 weeks. All patients kept a 3-day frequency-volume charts (FVC). The efficacy assessments was based on data from the patients' FVC after the 4-week treatment period. The safety of oral desmopressin was evaluated based on the collected adverse events such as headache, nausea, vomiting, and laboratory data with an emphasis on serum sodium levels.

RESULTS

In the conducted study there were 22 number of males in desmopressin treated group as opposed to 23 males in placebo group. While the number of females were 3 in desmopressin treated group and 2 in placebo treated group.

The age of the patients fell into four age groups 40-50, 50-60, 60-70 and 70-80 years respectively. The no. of patients in the aforementioned respective age groups in desmopressin treated category were 4,6,12, and 3 whilst the no. of patients in placebo treated category were 3,5,13 and 4 respectively.



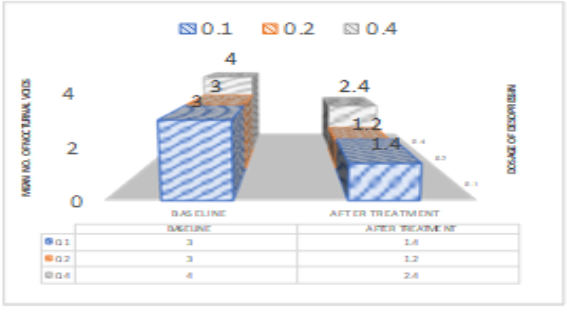
	NO OF PATIENTS RECEIVING THE DOSE	NO OF PATIENTS SHOWING DECREASE IN NOCTURNAL VOID BY ≥50 PERCENT
0.1	25	6
0.2	19	12
0.4	7	2

Chart1- Relation Of Different Dosage Of Desmopressin With No. Of Patients Showing ≥50% Decrease In Mean Nocturnal Voids During Titration Phase

Total 25(n) patients were treated with desmopressin in the dose titration phase starting with the minimal dose in order to find the optimal dose, hence all of them were given 0.1 mg dose of desmopressin in the 1st week of dose titration phase.Of them 6 had their mean nocturnal voids decreased by ≥50% so 0.1 mg was selected as optimum dose for such patients. They were treated with 0.1 mg for 4 weeks considering 0.1 mg as an optimal dose.

19 patients which did not show ≥50% decrease in mean nocturnal voids were given 0.2 mg of desmopressin, out of which 12 patients responded by showing mean nocturnal voids decrease by ≥50% so in these 12 patients optimal dose was considered to be 0.2 mg. Remaining of the 7 patients were treated with 0.4 mg of desmopressin considering it to be the optimal dose, out of which 2 showed a ≥50% decrease in mean nocturnal void. The 5 patients who did not show response to 0.4 mg dose of desmopressin were still given 0.4 mg in treatment considering it to be an optimal dose.

After the titration phase once the optimal dose has been chosen, the results showed that 24% of patient had an optimal dose of 0.1 mg, 48% of the patients had an optimal dose of 0.2 mg and 28% had 0.4 mg as an optimal dose of the total 25 patients.

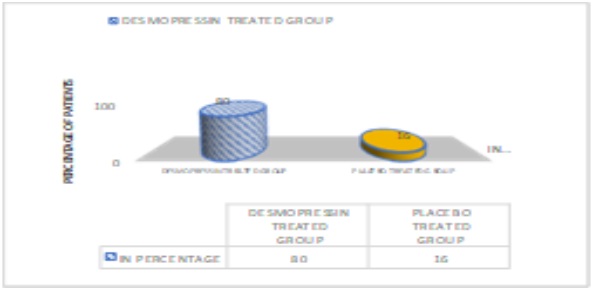


	BASELINE	AFTER TREATMENT
0.1	3	1.4
0.2	3	1.2
0.4	4	2.4

Chart 2- Comparison Of Decrease In Mean No. Of Nocturnal Voids With Different Dosage Of Desmopressin Before And After Treatment

The three group of patients treated with 0.1,0.2 and 0.4 mg dosage of desmopressin were 6, 12, and 7 in no. respectively having mean no. of nocturnal voids being 3, 3 and 4 respectively before the start of treatment which after the course of treatment improved to become 1.4, 1.2 and 2.4 respectively.

The mean nocturnal volume of the 25 patients who were treated with desmopressin for 4 weeks after the treatment was 500 ml while before start of the treatment it was 850 ml.



	DESMOPRESSIN TREATED GROUP	PLACEBO TREATED GROUP
IN PERCENTAGE	80	16

Chart3-Comparison Of Percentage Of Patients Having Decrease In Mean No. Of Nocturnal Voids ≥ 50% In Desmopressin Vs Placebo Treated Groups

The no. of patients who had their nocturnal voids decreased by ≥ 50% were 18 of the total 25 patients treated with desmopressin comprising 80% while there were 4 patients of out of 25 treated with placebo who had shown decrease in their mean nocturnal voids ≥ 50%, comprising 16% of the total 25 patients. It is here to be noted that out of 7 patients who were given 0.4 mg of desmopressin in the treatment phase, 5 did not show decrease in mean nocturnal void by ≥ 50%.

Various side effects were encountered during the course of study, most commonly being headache encountered in 17% of patients given 0.1 mg dose of desmopressin, 17% in the patients who received 0.2

mg of desmopressin and in 29% who were given 0.4 mg of desmopressin. Next most commonly found side effect was nausea found in 17%, 8% and 29% of patients given 0.1, 0.2 and 0.4 mg respectively. Next common side effect was vomiting found in 0%, 8% and 14% patients given 0.1,0.2 and 0.4 mg respectively. Least common side-effect was hyponatremia found in 0%, 0% and 14% patients of 0.1, 0.2 and 0.4 mg group patients respectively.

DISCUSSION

Rembratt and colleagues recruited 72 patients with a median age of 75.5 (range 66–90), all of whom experienced two or more voids per night and completed frequency– volume charts for 72 hours while taking 0.2 mg of desmopressin tablets. [Rembratt et al. 2003]$_5$ Primary endpoint was safety in regard to serum sodium. Despite the fact that 34 patients (47%) reported a total of 49 adverse events, headache being most frequent (16%), only four patients experienced serum sodium <134 mmol/l, and all were at least 79 years of age. There were no serious adverse effects. The authors concluded that desmopressin tablets were well tolerated in the short term.

Kuo aimed to examine the efficacy of desmopressin tablets in patients >65 years old, safety and adverse effects being reserved as secondary end-points.[Kuo 2012]$_6$ He recruited patients with more than three episodes of nocturia as well as nocturnal polyuria (>35% of total voided volume at night) according to frequency–volume charts. Those with normal serum electrolytes and complete frequency–volume charts (72 hours of data) were eligible. Desmopressin tablets at a dose of 0.1 mg were administered for 4 weeks; a visit at the 2-week mark was carried out in order to collect another 3-day frequency–volume chart, as well as urine for specific gravity and serum electrolytes. The patients were followed for 4 weeks after stopping desmopressin. Quality of life was also examined. A total of 30 patients ultimately underwent medication administration; 25 men and five women, mean age 75.4 ± 6.6 years, range 65–84. Five patients

(16.7%) reported side effects, namely dizziness and headache, generalized erythema, general weakness and increased urinary frequency.Kuo concluded that desmopressin tablets were safe and effective for administration in the elderly in the short term.

CONCLUSION

Patients with nocturia who had a pharmacological response to desmopressin were treated with desmopressin. Desmopressin given orally at bedtime at doses of 0.1, 0.2 or 0.4 mg led to a 80% reduction in night time voids of patients with nocturia, whereas only 16% receiving placebo had a clinical response.

The optimal dose of desmopressin was 0.2 mg in maximum people.

The three group of patients treated with 0.1, 0.2 and 0.4 mg dosage of desmopressin were 6, 12, and 7 in no. respectively having mean no. of hours of nocturnal voids being 3, 3 and 4.0 respectively before the start of treatment which after the course of treatment improved to be 1.4, 1.2 and 2.4 respectively.Hence it was concluded desmopressin helped in comparison to placebo.

The mean nocturnal volume of the 25 patients who were treated with desmopressin for 4 weeks also decreased.

Various side effects were encountered during the course of study,

most commonly being headache. Next common side effect was vomiting and least common side-effect was hyponatremia.

Hence on the basis of our study we concluded that Desmopressin was more efficient in decreasing mean nocturnal voids as opposed to the placebo. And of all the three doses of desmopressin 0.2 mg of desmopressin was recommended as it was better in terms of decreasing mean nocturnal voids and mean nocturnal volume and also side-effects encountered.

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