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IMPROVEMENT OF SLEEP AND QOL IN PATIENTS WITH LUTS/BPH AND PREDOMINANT NOCTURIA FOLLOWING TREATMENT WITH DESMOPRESSIN.

Hypothesis / aims of study

Nocturia is a highly prevalent condition in adults and is the most bothersome symptom for patients with lower urinary tract symptoms (LUTS) suggestive of benign prostate hyperplasia (BPH), affecting 80% of those patients(1). Although the causes of nocturia are generally considered multifactorial, in a high proportion of patients the underlying pathogenesis is nocturnal polyuria (2).

Nocturia is the leading cause of sleep disturbances or sleep fragmentation. An increased impairment in overall and health related quality of life (QoL) is associated with the severity of nocturia. Reduction of the first sleep period (SWS) leads to a negative effect on daytime activity (3).

It has been previously demonstrated that Desmopressin increases the first sleep period in nocturic patients. The primary aim of this observational study for treatment of nocturia associated with nocturnal polyuria was to examine the effect of Desmopressin therapy on quality of sleep and hence QoL in patients with LUTS/BPH and nocturia as the predominant symptom. As alpha(1)-adrenoceptor antagonists and other additional products acting on bladder neck or detrusor muscle are considered to have a beneficial effect on LUTS/BPH patients, it was of additional interest to see if Desmopressin could further improve the nocturia component of LUTS in these patients.

Study design, materials and methods

A total of 109 patients with LUTS suggestive of BPH and nocturia as the predominant symptom were included in this observational study in 47 centers in Germany. Patients were treated with Desmopressin tablets for 3 months; LUTS/BPH co-medication was recorded but remained unchanged. Patients were asked to fill in a bladder diary to record times of micturitions and voided volumes as well as fluid intake. To investigate the impact of therapy on QoL patients were asked to fill in the International Consultation on Incontinence Modular Questionnaire-Nocturia (ICIQ-N) before and during therapy as well as the Leeds sleep evaluation questionnaire (LSEQ) which documents changes in sleep evaluation compared to usual.

Statistical analysis: The non-parametric correlation between changes in duration of first sleep period and LSEQ items was studied using Spearman's correlation.

Results

104 (95%) of patients completed therapy. 5 patients withdrew. Withdrawals were due to adverse events (N=2), lack of efficacy (N=2) or non compliance (n=1). Age range was 46 – 82 years (median 63). Median IPSS was 17 and median nocturia episodes per night were 4. 87,2% of patients were treated with Desmopressin 0,1 mg tablets. 61,5% of the patients were on co-medication, with alpha(1)-adrenoceptor antagonists being the most frequently used medication (47,7%). The percentage of nocturnal urine volume of total 24h urine volume was <30% in 23,4%, 30-40% in 51,1%, >40% in 25,5% of patients. 40,3% of the patients had >8 daytime voids. Median duration of the first undisturbed sleep period was 2h. Median degree of bother from nocturia obtained from ICIQ-N was 8.

Following onset of Desmopressin median IPSS reduction from 17 to 12 and median reductions of nocturia episodes from 4 to 2 was observed. The median degree of bother (ICIQ-N) from nocturia decreased from 8 to 3 (on a scale from 0 (no problem)-10 (big problem)). During therapy the median percentage of nocturnal urine volume/24h decreased significantly from 34% to 20%.The median duration of the first sleep period increased from 2 h to 4 h with the percentage of patients benefitting from sleep duration above 4 hours increased from 5,1% to 76,8%. The LSEQ analysis showed an overall significant effect of therapy on improving sleep ($p<0,0001$) and calmer sleep ($p<0,0001$), fewer awakenings ($p<0,0001$), easier awakening in the morning ($p<0,0001$) as well as being more alert with less disrupted co-ordination after waking up ($p<0,0001$), respectively.

Subgroup analysis for patients (n=34) with nocturnal urine volume >30%/24h although already receiving alpha(1)-adrenoceptor antagonists co-medication (at least 4 weeks before start of desmopressin treatment) could demonstrate a significant decrease in median nocturia episodes (from 4 to 2) and median IPSS (from 18 to 14). Baseline nocturia episodes and IPSS of this subgroup were comparable to the subgroup of patients without co-medication and nocturnal urine volume >30%/24h.

Desmopressin was well tolerated with 2,8% AE's (n=3) and no occurrence of a severe event.

Tolerability and efficacy was evaluated as very good or good by 84,9% of patients or 85,6% of doctors.

Interpretation of results

Consistent with other studies Desmopressin therapy had significant impact on the prolongation of the first sleep period as well as the reduction in number of nocturia episodes and lowering the percentage of nocturnal urine volume/24h urine output compared to baseline. As expected the ICIQ-N (item 3 and 4) demonstrates a significant decreases in QoL with increasing number of nocturia episodes ($p<0,0001$) as well as improvement in QoL during desmopressin therapy.

Consistent with the prolongation of the first sleep period the LSEQ was able to detect an overall improvement in sleep (4 items: getting to sleep – GTS; quality of sleep – QOS; awake following sleep – AFS; behaviour following awakening BFW) during desmopressin therapy as compared to usual. In addition, when looking at specific items of the LSEQ the item "behaviour following wakening" (BFW) correlated with changes in duration of the first undisturbed sleep period ($0,221$, $p<0,0312$). Longer first sleep period changes led to patients being more alert and less tired when waking up and during the daytime as well as showing less disrupted balance and co-ordination upon awakening.

The results of the study showed significantly improved sleep quality as well as QoL in nocturia patients with LUTS/BPH during desmopressin therapy.

Subgroup analyses demonstrate a significant reduction in nocturia episodes and IPSS for patients with alpha(1)-adrenoceptor antagonist co-medication.

Concluding message

In LUTS patients treated with conventional BPH medication nocturia is poorly managed as nocturnal polyuria persists. Reduction of nocturia episodes due to Desmopressin treatment has a significant positive impact on sleep quality and QoL. This supports the importance of an individual treatment approach that addresses the aetiology for patients with LUTS/BPH and nocturia as the predominant symptom.

References

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What were the subjects in the study?	**HUMAN**
Was this study approved by an ethics committee?	**No**
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Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**