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SCIENTIFIC INVESTIGATIONS

Does Zolpidem Enhance the Yield of Polysomnography?

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Study Objectives: An uncomfortable environment or continuous positive airway pressure (CPAP) intolerance may cause poor sleep efficiency during polysomnography and result in a poor-quality study. Unsatisfactory polysomnograms often must be repeated. Nonbenzodiazepine hypnotics may improve sleep efficiency without disruption of sleep architecture. We hypothesized that premedication with zolpidem improves polysomnogram quality and decreases the need to restudy.

Methods: We retrospectively reviewed 200 consecutive polysomnograms. Zolpidem premedication was not standardized and was prescribed at the discretion of consulting sleep physicians, who were unaware of this study. We compared the quality of polysomnograms between patients who received zolpidem 10 mg prior to polysomnography and those who did not. A poor-quality polysomnogram was defined as having insufficient sleep time to allow for diagnosis, incomplete CPAP titration with a resulting apnea-hypopnea index > 10 on the highest level of CPAP achieved, or complete CPAP intolerance.

Results: Of 200 records reviewed, 54 patients (27%) received zolpidem. Demographics did not differ between groups. Premedication with zolpidem resulted in improved sleep latency (11.8 ± 9.5 minutes vs 26.0 ± 19.9 minutes, $p = .002$) and sleep efficiency (89.5% ± 5.6% vs 78.8 ± 12.3, $p < .0001$). Zolpidem premedication resulted in significantly fewer studies meeting criteria for poor quality (7.4% vs 33.6%, $p = .005$). Of the 49 studies meeting criteria for poor quality, 21 were repeated using zolpidem, showing significant improvements in sleep latency (10.8 ± 7.1 minutes vs 42.8 ± 30.5 minutes, $p = .0004$) and sleep efficiency (89.5% ± 4.9% vs 61.8% ± 13.7%, $p < .0001$). No study repeated with zolpidem met criteria for poor quality.

Conclusions: Pretreatment with zolpidem significantly improved polysomnographic quality and may decrease the need to repeat polysomnograms.

Key Words: Zolpidem, polysomnography, sleep study, sleep latency, sleep efficiency, CPAP titration

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The increasing awareness of sleep-disordered breathing has created a tremendous demand for polysomnography (PSG). Waiting times in many laboratories are often excessive, prompting efforts to improve the efficiency of sleep centers and streamline PSG evaluations. Poor-quality studies may lead to an inability to make a diagnosis or to adequately titrate continuous positive airway pressure (CPAP) therapy. Unsatisfactory studies may need to be repeated, further adding to the demand for PSG.

Commentary Follows on Pages 133-135

Multiple factors may lead to inadequate or poor-quality studies. An unfamiliar or uncomfortable environment, contributing to what is called the "first-night effect," may prolong sleep latency and decrease sleep efficiency. Likewise, CPAP intolerance in those initially treated or being titrated to higher levels may also reduce the quality of PSG.

Prestudy sedation may improve patient tolerance of both the lab environment and CPAP titration, resulting in an improved quality and greater yield of PSG. Ideally, this sedating agent would improve sleep efficiency without disrupting sleep architecture. Nonbenzodiazepine hypnotics, such as zolpidem, have been shown to decrease sleep latency and increase total sleep time and efficiency.[1-3] Additionally, they have minimal effects on sleep architecture and respiratory events.[1,3-5] Significant side effects and post-study hypersomnolence are infrequent.[2,3]

We hypothesized that premedication with the nonbenzodiazepine hypnotic agent zolpidem prior to PSG will improve sleep efficiency and patient tolerance to CPAP. These improvements are expected to improve the quality of PSG, resulting in a higher diagnostic yield, better CPAP titration and a decreased need to restudy.

METHODS

Patients

We conducted a retrospective review of consecutive PSG records performed at our sleep laboratory over a 2-month period. Our sleep center is part of an academic, military referral hospital, which serves military service members, retired military members, and their civilian dependents. Our patient population, therefore, comprises both men and women of all ages. We excluded patients younger than 18 years of age and those who received a 5 mg dose of zolpidem prior to PSG. The protocol was approved by our institution's scientific research review committee.

Patients were divided into 2 groups based upon whether or not they received zolpidem 10 mg prior to the start of PSG. Zolpidem was taken within 60 minutes prior to the start of the test.

Disclosure Statement

Drs. Lettieri, Eliasson, Andrada, Khramtsov, and Kristo have indicated no financial conflicts of interest.

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Zolpidem premedication was not standardized and was prescribed at the discretion of the consulting sleep physicians who were unaware of this study. We compared patient demographics and PSG data and the need to restudy between patients who received zolpidem 10 mg and those who did not.

Data

Demographic data, including age and gender, were recorded for analysis. PSG data collected for analysis included sleep latency, sleep efficiency, apnea-hypopnea index (AHI), and final diagnosis. For those undergoing CPAP titration, the AHI on the highest level of CPAP during the PSG was also recorded. Sleep latency was defined as the time, in minutes, from the start of the PSG (lights out) to the onset of sleep. Sleep onset was determined by 3 consecutive epochs of stage 1 sleep or 1 epoch of any other sleep stage. Sleep efficiency was defined as the percentage of the total time with electroencephalographic confirmation of sleep divided by the total time in bed. The AHI reflected the average number of respiratory events per hour of sleep. Respiratory events were defined as apneic episodes lasting longer than 10 seconds or hypopneas (greater than 50% reduction in airflow) associated with an electroencephalographic arousal lasting 3 or more seconds or at least a 4% desaturation, as assessed by noninvasive pulse oximetry.

Endpoints

The primary endpoint of this study was the quality of PSG data. We defined a poor-quality PSG as one with insufficient sleep time to allow for diagnosis, insufficient CPAP titration (AHI greater than 10 on highest CPAP attained), or complete intolerance of CPAP. A PSG was determined to be of poor quality if the interpreting physician felt that a repeat study was necessary to make a diagnosis or to determine a therapeutic CPAP level. Secondary endpoints included the effects of zolpidem on sleep latency, sleep efficiency, and AHI.

Statistical Analysis

Data are presented as mean ± SD and were analyzed with the Student *t* test. All tests were 2 tailed. *P* values of < .05 were assumed to represent statistical significance. All analyses were performed using the Statistical Package for the Social Sciences 11.0 (SPSS Inc, Chicago, IL).

RESULTS

Of the 205 consecutive studies that were evaluated, 2 were performed on children and were excluded from analysis. Two patients received zolpidem 5 mg prior to the study and were also excluded, as this small number would not allow for an adequate subgroup analysis. One patient was receiving chronic zolpidem therapy, and it could not be adequately determined if the medication was taken prior to the study. Of the 205 studies reviewed, data from 200 were included in the final analysis.

Of 200 patients meeting inclusion criteria, 54 (27%) received zolpidem 10 mg prior to PSG. Age and sex did not differ between the groups. Premedication with zolpidem resulted in a significant reduction in sleep latency (11.8 ± 9.5 minutes versus 26.0 ± 19.9 minutes, $p = .002$). Sleep efficiency was also significantly improved with zolpidem pretreatment (89.5% ± 5.6% versus 78.85 ± 12.3%, $p < .0001$). There was no statistical difference in AHI with or without zolpidem (32.4 ± 12.7 versus 30.1 ± 11.9, $p = .28$). The quality of the study was also significantly improved in those receiving zolpidem. Of the studies performed without zolpidem, 33.6% met our definition for poor quality, whereas only 7.4% in those pretreated met this definition ($p = .005$). Comparisons between the 2 groups are depicted in Table 1.

Among the 49 PSGs meeting criteria to be repeated, 30 were repeated during the study period. Of those repeated PSGs, 21 were completed with zolpidem pretreatment, and 9 were completed without zolpidem. Comparing the 21 repeat studies done with zolpidem to their initial study performed without zolpidem, there were significant improvements in both sleep latency (10.8 ± 7.1 minutes versus 42.8 ± 30.5 minutes, $p = .0004$) and sleep efficiency (89.5% ± 4.9% versus 61.8% ± 13.7%, $p < .0001$). Of these 21 PSGs repeated with zolpidem, none met criteria for poor quality. Of the 9 studies repeated without zolpidem, a shorter sleep latency and improved sleep efficiency (less first-night effect) was observed in 3, sleep latency and efficiency were worse in 2, and 5 were of similar quality to their initial studies.

In this study, zolpidem pretreatment resulted in a 78% relative risk reduction for a poor-quality study. In this cohort, the number needed to treat in order to prevent 1 poor-quality study was 3.8, reflecting an absolute risk reduction of 26.2% and a 19.6% reduction in total PSG studies needing to be performed.

DISCUSSION

Our findings suggest that routine premedication with zolpidem may enhance the yield of PSG. In this study, pretreatment with zolpidem 10 mg prior to PSG significantly improved the quality of PSG. The significant improvement in quality and diagnostic yield of PSG and nearly 20% reduction in total studies needing to be performed may result in greater efficiency and lower cost for sleep laboratories.

Our data showed that zolpidem significantly shortened sleep latency and improved sleep efficiency. Zolpidem has been previously shown to improve both objective and subjective sleep quality.[1] Our results are similar to those of previous studies that showed that the use of nonbenzodiazepine hypnotics results in an increase in total sleep time, an increase in sleep efficiency, and a decrease in sleep latency.[1-3] Several studies have shown that nonbenzodiazepine hypnotic agents are effective in both acute and chronic treatment of insomnia.[6,7] When used as a pretreatment for PSG, these effects can result in greater time asleep, allowing for more data collection, thus increasing the diagnostic yield of PSG.

Table 1—Demographic and Polysomnographic Comparisons According to Pretreatment

	No Pretreatment (n = 146)	Pretreatment (n = 54)	*p* value
Age, y	46.5 ± 9.5	43.9 ± 9.9	.26
Men, %	73.2	74.1	.45
Sleep latency, min	26.0 ± 19.9	11.8 ± 9.5	.002
Sleep efficiency, %	78.8 ± 12.3	89.5 ± 5.6	< .0001
Apnea-hypopnea index, no./h	30.1 ± 11.9	32.4 ± 12.7	.28
Poor-quality studies, %	33.6	7.4	.0005

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Similarly, mild sedation can assist with initial tolerance of CPAP therapy, allowing adequate titration.

The effects of any medication, whether used chronically or as premedication, must be considered, and those that alter the results of PSG data could lead to inaccurate diagnoses. Although not addressed in this study, previous studies have found that nonbenzodiazepine hypnotics have minimal effects on sleep architecture. These agents result in a modest increase in stage 3 and 4 sleep and a minimal decrease in rapid eye movement sleep, without alterations of stage 1 and 2 sleep or oxygenation.[1-3] These alterations are less marked than those seen with benzodiazepines.[3-5] Quera-Salva and colleagues[2] reported that, in nonapneic subjects, respiratory events were increased with zolpidem use. However, in all but 1 patient, the AHI changed less than 5 events per hour with zolpidem. This is similar to our findings in which patients treated with zolpidem showed a nonsignificant increase in AHI. In both studies, this minimal increase would be unlikely to lead to an alteration in diagnosis. However, this effect should be considered in patients with mild disease, and the true effect of zolpidem on patients with sleep-disordered breathing needs to be prospectively evaluated.

Significant side effects of zolpidem are rarely reported but must be considered. Hypersomnolence and imbalance shortly after ingestion have been reported. However, zolpidem does not cause significant somnolence after awakening.[2,3] We did not address side effects or adverse reactions to zolpidem in this study. However, there were no reported complications during this study period.

Our study has several limitations. We did not perform purely diagnostic PSGs both with and without zolpidem in the same patient. Therefore, we could not directly assess the effects of zolpidem on sleep architecture or respiratory events. Additionally, we could only assess the first-night effect in 9 subjects. Among these, one-third showed improvements on subsequent studies. This effect may have added to the improvement seen in our patients who completed studies both with and without zolpidem. Premedication with zolpidem was not standardized, and we were unable to determine if it was withheld due to contraindications. We also did not test the effects of zolpidem 5 mg. Intuitively, if this dose resulted in similar findings, it would be preferred given the potential for less toxicity and inherently lower cost. Finally, this was a retrospective study and lacks the benefit of a randomized, double-blind, placebo-controlled design. Although significant, our findings should be confirmed with a larger prospective study that also includes the rate of adverse events and a direct comparison of PSG data.

In conclusion, our study suggests that zolpidem premedication may enhance the yield of PSG. The minimal risk and contraindications of nonbenzodiazepine hypnotics must be considered. However, the routine use of premedication may lead to an improvement in the quality of PSG data and a reduction in studies needing to be performed. In turn, improved efficiency of the sleep laboratory may enhance access to sleep diagnostic services.

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