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TREATMENT OF NOCTURIA INCREASES QOL

Hypothesis / aims of study

Nocturia, the need to wake at night to void, is proven to be one of the most bothersome lower urinary tracts symptoms (1). The severity is traditionally measured by number of nocturnal voids and sleep duration. Lately, however, several large epidemiological studies have linked the number of nocturnal voids with a decrease in quality of life (QoL) and have found a close correlation: the more nocturnal voids, the worse the QoL (2,3). Despite these studies, nocturia is still often left untreated and the patient is told that increased nocturnal voiding is a natural part of aging.

Several studies have shown that nocturia can be treated effectively, reducing the number of voids and increasing the length of the initial period of undisturbed sleep. We wanted to explore the relation between the reduction in nocturia symptoms and increase in QoL and whether the impact on QoL differs between age groups.

Study design, materials and methods

This was a phase 3 randomized, double-blind, placebo-controlled, multicenter study investigating the efficacy and safety of desmopressin orally disintegrating tablet in adults with ≥2 voids per night. The study was conducted at 78 study centers in the USA and Canada. In total 799 subjects were randomized to placebo or one of four different doses of desmopressin administered sub-lingually 1 hour before bedtime. 717 subjects providing data at both baseline and end of study are included in this analysis.

At baseline and Day 28 patients were asked to complete a 3-day voiding diary, with information on number of voids, a sleep diary, including information on initial period of undisturbed sleep, and a disease-specific QoL questionnaire, the N-QoL. The N-QoL is a 13-item questionnaire consisting of 12 core items arranged in two domains (sleep/energy and bother/concern) and a total score.

The impact on QoL of a change in number of nocturnal voids was investigated by an ANCOVA model using the change from baseline in QoL as outcome (dependent) variable. Age (<65, ≥65 years) was included as a factor and change from baseline in nocturnal voids and the baseline QoL score were used as covariates. This analysis was performed for the overall N-QoL score and for each of the two domains. A similar model was used for exploring the relationship between change in initial period of undisturbed sleep (hours) and QoL. Estimates are presented with 95% confidence limits.

Results

Table 1. Mean total N-QoL score (and standard deviation) at baseline and Day 28 by change in number of nocturnal voids

		Worsened (>0.5 voids) N=57	Stable (0 ± 0.5 voids) N = 175	-1 void (-1 ± 0.5 voids) N=241	-2 voids (-2 ± 0.5 voids) N=183	-3 + voids (<-2.5 voids) N=61
<65 years	Baseline	49.0 (22.9)	46.5 (20.8)	46.8 (19.2)	45.7 (20.3)	35.0 (17.2)
	Day 28	53.2 (27.2)	59.2 (22.3)	64.6 (20.7)	70.9 (20.0)	68.7 (22.2)
≥65 years	Baseline	54.6 (19.1)	55.2 (21.9)	58.0 (19.0)	50.9 (21.0)	42.1 (18.0)
	Day 28	60.8 (20.1)	64.2 (20.8)	72.2 (16.7)	71.6 (19.4)	68.3 (21.2)

Table 2. Effect of a change in number of voids on N-QoL (total, sleep/energy domain and bother/concern domain)

		Change in N-QoL per void (95% confidence limits)
<65 years	N-QoL (total score)	5.59 (4.06, 7.12)*
	N-QoL (sleep/energy)	4.47 (2.85, 6.09)*
	N-QoL (bother/concern)	6.51 (4.78, 8.24)*¤
≥65 years	N-QoL (total score)	3.77 (2.28, 5.26)*
	N-QoL (sleep/energy)	4.02 (2.43, 5.61)*
	N-QoL (bother/concern)	3.55 (1.87, 5.23)*¤

*P<0.0001.

¤The decrease in QoL per additional void was significantly larger for patients <65 years, p<0.015

Table 3. Effect of a change of 1 hour in initial period of undisturbed sleep on N-QOL score (total, sleep/energy domain and bother/concern domain).

		Change in N-QoL per hour change in first period of undisturbed sleep (95% confidence limits)
<65 years	N-QoL (total score)	4.02 (3.13, 4.91)*
	N-QoL (sleep/energy)	3.35 (2.40, 4.30)*
	N-QoL (bother/concern)	4.64 (3.63, 5.65)*¤
≥65 years	N-QoL (total score)	3.34 (2.25, 4.43)*
	N-QoL (sleep/energy)	3.20 (2.03, 4.36)*
	N-QoL (bother/concern)	3.46 (2.23, 4.69)*¤

*P<0.0001.

¤The increase in QoL per additional hour during the initial period of undisturbed sleep was significantly larger for patients <65 years, p<0.013

Interpretation of results

The analyses showed improvement on the total score from baseline to Day 28 for all groups (see Table 1). Furthermore, the ANCOVA analysis showed that for every reduction of one nocturnal void, the QoL of the patient will increase 5.59 for those <65 years and 3.77 for those ≥65 years on the total QoL score (Table 2). When looking at the domains, the QoL increase per void is larger in the area of bother/concern compared with sleep/energy for those <65 years. For every 1 hour increase in the first period of undisturbed sleep, total QoL increased by 4.02 in those <65 years and 3.34 in those ≥65 (Table 3). Bother/concern showed a larger increase per hour gained compared with sleep/energy for all patients.

The differences in improvement in N-QoL score between those over and under 65 years were only statistically significant when looking at the bother/concern domain, with younger patients experiencing significantly greater improvements in bother/concern with a reduction of one void per night and with an increase of 1 hour in the initial period of undisturbed sleep (Tables 2 and 3).

Concluding message

QoL of nocturia patients increases significantly for every reduction of one void and for every hour the first period of sleep increases. Improvements in total QoL and both domains of QoL (as measured by the N-QoL questionnaire) were numerically greater in younger patients than older patients, and were significantly greater in younger patients for the bother/concern domain. This may reflect a superior benefit of treatment for patients who are still active in the workforce. Overall, treatment of nocturia does significantly improve the QoL of the patient, and this indicates that both diagnostic and therapeutic follow-up of nocturia patients is warranted.

References

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Specify Name of Public Registry, Registration Number	**The study was registered on www.clinicaltrials.gov (NCT00477490, NCT00615836)**
Is this a Randomised Controlled Trial (RCT)?	**Yes**
What were the subjects in the study?	**HUMAN**
Was this study approved by an ethics committee?	**Yes**
Specify Name of Ethics Committee	**The study was approved by the institutional review board or ethics committee for each site.**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**