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Lose G. [1], Mattiasson A. [2]
1. County Hospital of Glostrup, 2. University Hospital of Lund, Sweden

ORAL DESMOPRESSIN (MINIRIN®) IN LONG-TERM TREATMENT OF MALE AND FEMALE PATIENTS WITH NOCTURIA

Aims of Study

Desmopressin (Minirin®) is a suitable treatment for nocturia caused by polyuria. However, long-term data does not exist. The aims of these studies were to investigate the long-term safety and efficacy of oral desmopressin in patients with nocturia.

Methods

The studies were international, multi-centre, open-labelled phase III studies. One study was performed in male and one in female patients. Otherwise the studies applied the same design. Desmopressin was administered in doses of 0.1 mg, 0.2 mg and 0.4 mg.
Patients, who had completed the 3-week short-term studies (1, 2) were offered to participate in the 10 to 12 month's long-term studies. The main inclusion criteria were consenting male or female aged ≥ 18 years with ≥ 2 voids per night and a nocturnal urine production greater than functional bladder capacity.

The primary outcome measure was

- to assess the safety (adverse events and fluctuations in serum sodium over time) of long-term treatment with desmopressin in nocturia patients who had been successfully treated during 3-week short-term studies

Secondary outcome measures were:

- number of nocturnal voids
- time from bedtime until the first nocturnal void
- proportion of responders (defined as ≥ 50% reduction in the number of nocturnal voids compared to baseline)

Results

Desmopressin was administered orally to 132 male and 117 female patients corresponding to 92% and 83% of the patients completing short-term studies, respectively. In all, 74% and 72% of the male and female patients completed the long-term studies. The main reasons for not completing the long-term studies were adverse events (14% male and 10% female) and lack of efficacy (4% male and 7% female).
Desmopressin in doses of 0.1 mg, 0.2 mg and 0.4 mg were administered to 14%, 34% and 52% of the male patients and to 15%, 38%, and 47% of the female patients. Very few patients changed dose during the studies.
Desmopressin was well tolerated in long-term treatment of nocturia. The frequency and type of adverse events was low and as seen in the short-term studies. For males the most frequent (≥3% of the patients) treatment-related adverse events were dizziness (5%) and headache (5%). For females, headache (7%), oedema peripheral (3%), increase in micturition frequency (3%), and urinary tract infection (3%) were the most frequent treatment-related adverse events.
The fluctuations seen in serum sodium were low and in most patients without clinical relevance. Overall, 35 out of 249 patients developed hyponatraemia of which 33 cases were evaluated as non-clinically relevant by the investigators. The majority of all hyponatraemia cases (33 out of 35) were borderline hyponatraemia (se-sodium below normal range but higher or equal to 130 mmol/l). Two patients developed Class I hyponatraemia (se-sodium higher or equal to 125 mmol/l but below 130 mmol/l). No patients developed Class II hyponatraemia (se-sodium below 125 mmol/l).
The statistically significant effect demonstrated in the desmopressin group compared to the placebo group in the short-term studies was maintained or even improved during desmopressin treatment in the long-term studies. That is, the reduction in mean number of nocturnal voids, the increase in mean duration of the first sleep period and the proportion of responders were improved during desmopressin treatment; Table 1.

Table 1: Summary of efficacy endpoints

	Baseline at short-term Mean (SD)	Start of long-term[a] Mean (SD)	10 months treatment Mean (SD)	12 months treatment Mean (SD)
Nocturnal voids				
Male	3.06 (1.08)	1.70 (0.90)	1.51 (0.92)	1.25 (0.76)
Female	2.89 (0.81)	1.57 (0.85)	1.22 (0.81)	1.19 (0.79)
Duration of first sleep period (minutes)				
Male	157 (51)	275 (91)	281 (100)	288 (109)
Female	142 (47)	277 (102)	307 (117)	310 (108)
Proportion of responders (≥50 reduction in number of nocturnal voids)				
Male	-	37%	52%	67%
Female	-	46%	66%	67%
Number of patients throughout the studies				
Male	N=132	N=75	N=95	N=33
Female	N=117	N=56	N=85	N=79

a) Results for patients treated with desmopressin in 3-week short-term studies. Comparison of baseline with start of long-term studies reflects the treatment effect obtained in 3-week short-term studies.

Conclusions

- Desmopressin is well tolerated in long-term treatment of nocturia
- Fluctuations in s-sodium are low and in most patients without clinical relevance
- The statistically significant efficacy of desmopressin obtained in the 3-week short-term studies was maintained or even improved during desmopressin treatment in the long-term studies