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BASELINE CHARACTERISTICS OF NOCTURIA PATIENTS IN A LARGE PHASE III CLINICAL TRIAL

Hypothesis / aims of study

The aim of this study was to investigate the demographic and clinical characteristics of people with nocturia who volunteered to participate in a large Phase III trial of nocturia therapy performed in the USA and Canada.

Study design, materials and methods

Patients were recruited from 83 study centers in the USA and Canada. Subjects were considered eligible if they were ≥18 years of age, had an average of ≥2 voids per night (determined using a 3-day frequency-volume chart), and provided informed consent. Subjects were excluded if genitourinary tract conditions were suspected. In males, this included suspicion of bladder outlet obstruction (BOO), or surgical treatment for BOO or benign prostatic hyperplasia (BPH) in the past 6 months. In females, this included pregnancy, use of a pessary for pelvic prolapse, or the presence of an unexplained pelvic mass. In both sexes, subjects were excluded if urinary retention was suspected, if they had ever experienced urological malignancies, or if there was a history of neurogenic detrusor activity. Other exclusions were cardiac failure, uncontrolled hypertension, uncontrolled diabetes mellitus, renal insufficiency, hepatic and/or biliary disease, hyponatremia, diabetes insipidus, Syndrome of Inappropriate Anti-Diuretic Hormone secretion (SIADH), psychogenic or habitual polydipsia and obstructive sleep apnea requiring therapy. Individuals were also excluded if there was known alcohol or substance abuse, if their work/lifestyle potentially interfered with regular night-time sleep (eg shift workers), if they had received previous desmopressin treatment for nocturia, or if they were receiving loop diuretics. Other classes of diuretics were permitted, either as monotherapy or combination therapy.

Baseline data collected included demographic characteristics, medical history and medication, as well as voiding characteristics and sleep characteristics (assessed using diaries and questionnaires).

Results

Of the 757 intention to treat (ITT) subjects, 341 (45%) were female and 416 (55%) were male; 80% of subjects were white, 15% were black/African American, 2% were Asian. Hispanics comprised 7% of the study population. The mean age of the ITT subjects was 62.0 years (median age: 64 years) and age ranged from 20 to 89 years. 382/757 participants were <65 years of age. Mean height was 1.7 m, mean weight was 85.8 kg, and mean body mass index (BMI) was 29.6 kg/m^2.

Almost all (97%) subjects reported a medical history. The most common medical histories overall were associated with renal and urinary disorders (65%), including frequency, urgency, incontinence and nocturia; musculoskeletal and connective tissue disorders (52%), including osteoarthritis (19%) and back pain (10%); gastrointestinal disorders (48%), including dry mouth (23%) and gastroesophageal reflux disease (GERD, 17%); reproductive system and breast disorders (45%), including BPH (49%) and erectile dysfunction (20%) in males; surgical and medical procedures (42%), including hysterectomy (28%) in females; vascular disorders (42%), including hypertension (39%); and metabolism and nutrition disorders (41%), including hypercholesterolemia (23%).

Based on the medical history collected, 37% of all subjects reported that they had ever been diagnosed with urinary urge incontinence (UUI), and 28% of all subjects reported that they had been diagnosed with overactive bladder (OAB). Since UUI represents a subset of the OAB patient population, these conditions grossly overlap. Of the 416 males, 214 (51%) reported that they had been diagnosed with BPH.

Most (90%) subjects used concomitant medications. Overall, the most common (≥10%) types of concomitant medications included lipid-modifying agents (34%), antithrombotic agents (31%), nonsteroidal anti-inflammatory/antirheumatic products (28%), combination multivitamins (26%), drugs for peptic ulcer and GERD (18%), other analgesics and antipyretics (15%), antidepressants (14%), beta blocking agents (14%), other urologicals including antispasmodics (13%), calcium (13%), angiotensin-converting enzyme (ACE) inhibitors (12%), and drugs used in BPH (10%).

At baseline, the median number of nocturnal voids overall was 3.0 and ranged from 2–8.7. 54% of subjects averaged ≤3 nocturnal voids, with 28% averaging 3–4 nocturnal voids and 11% averaging 4–5 nocturnal voids. 6.7% had an average of >5 voids per night. 21.2% voided more than 8 times during the daytime on average, indicating increased daytime frequency. 683/757 (90%) of participants were found to have nocturnal polyuria (NP), defined as a ratio of night-time urine volume/24-hour urine volume of ≥33%. Sleep and night-time voiding characteristics are summarized in Table 1.

Table 1: Sleep and nocturia characteristics of patients at baseline

	Mean	**SD**	**Median**	**Range**
Mean number of voids	3.3	1.14	3	2, 8.7
Wake ups during night	3.4	1.3	3.3	1, 10.3
Reported overall sleep duration (minutes)	406.0	79.8	408.3	76.7, 673.7
Estimated awake duration (minutes)	65.8	66.1	50	0, 860.0
Initial period undisturbed sleep (minutes)	114.7	64.0	106.7	0, 470.0
Global PSQI score (≥5 indicates poor sleeper)	8.4	3.9	8.0	0, 20

*PSQI: Pittsburgh Sleep Quality Index

Interpretation of results

Patients in the ITT sample experienced an average of 3.3 voids per night, but this ranged up to 8.7 voids per night; as many as 46% of patients had an average of >3 voids per night. The initial period of undisturbed sleep was under 2 hours on average. It is therefore likely that nocturia patients' sleep is routinely being disrupted during the important phase of restorative slow-wave sleep in the early part of the night (1). Indeed, the mean global PSQI score indicated that the patient group had clinically poor sleep quality.

The impact of nocturia on sleep is, therefore, serious and the condition should be regarded as non-trivial and worthy of treatment in those who are bothered by night-time voiding.

28% of all subjects reported that they had been diagnosed with OAB, and 51% of men reported that they had been diagnosed with BPH. Furthermore, 13% of patients were receiving antispasmodics and 10% were receiving drugs used in BPH. It can be hypothesised that those who were not currently receiving treatment for diagnosed OAB or BPH had previously been prescribed treatment for these conditions. However, for all of these patients, nocturia had persisted. This suggests that, despite a diagnosis of BPH in the majority of men, and of OAB in nearly 30% of participants, nocturia remained problematic and had not been resolved with treatment for these conditions. 90% of participants were found to have NP and this may indicate that nocturia for these patients, including those with an OAB/BPH diagnosis, is at least partially attributable to an overproduction of urine at night.

Concluding message

At baseline, nocturia patients in this trial had an initial sleep duration of less than 2 hours and clinically impaired sleep quality. Nocturia is, therefore, a condition with a clear impact on sleep, and like sleep disorders, should be considered a non-trivial condition worthy of proactive management. Many patients in this study of nocturia therapy had previously received a diagnosis of OAB and/or BPH, but nocturia had persisted and led to their involvement in this trial. The persistence of nocturia in these patients may be in part due to the presence of NP in the large majority of patients: amongst the broad range of patients investigated, 90% of the ITT population were found to have NP. Effective management of nocturia should take into account the high probability of NP, which can be detected using a frequency-volume chart. Traditional therapies for conditions such as OAB and BPH do not target NP; treatment selection should therefore be tailored to the etiology of nocturia, and specifically to the overproduction of urine at night if NP is present.

References

1. Stanley. Eur Urol Suppl 2005;4:17–19

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Specify Name of Public Registry, Registration Number	**Clinicaltrials.gov NCT00477490**
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Was this study approved by an ethics committee?	**Yes**
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Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**