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THE EFFICACY AND SAFETY OF ORAL DESMOPRESSIN IN THE TREATMENT OF NOCTURIA IN MEN AND WOMEN

Aims of Study

Nocturia, defined as waking at night to void, is caused by several factors including nocturnal polyuria. The aims of this study were to investigate the efficacy and safety or oral desmopressin, an antidiuretic agent, in the treatment of nocturia in men and women.

Methods

The study (NOCT 4) was an international, multi-centre, phase IIIB study. Women and men aged ≥ 18 years were screened using frequency-volume charts and were eligible to take part if they had verified nocturia (defined as ≥ 2 voids per night on average).

An open-label dose-titration period established the optimal dose for each patient using 0.1 mg, 0.2 mg and 0.4 mg of desmopressin (Minirin®) for one week each. After a one-week washout period, patients were randomised to receive either placebo or desmopressin at the optimal dose for a three-week double-blind period. Optimal desmopressin dose and placebo were compared for the primary endpoint; proportion of patients with at least 50% reduction in the mean number of nightly voids. Secondary endpoints included changes in mean number of voids per night and duration of the period until the first nocturnal void. Safety parameters included incidence of adverse events, vital signs and measurement of serum sodium levels.

Results

In all 271 patients were screened of which 184 entered the dose-titration period. Fifty-seven (31%) patients were withdrawn. The most frequent reasons for withdrawal were adverse events (14 patients), nocturnal diuresis not returning to pre-treatment levels during wash-out (13 patients) and lack of efficacy (12 patients). The population for the main analysis (the intent-to-treat population) consisted of 60 patients on desmopressin and 66 patients on placebo.

The proportion of patients who obtained at least a 50% reduction in the number of nocturnal voids was significantly greater (p=0.0014) in the desmopressin group (n=20; 33%) than in the placebo group (n=7; 11%). Further, significant differences between the two groups were demonstrated for number of nocturnal voids and duration of first sleep period; Table 1.

Table1: Summary of secondary endpoints

	Desmopressin Mean (SD)			Mean[b]	95% Confidence interval
	Baseline N=60	**Treatment N=60**	**% Change[a]**		
Mean number of nocturnal voids	3.26 (0.96)	2.01 (0.96)	- 37.8	–0.84	[–1.12 to –0.57][c]
Duration of first sleep period (min)	139 (49)	247 (95)	+ 74.7	67.2	[39.0 to 95.4][c]

[a] Median percentage difference between end of treatment values compared with baseline values
[b] Difference between desmopressin and placebo in terms of the absolute change in mean values
[c] p<0.0001

A total of 175 adverse events were reported by 93 (51%) patients during dose titration/washout. In the double-blind period 15 (25%) patients on desmopressin and 15 (23%) patients on placebo had a total of 40 adverse events. During dose-titration 52 (28%) patients reported 75 treatment-related adverse events. During the double-blind period four (7%) patients on desmopressin and one (2%) patient on placebo reported treatment-related adverse events. Headache (9%), abdominal pain (4%), hyponatraemia (3%), and dry mouth (3%) were the most frequently reported treatment-related adverse events. Three patients reported six serious

adverse events during dose-titration. In the double-blind period two serious adverse events were reported; one in each treatment group. None of the serious adverse events in the study was judged to be treatment related. Serum sodium levels below the normal range were recorded at least once for 26 (14%) patients, of which 17 (9%) patients had serum sodium levels below 130 mmol/l. Of these one patient had symptoms that could be associated with hyponatraemia. All cases of hyponatraemia occurred in the dose-titration period and were mainly observed in patients above the age of 65 years.

Conclusion

- Orally administered desmopressin is found to be superior to placebo in the treatment of nocturia. It reduces the number of nocturnal voids and prolongs the period of sleep before the first nocturnal void.
- Both the efficacy and the safety results of this study (NOCT 4) reflect the findings of two previous studies, one in men (NOCT 2A) and one in women (NOCT 3A).
- The use of desmopressin for the treatment of nocturia is safe in the dose levels tested. The type of reported adverse events were comparable with previous experience. The elderly (over 65 years) seem to be more susceptible to develop hyponatraemia than patients aged below 65 years.