Short Time to First Void Is Associated with Lower Whole-Night Sleep Quality in Nocturia Patients

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Study Objective: To examine associations between diary-based reports of the time to first void and a commonly used measure of sleep across the entire night, the Pittsburgh Sleep Quality Index (PSQI).

Design and Setting: Data from the Baseline phase of a large, multi-site, US-based, randomized clinical trial of a nocturia medication were analyzed. We examined age-adjusted associations between time to first void as reported in a 3-day diary and PSQI Global and individual subscale scores.

Patients: 757 patients with nocturia completing Baseline measurements

Interventions: None.

Measurements and Results: Using quartile analysis, higher scores indicating poorer sleep on all PSQI scales were associated ($p \leq 0.05$) with short time to first void durations.

Among individuals in the lowest quartile of time to first void (< 1.17 hours), the odds ratio (OR) of a PSQI Global score > 5 was nearly 3 times (2.96; 95% CI 1.75–5.01) that of those in the highest quartile (> 2.50 h). Shorter time to first void was associated with lower sleep quality, shorter sleep duration, poorer sleep efficiency, and greater daytime dysfunction.

Conclusions: Time to first void may serve as a valuable adjunctive, self-report measure for characterizing poor sleep among populations with nocturia.

Keywords: nocturia, nocturnal micturition, self-reports, insomnia, PSQI

Citation: Bliwise DL, Holm-Larsen T, Goble S, Nørgaard JP. Short time to first void is associated with lower whole-night sleep quality in nocturia patients. *J Clin Sleep Med* 2015;11(1):53–55.

The time to first void refers to the interval before an individual awakens to urinate for the first time during a night of sleep. As a self-report, time to first void has been used by some pharmacologic studies of nocturia^{1,2} to estimate the extent to which sleep is disrupted by associated trips to the bathroom, specifically the initial bathroom trip of the night. Although nocturia has typically been defined as one or more nocturnal voids preceded and followed by sleep by the International Continence Society,¹ or alternatively, as at least two-thirds of nocturnal awakenings associated with voiding as recorded on overnight sleep diaries,³ the relative simplicity of the time to first void makes it an attractive measure for subjective recall. Despite this intuitive appeal, this measure may or may not be related to the quality of entire night of sleep, and no data have related individual differences in it to more conventional measures of subjective sleep quality. In this study we examined associations between time to first void and a widely used self-reported measure of sleep, the Pittsburgh Sleep Quality Index (PSQI)⁴ to determine the utility of the measure as a marker of general sleep quality.

METHODS

The baseline data (i.e., prior to ingestion of first medication) from patients in a previously published randomized clinical trial of a nocturia medication⁵ were analyzed. All participants in the trial provided Informed Consent and all study procedures complied with the ethical standards of the relevant national and institutional committees on human experimentation and with the

BRIEF SUMMARY

Current Knowledge/Study Rationale: This study sought to determine to what extent poor sleep quality, as measured by the Pittsburgh Sleep Quality Index (PSQI), was related to a commonly used measure in studies of nocturia, the time to first void.

Study Impact: The data presented here indicate that time to first void is a good proxy for many aspects of sleep assessed by the PSQI, including sleep quality, depth, duration and even daytime sleepiness. The overall magnitude of effects were relatively small, but the ease of collecting this self-reported measure related to nocturnal voiding suggests that it could have value in future studies.

Helsinki Declaration of 1975, as revised in 2008. Patients in the trial completed a 3-day sleep and voiding diary during the screening phase, in which all were asked to record the time of going to bed, the time of their voids during the night, and the time of their morning wake-up. The endpoint of the time to first void (referred to as the initial period of undisturbed sleep in the clinical trial) was defined as the mean time in minutes from turning off the light with the intention of going to bed until the first nocturnal void or until the time of final awakening (if no void occurred) averaged across all 3 nights. All patients were also asked to complete the PSQI, which employs a 30-day recall period and collects data on sleep quality, duration, and latency and other features of sleep over the entire night. The PSQI is a widely used sleep questionnaire and generates scores on 7 different subscales as well as a Global summary score.⁴ It has both high test-retest reliability and strong discriminant validity for good versus poor sleep.⁶ Each

Figure 1—Frequency distribution for time to first void. **Table 1**—Scores on Pittsburgh Sleep Quality Index (PSQI) for study population.

PSQI Variable	N	Mean	SD
Global Score	726	8.45	3.86
Quality	755	1.51	0.77
Latency	730	1.37	0.96
Duration	753	0.97	1.01
Efficiency	751	1.25	1.13
Sleep Disturbance	755	1.60	0.65
Sleep Medication	755	0.56	1.02
Daytime Dysfunction	754	1.24	0.86

PSQI scale score was analyzed with summary statistics, and we examined the distributions of the time to first void and the PSQI Global score across participants. Associations between time to first void and PSQI scale scores were analyzed using age-adjusted Pearson correlation statistics. In order to further explore the relationship between time to first void and PSQI, we examined individual PSQI scale scores across quartiles (Q) of time to first void (Q1: < 1.17 h; Q2: 1.17–1.78 h; Q3: 1.79–2.50 h; Q4: > 2.50 h) using an analysis of covariance, with each PSQI scale score as the dependent variable, quartile group as a factor and both age and sex as adjustment covariates. The proportion of patients with PSQI global score > 5 (indicating relatively poor sleep) among the patients in the lowest quartile compared to those in the highest quartile was compared using logistic regression with the quartile group as a factor and age and sex as adjustment covariates.

RESULTS

There were 757 patients with a mean age of 62 years (range 20–89) in the intent-to-treat population for this US-based study. The study used stratified randomization 1:1 for < 65 versus ≥ 65 years old and consisted of 416 (55%) men and 341 (45%) women. Mean number of nocturnal voids per night was 3.22 (SD 1.14) and the mean time to first void was 1.91 h (SD 1.07). **Figure 1** shows the distribution of time to first void across these patients with nocturia. The distribution approximated normality with a mean (SD) of 1.91 (1.07) h and a median of 1.78 hours. PSQI Global Score is plotted in **Figure 2** and also approximates a normal distribution. **Table 1** shows

Figure 2—Frequency distribution for Pittsburgh Sleep Quality Index (global score). **Table 2**—Age- and sex-adjusted correlations between Pittsburgh Sleep Quality Index (PSQI) and time to first void.

PSQI Variable	rho	p
Global Score	-0.20	< 0.0001
Quality	-0.13	0.0004
Latency	-0.20	< 0.0001
Duration	-0.12	0.0017
Efficiency	-0.12	0.0017
Sleep Disturbance	-0.07	0.0481
Sleep Medication	-0.06	0.1032
Daytime Dysfunction	-0.09	0.0210

mean values for PSQI Global score and individual subscale scores for this sample and indicates at least moderate subjective sleep disturbance among these patients. Modal PSQI Global score was 8, which falls within the range usually associated with poor sleep (i.e., > 5).^{4,6} Age- and sex-adjusted correlations (**Table 2**) between time to first void and PSQI scores were statistically significant (all p values ≤ 0.05), with the exception of the sleep medication subscale score, all in the direction of poorer sleep associated with shorter time to first void.

When comparing the average PSQI scores among those in the lowest compared to the highest quartile of time to first void (**Table 3**), there was a statistically significant difference among all PSQI subscales. The PSQI Global score was on average 2.23 points higher among patients with a short time to first void when compared to patients with a longer time to first void (9.62 versus 7.39, $p < 0.0001$). The age- and sex-adjusted odds ratio of a PSQI Global score > 5 for those patients in the shortest time to first void quartile (relative to longest quartile) was 2.96 (95% CI: 1.75–5.01; $p < 0.0001$). These data indicated that the longer the individual's initial uninterrupted sleep period, the higher they rated the depth, the length, and the quality of their sleep for the entire night.

DISCUSSION

As a seldom used marker of general sleep quality for the entire night, time to first void retains clear associations with many specific aspects of sleep as measured by the PSQI, at least in these patients with nocturia. The magnitude of the effects

Table 3—Comparison of age- and sex-adjusted PSQI Scores across quartiles of time to first void.

PSQI Variable	First (Shortest) Time to First Void Quartile Mean (SE)	Second Time to First Void Quartile Mean (SE)	Third Time to First Void Quartile Mean (SE)	Fourth (Longest) Time to First Void Quartile Mean (SE)	p
Global Score	9.62 (0.27)	8.54 (0.28)	7.75 (0.28)	7.39 (0.27)	< 0.0001
Quality	1.62 (0.05)	1.57 (0.05)	1.43 (0.05)	1.34 (0.05)	0.0015
Latency	1.70 (0.07)	1.39 (0.07)	1.19 (0.07)	1.11 (0.07)	< 0.0001
Duration	1.16 (0.07)	0.98 (0.07)	0.83 (0.07)	0.80 (0.07)	0.0020
Efficiency	1.50 (0.08)	1.24 (0.08)	1.04 (0.08)	1.10 (0.08)	0.0005
Sleep Disturbance	1.68 (0.05)	1.63 (0.05)	1.54 (0.05)	1.50 (0.05)	0.0358
Sleep Medication	0.73 (0.07)	0.47 (0.07)	0.50 (0.07)	0.50 (0.07)	0.0486
Daytime Dysfunction	1.37 (0.06)	1.26 (0.06)	1.18 (0.06)	1.12 (0.06)	0.0241

is small, however, but the effects are consistent and uniform across all but one subscale. Recently, increased attention has been directed to awakening during the sleep period to void as a potential cause of poor sleep,^{7–9} although causality may be complex. In some cases, nocturia is comorbid with other conditions associated with increased nocturnal diuresis (e.g., congestive heart failure, sleep apnea),^{10,11} whereas in other cases, nocturia may be associated with conditions that awaken the individual for other reasons (e.g., chronic pain, restless legs syndrome)¹² that lead to bathroom trips, perhaps because of convenience. Even though causes of this phenomenon are multifactorial, the fact that the time to first void relates to many diverse aspects of the sleep experience, as reported on the PSQI, suggests that this might be a potentially important marker to include in population-based studies incorporating self-reports of sleep.

There are several limitations of these data. First, we have demonstrated relationships between time to first void and sleep quality only for a clinical population complaining of nocturia. It remains to be seen whether this metric also retains value in the general population, although studies of nocturia in more representative samples^{8,12} certainly suggest that nocturia is strongly associated with diminished sleep quality in populations not selected specifically for having nocturia. Secondly, the time to first void cannot necessarily be equated with uninterrupted sleep, since the elapsed duration of time may also include awakenings from other causes (e.g., spontaneous awakenings, environmental noise). It is possible that such events may then have led to a bathroom trip, essentially making nocturia secondary to awakenings from other causes. In that sense, the fidelity of time to first void in the current population enriched with nocturia patients may be somewhat higher than when used in the general population. Thirdly, as examined in these data, time to first void is a self-reported measure. It is intuitively possible that a longer initial period of sleep is associated with relatively higher levels of polysomnographically defined features of sleep (e.g., slow wave activity), but this remains unproven. Future polysomnographic studies will be required to document its utility in that regard.

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ACKNOWLEDGMENTS

The authors express our appreciation to Caroline Loat and Allan Blemings for their assistance in various aspects of manuscript preparation and statistical analyses, respectively. Author contributions: Conception (Bliwise, Holm-Larsen, Nørgaard); Data Collection (Holm-Larsen, Goble, Nørgaard); Data Analyses (Bliwise, Holm-Larsen, Goble); Initial Draft of Manuscript (Bliwise); Editing of Manuscript for Critical Content (Bliwise, Holm-Larsen, Goble, Nørgaard).

SUBMISSION & CORRESPONDENCE INFORMATION

Submitted for publication July, 2014

Submitted in final revised form September, 2014

Accepted for publication September, 2014

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DISCLOSURE STATEMENT

This work was supported in part by United States National Institutes of Health grant NS-050595 to Dr. Bliwise and by Global Research and Development Division of Ferring Pharmaceuticals. Drs. Bliwise and Holm-Larsen are paid Consultants of Ferring Pharmaceuticals. Drs. Goble and Nørgaard are employees of Ferring Pharmaceuticals.