Sleep and Breathing (2019) 23:49–56
https://doi.org/10.1007/s11325-018-1653-3

SLEEP BREATHING PHYSIOLOGY AND DISORDERS • ORIGINAL ARTICLE

The effect of temazepam on assessment of severity of obstructive sleep apnea by polysomnography

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Received: 10 January 2018 / Revised: 4 March 2018 / Accepted: 12 March 2018 / Published online: 19 March 2018

Abstract

Purpose To determine the effect of temazepam on assessment of the severity of obstructive sleep apnea (OSA) by polysomnography (PSG).

Methods Analysis of diagnostic laboratory-PSG studies was performed in OSA patients who were administered temazepam (10 mg) to facilitate sleep ("temazepam group", $n = 73$) and in OSA patients (matched for age, gender, body mass index and study date) in whom temazepam was not administered ("control group", $n = 73$). Sleep- and respiratory-related variables were compared between the groups for the (i) first 3 h of study following temazepam in the temazepam group (when peak blood concentration is expected) or following lights out in the control group, and (ii) entire study duration.

Results Within the first 3 h, no differences in sleep-related variables were observed between the groups. Over the entire study duration, the temazepam group had a reduced total sleep time compared to the control group, likely due to the overnight sleep difficulties that led to its use. Whether measured during the first 3 h of study or over the entire study duration, no significant differences were detected between the groups for any respiratory-related variable, including apnea hypopnea index, arousal index, oxygen desaturation, apnea index, hypopnea index, and event duration. When patients were considered in terms of OSA severity, decreased arousal index was noted in the temazepam group over the entire study duration, but only in those with severe OSA.

Conclusion Oral administration of 10 mg of temazepam during the course of PSG does not systematically affect assessment of the severity of OSA by PSG.

Keywords Respiratory sleep disorder · Benzodiazepine · AHI · Airway obstruction · Sedatives · Airway collapsibility

Introduction

Sleep may be difficult to achieve in the unfamiliar environment of a sleep laboratory and hypnosedatives, such as the benzodiazepine temazepam, are frequently used to facilitate it, even though they have the potential to change sleep behaviors. Apart from the effects on sleep initiation and consolidation [1], desired for these purposes, temazepam has the capacity to depress ventilatory drive, muscle activation and arousal responses [2–5]. In patients with obstructive sleep apnea (OSA) and low arousal thresholds (i.e. a ready propensity to arouse), the latter effect may act to dampen upper airway obstruction-related arousals and sleep disruption, particularly at sleep onset. While some argue this is a desirable clinical effect for milder forms of OSA [6], in the setting of a sleep laboratory, it has the potential to mislead investigation by

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reducing the true impact of obstructive events on sleep continuity. Furthermore, there is a concern, both from the clinical and investigative points of view, that where arousal thresholds are high and/or sleep apnea is severe, temazepam could worsen OSA severity because it may further depress these arousal responses during sleep [4] and prolong obstructive events. Also of potential concern is the capacity of temazepam to attenuate upper airway muscle activity [2, 3] within those with OSA, which may further compromise airway patency. Hence, it is possible that this relatively common use of temazepam during the conduct of PSG could influence the results of the studies it is used to facilitate, thereby compromising their veracity and validity.

Despite this concern, temazepam is often administered in clinical sleep laboratories to assist with acclimation to positive airway pressure (PAP) therapy during pressure titration studies and/or to aid sleep initiation and maintenance in those undergoing diagnostic polysomnography (PSG). Even though the possibility exists that it is biasing the results of investigation, there is a paucity of data on which to adjudicate this concern. To date, only two small-scale studies have investigated the influence of temazepam on the severity of OSA assessed during PSG. Neither identified a difference in the apnea hypopnea index (AHI) during temazepam-induced and natural sleep in patients with mild-moderate OSA [5, 7]. No study has examined the effect of temazepam in patients with severe OSA.

To help address these issues, this study sought to determine the effect of orally administered temazepam on the severity of OSA assessed during PSG: (i) in the initial few hours of study following its administration, during which time plasma temazepam concentration would be expected to be maximal; and (ii) over the whole night of sleep. We utilized data obtained during routine overnight PSG from a clinical sleep laboratory to ensure its applicability to everyday clinical practice. Our aim was to compare OSA severity in a cross-section of patients, closely matched for anthropometric variables and time of study, who were either administered temazepam or not during the course of the PSG undertaken for investigation of suspected uncomplicated OSA. On the basis of previous work [5, 7] and our clinical impressions, we hypothesized that temazepam would have little effect on the assessed severity of OSA.

Materials and methods

Participants

Patients were selected in reverse chronological order from successive eligible patients with suspected uncomplicated OSA who had attended the sleep laboratory at Sir Charles Gairdner Hospital, Perth, Australia, for a diagnostic PSG between August 2005 and December 2011 and who demonstrated the presence of OSA (AHI ≥ 5 events.h^{-1}). Two groups of patients were identified: (i) those who had been administered 10 mg temazepam on the night of their PSG study (temazepam group); and (ii) a matched group who were not administered temazepam on the night of their PSG study (control group). Selection was performed on the following basis.

Patients were included in the *temazepam group* if they had OSA (AHI≥ 5 events.h^{-1}), had been administered 10 mg of temazepam prior to 1:00 am, had a minimum of 2 h sleep, of which at least 1 h was within 3 h of temazepam administration, and had a suitable matched control patient. Patients were administered temazepam if they reported a history of difficulty achieving or maintaining sleep in the sleep laboratory or unfamiliar environments, or if they were unable to establish sleep on the night of the study.

Control group patients were selected after each temazepam patient had been recruited from patients whose studies had been performed in close temporal proximity and who were matched for gender (male/female), age (± 2 years) and body mass index (BMI) (± 1 kg.m^{-2}). Where multiple patients fulfilled these criteria, the patient whose sleep study was temporally the closest to the sleep study of the temazepam patient was selected. Control patients were also required to have OSA (AHI ≥ 5 events.h^{-1}) and to have slept for at least 2 h, with a minimum of 1 h being within the first 3 h following lights out.

Exclusion criteria, applicable to all patients, included use of barbiturates or other hypnosedatives (apart from *per protocol* use of temazepam); antidepressant or other psychoactive drugs; opioid analgesics; antihistamines; anticholinergics; > 10 mg temazepam; alcohol (> 2 standard drinks, 10 g alcohol) on the study night (patients attending for sleep studies are asked to consume their habitual evening alcohol intake)); antispasmodics; or use of any OSA treatment including positive airway pressure devices or oral appliances.

Polysomnography study

Standard PSG was performed on all patients including central electroencephalogram (EEG), chin and anterior tibialis electromyogram (EMG), electrooculogram (EOG), and electrocardiogram (ECG). In addition, abdominal and thoracic breathing effort, respiratory airflow, nasal air pressure, pulse oximetry, sleep position and sound were recorded. All signals were continuously recorded (E series; Compumedics, Melbourne, Australia) and PSGs were analyzed by trained technologists using Rechtschaffen and Kales criteria to score sleep and the "Chicago" criteria to score respiratory events [8, 9]. Apneic events were defined as a reduction in oronasal airflow to < 10% of baseline for at least 10 s. Hypopneic events were defined as a clear reduction in nasal pressure for at least 10 s that were either (i) to < 50% of baseline pressure or (ii) were associated with an oxygen desaturation of > 3% or an arousal [8].

Polysomnographic analyses

The PSG reports were generated for two time periods: (i) the first 3 h—from time zero to the end of 3 h and (ii) the whole night—from time zero to the end of the study. Time zero was defined as the time at which temazepam was administered (temazepam group), any time prior to 1.00 am, or when lights were switched off (control group).

Variables included in the reports were total sleep time (TST), sleep efficiency (SE) (%), time in bed (TIB), sleep onset latency (SOL), wake after sleep onset (WASO) (%), time in rapid eye movement (REM) sleep (%), time in stage 1 non-rapid eye movement (NREM) sleep (%), time in stage 2 NREM sleep (%), time in slow wave sleep (SWS) (%), apnea hypopnea index (AHI), obstructive apnea index (OAI), central apnea index (CAI), hypopnea index (HI), total arousal index (ArI), spontaneous ArI, respiratory ArI, mean SaO_2 desaturation, nadir SaO_2, mean obstructive apnea duration, mean central apnea duration, mean hypopnea duration, supine AHI, non-supine AHI.

The presence of a low arousal threshold was predicted from PSG based on criterion developed by Edwards et al. [10]. Briefly, patients were deemed to have a low arousal threshold if they met two or more of three criteria which included: AHI < 30 events.h^{-1}; nadir $SaO_2 > 82.5\%$; and proportion of hypopnoeas $> 58.3\%$.

Statistical analysis

Power calculations were based on a clinically relevant mean difference in AHI of 10 ± 30 events.h^{-1}, with $\beta = 0.8$ and $\alpha = 0.05$ and indicated that a total of 143 patients should be studied. The overall total of 146 studied slightly exceeded this (i.e. 73 patients in each group). Data were analyzed using the R environment for statistical computing [11]. Linear mixed models were used to compare groups within each of the two time periods with respect to sleep variables. Fixed effects of group, age and BMI were included in the model as well as a random effect of matched pair. To adjust for multiple comparisons ($n = 23$), Bonferroni adjustment was applied and significance was accepted as $p < 0.002$ (i.e. 0.05/23). Secondary analyses included linear regression to investigate the interaction of groups and OSA severity groups (mild, $5 \leq 15$; moderate, $15 \leq 30$ and; severe, ≥ 30 events.h^{-1}) on respiratory measures, after adjusting for age and BMI. To adjust for the number of comparisons ($n = 14 \times 3$ severity groups), Bonferroni adjustment was applied and significance was accepted as $p < 0.0009$. For analysis purposes, WASO (%), stage 1, mean OA duration, mean CA duration, OAI, CAI, HI, supine AHI, spontaneous ArI, respiratory ArI and total ArI were log-transformed. The proportion of patients with predicted low arousal threshold in each of the temazepam and control groups was examined with chi-square analysis. Data are reported as mean ± SD and significance was accepted as $p < 0.05$ unless otherwise specified.

Results

A total of 73 studies were identified in patients who had been administered temazepam (28 females; group mean age 55.6 ± 14.0 years, BMI 33.1 ± 6.3 kg.m^{-2}). Control patients ($n = 73$, 28 females) were well matched for age (55.5 ± 13.8 years) and BMI (33.1 ± 6.0 kg.m^{-2}). When subdivided by OSA severity category, similar numbers of patients from the control and temazepam groups were classified as having mild OSA ($n = 15$ and 20, respectively), moderate OSA ($n = 27$ and 21, respectively) and severe OSA ($n = 31$ and 32, respectively).

First 3-h comparisons

Considering just the first 3 h of study from lights off (control group) or temazepam administration (temazepam group), none of the 22 variables of interest, including respiratory related variables, were significantly different (at the $p < 0.002$ level) between the groups (Table 1). In particular, mean AHI was similar in the control and temazepam groups (36.5 ± 31.2 and 34.4 ± 25.0 events.h^{-1}, respectively) (Table 1).

When data were analyzed by OSA severity category, no differences in respiratory measures were identified as being different between the control and temazepam groups. The proportion of patients in the temazepam group classified as having a low arousal threshold (56/73) was not different to the proportion of patients in the control group with a low arousal threshold (58/73).

Whole night comparisons

Considering the entire night, compared to the control group, the temazepam group slept for a shorter period of time (TST; $p < 0.002$) and spent less time in bed ($p < 0.002$) (Table 2).

There were no differences in any measure of sleep-disordered breathing between the two groups overall (Table 2). In particular, mean AHI was not significantly different between the control and temazepam groups (36.7 ± 27.9 and 32.6 ± 22.1 events.h^{-1}, respectively) (Table 2, Fig. 1).

When analyzed by OSA severity category, significant differences in arousal indices were identified between the control and temazepam groups, but only in those patients with severe OSA. Specifically, compared to the control group those in the temazepam group had a lower respiratory ArI (45.6 ± 19.4 vs 32.5 ± 18.4 events.h^{-1}, respectively, $p < 0.0009$) and total ArI (50.7 ± 18.2 vs 37.3 ± 17.5 events.h^{-1}, respectively, $p < 0.0009$). No other measures were different within any of the severity categories. The proportion of patients in the temazepam (50/73) and control groups (51/73) classified as having a low arousal threshold over the whole night was not different.

Table 1 Sleep and respiratory data from first 3 h

Variable	Control ($n = 73$)	Temazepam ($n = 73$)	p value
Sleep-related measures			
SOL (min)	21.6 ± 20.4	28.8 ± 15.4	0.016
TST (min)	125.5 ± 28.0	129.1 ± 24.1	0.400
WASO (% of TST)	31.0 ± 29.3	19.7 ± 22.1	0.009
SE (%)	69.9 ± 15.6	72.0 ± 13.1	0.371
Stage REM (% of TST)	10.7 ± 9.0	11.4 ± 8.9	0.616
Stage 1 NREM (% of TST)	3.9 ± 4.6	2.8 ± 3.7	0.102
Stage 2 NREM (% of TST)	65.2 ± 15.6	68.0 ± 16.4	0.282
SWS (% of TST)	20.2 ± 15.4	17.7 ± 16.3	0.346
Respiratory-related measures			
AHI (events.h^{-1})	36.5 ± 31.2	34.4 ± 25.0	0.642
OA index (events.h^{-1})	6.6 ± 9.0	8.6 ± 13.0	0.474
CA index (events.h^{-1})	3.6 ± 6.3	6.3 ± 16.1	0.604
HI (events.h^{-1})	33.2 ± 28.5	28.4 ± 19.6	0.244
Supine AHI (events.h^{-1})	40.2 ± 38.8	39.6 ± 33.1	0.912
Non-supine AHI (events.h^{-1})	27.5 ± 30.2	26.8 ± 28.5	0.893
Mean OA duration (sec)	17.8 ± 7.1	22.7 ± 9.3	0.018
Mean CA duration (sec)	17.9 ± 6.5	24.8 ± 13.4	0.127
Mean hypopnea duration (sec)	22.0 ± 6.5	23.3 ± 7.1	0.265
Mean SaO_2 desaturation (%)	4.2 ± 3.0	4.5 ± 2.7	0.448
SaO_2 nadir (%)	85.1 ± 7.0	84.6 ± 6.9	0.668
Total ArI (n.h^{-1})	35.5 ± 24.3	28.3 ± 18.8	0.048
Spontaneous ArI (n.h^{-1})	9.4 ± 8.3	7.0 ± 5.2	0.041
Respiratory ArI (n.h^{-1})	26.1 ± 25.6	21.3 ± 19.1	0.201

Values are reported as mean ± SD. No statistically significant ($p < 0.002$) differences were observed between the two groups

SOL sleep onset latency; *TST*: total sleep time; *WASO* wake after sleep onset; *SE* sleep efficiency; *REM* rapid eye movement; *NREM* non-rapid eye movement; *SWS* slow wave sleep; *AHI* Apnea Hypopnea Index; *HI* Hypopnea Index; *OA* obstructive apnea; *CA* central apnea; *SaO_2* blood oxygen saturation; *ArI* Arousal Index

Discussion

This study sought to determine whether use of temazepam to facilitate sleep in patients with suspected OSA during overnight laboratory PSG affects assessment of its severity. Our interest was driven by a concern that, while frequently needed to help secure sleep, temazepam has the potential to dampen arousal responses, ventilatory drive and muscle activation thereby aggravating OSA and affecting the study outcomes.

To pursue this question, two age-, gender- and BMI-matched groups were selected from our sleep clinic records: one group of patients who had been administered 10 mg oral temazepam early in the course of their laboratory-based PSG study and another group who did not receive temazepam. No differences were seen between the groups in the number or duration of apneas or hypopneas, or in the number of arousals or the severity of oxygen desaturation, regardless of whether data were analyzed from only the first 3 h after temazepam administration (when plasma temazepam concentration would be expected to be greatest) or from the whole night, or whether the patients were analyzed as a single group or by subgroups of OSA severity, apart from some arousal-related changes over the whole night in those with severe OSA. These findings suggest that temazepam has no systematic effect on the severity of OSA.

Temazepam binds to and activates $GABA_A$ receptors resulting in dose-related hypnosis, sedation, depression of arousal responses and muscle relaxation. It inhibits hypoglossal motoneuron activity [12], which has traditionally been thought to inhibit post-synaptic pharyngeal muscle tone [13]. Indeed, benzodiazepines have been shown to have myorelaxant effects when administered locally at the hypoglossal motor nucleus in rats, although when administered systemically genioglossus activity in rats is increased [12]. Direct measures of the effect of benzodiazepines on hypoglossal motoneuron or pharyngeal muscle activity have not been performed in sleeping or anesthetized humans although the common notion, and a basis for concern

Table 2 Sleep and respiratory data from whole night

Variable	Control ($n = 73$)	Temazepam ($n = 73$)	p value
Sleep-related measures			
SOL (min)	21.6 ± 20.4	28.8 ± 15.4	0.016
TST (min)	357.4 ± 66.1	283.8 ± 59.6 *	< 0.0001
WASO (% of TST)	32.5 ± 20.5	23.5 ± 25.4	0.020
SE (%)	73.6 ± 11.0	76.4 ± 10.7	0.115
Time in bed (min)	485.2 ± 49.8	374.5 ± 75.0 *	< 0.0001
Stage REM (% of TST)	19.6 ± 7.0	17.8 ± 8.2	0.149
Stage 1 NREM (% of TST)	3.4 ± 3.2	2.6 ± 3.5	0.177
Stage 2 NREM (% of TST)	64.4 ± 10.5	67.1 ± 13.0	0.162
SWS (% of TST)	12.6 ± 9.1	12.0 ± 10.5	0.717
Respiratory-related measures			
AHI (events.h^{-1})	36.7 ± 27.9	32.6 ± 22.1	0.329
OA index (events.h^{-1})	5.7 ± 9.0	6.0 ± 11.6	0.901
CA index (events.h^{-1})	3.2 ± 6.2	4.2 ± 11.5	0.704
HI (events.h^{-1})	33.3 ± 24.7	27.1 ± 17.6	0.148
Supine AHI (events.h^{-1})	45.5 ± 32.1	43.2 ± 29.7	0.648
Non-supine AHI (events.h^{-1})	29.1 ± 28.3	25.6 ± 25.2	0.423
Mean OA duration (sec)	19.4 ± 6.1	23.5 ± 8.1	0.008
Mean CA duration (sec)	20.4 ± 7.5	22.9 ± 10.7	0.365
Mean hypopnea duration (sec)	22.5 ± 4.9	23.7 ± 6.0	0.194
Mean SaO_2 desaturation (%)	4.5 ± 2.7	4.7 ± 2.8	0.739
SaO_2 nadir (%)	81.2 ± 9.6	82.7 ± 7.1	0.291
Total ArI (n.h^{-1})	33.1 ± 20.1	26.8 ± 15.9	0.038
Spontaneous ArI (n.h^{-1})	7.6 ± 5.2	6.7 ± 4.1	0.232
Respiratory ArI (n.h^{-1})	25.4 ± 21.8	20.1 ± 16.8	0.099

Values are reported as mean ± SD. * $p < 0.002$ between the two groups

SOL sleep onset latency; *TST* total sleep time; *WASO* wake after sleep onset; *SE* sleep efficiency; *REM* rapid eye movement; *NREM* non-rapid eye movement; *SWS* slow wave sleep; *AHI* Apnea Hypopnea Index; *HI* Hypopnea index; *OA* Obstructive Apnea; *CA* Central Apnea; *SaO_2* blood oxygen saturation; *ArI* Arousal Index

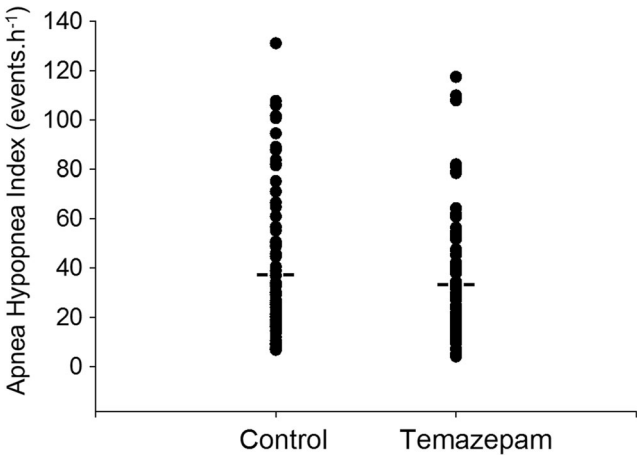

Fig. 1 Apnea hypopnea index for the whole night for control and temazepam patients. Group mean values, indicated by black lines, were not significantly different

regarding benzodiazepine use in OSA patients, is that benzodiazepines induce myorelaxation and compromise airway patency.

Supporting this construct, an early case report described an increased AHI following two nights of 30 mg flurazepam [14] in a 38-year-old male with mild OSA. Similarly, a placebo-controlled trial of 20 subjects ($n = 17$ male, mean age 49) reported a significant, although small, increase in the frequency of sleep disordered breathing events with flurazepam, from 3.0 to 4.2 events.h^{-1} [15]. Conversely, and consistent with the results of the present study, a number of other studies involving predominantly elderly male subjects have reported no adverse influence of temazepam or other benzodiazepines on the severity of sleep-disordered breathing [5, 7, 16–19]. With limited participant age ranges, OSA severity and male predominance many of these previous studies have lacked external validity. It is notable that the characteristics of the present study population are as might be expected

for patients presenting for adult laboratory PSG with an age range of 26–84 years, an increased proportion of males (64%), elevated BMI (33.1 ± 6.1 kg.m^{-2}) and a broad spread of OSA severities (21% mild, 34% moderate and 45% severe).

Temazepam could also increase the severity of OSA by increasing the threshold for arousal from sleep. Berry et al., demonstrated that the esophageal pressure immediately prior to termination of apnea in patients with severe OSA was increased (i.e. more negative) with benzodiazepines compared to placebo [16, 19]. Such an elevated arousal threshold would be expected to result in longer mean event duration, inadequate ventilation and consequent augmented PCO_2 accumulation and SaO_2 decline before arousal occurs. In the present study, the respiratory ArI over the whole night was, on average, reduced in those who took temazepam compared to those who did not, although this reduction was limited to patients with severe OSA. However, mean event duration and indices of SaO_2 desaturation over the entire night were not different between those who ingested temazepam compared to those who did not. Even considering data from just the first 3 h following temazepam administration, when peak plasma levels would be greatest, no differences in event duration or desaturation were identified. Such findings are consistent with those of other studies investigating the effect of relatively low (hypnotic) doses of benzodiazepines on OSA which have shown no differences in mean or minimum SaO_2 levels during benzodiazepine-induced sleep versus control or placebo in groups of middle aged [18] or elderly [7] mild-moderate sleep apneics or in patients of mixed age and OSA severities [5].

It is also possible that increasing the threshold for arousal could *reduce* OSA severity [20]. The mechanism for this is related to the increase in ventilatory drive and greater pharyngeal negative pressures in response to pharyngeal obstruction/narrowing, which could augment pharyngeal dilator muscle activity and act to restore airway patency [6]. Hence, patients with low arousal thresholds may benefit from sedatives which act to increase the arousal threshold [21–23]. Using the criteria developed by Edwards et al. [10], more than 75% of patients in the present study were predicted to have a low respiratory arousal threshold over the first 3 h and almost 70% of patients had a predicted low arousal threshold over the whole night. However, the proportions of those with predicted low arousal threshold were not different between the temazepam and control groups. These findings are comparable to a recent study showing that administration of either of the non-benzodiazepine sedatives eszopiclone or zolpidem did not influence the prevalence rates of a low arousal threshold or the AHI [24].

While such findings argue against temazepam having a systematic effect on arousal threshold, they do not exclude the possibility that temazepam, or other benzodiazepines, may have adverse, or beneficial, effects in higher doses or in select individuals with particular sensitivities or phenotypes. In this regard, Wang et al. have recently reported that OSA patients with increased central chemosensitivity appear most vulnerable to respiratory depression during temazepam-induced sleep [5]. We also cannot exclude the possibility that the effect of temazepam may be reduced in some individuals who were regularly using temazepam at home. However, many such patients use more than the 10 mg dose specified in the protocol. Where this was the case they were excluded from the study.

The present study was based on patients who had ingested 10 mg of temazepam. It is possible that greater doses of temazepam are required before any detrimental effects on OSA are observed. Supporting this notion are studies showing that OSA is worsened with administration of 30 mg of the benzodiazepine flurazepam [14, 15, 17], however bioequivalency between flurazepam and temazepam is not assured [25]. Arguing against moderately higher doses of temazepam being detrimental to OSA are findings by Camacho et al. who reported no detrimental effect of 15–30 mg of temazepam on OSA severity [7]. In addition, Park et al. showed in a rat model, that systemic administration of lorazepam produces dose dependent *increases* in genioglossus muscle activity [12].

Both body posture and sleep stage have been implicated in OSA severity [26–28]. Although the retrospective design of the current study did not allow for control of these factors, indices of OSA severity were analyzed in both the supine and non-supine postures and REM and non-REM sleep. No between-group differences in AHI were observed when in supine or non-supine postures or between REM and non-REM sleep; hence, postural influences did not affect these findings.

Temazepam is an effective hypnosedative that is frequently utilized within sleep clinics to facilitate patients' sleep onset and efficiency. However, contrary to the expectation that the temazepam group would have had a higher TST and sleep efficiency [29], a reduced TST over the whole night was observed in this group. Sleep efficiency was slightly, although not significantly, improved in the temazepam group in both the initial 3 h and over the whole night. It is likely that these findings are more a consequence of the experimental design than a true effect of temazepam because in this study temazepam was administered to patients who had difficulty initiating or maintaining sleep or were anxious. This, by design, reflects actual sleep laboratory practice. Thus, not surprisingly, the probability of patients having a decreased TST and sleep efficiency was increased for patients in the temazepam group. In addition, the design of the current study whereby time zero for the control group was at "lights out" and time zero for the temazepam group was at the time of temazepam administration, any time prior to 1:00 am and potentially a significantly later time than "lights out," is likely to contribute to the lower TIB and TST in the temazepam group. To address this potential limitation, we have only presented respiratory and arousal data that were normalized for TST.

The clinical purpose of a PSG study is to observe overnight sleep behavior and determine the presence/absence of a sleep disorder. Sleep is therefore essential for a PSG study to have any value and studies in which patients do not achieve sleep represent an expensive, wasted resource. In the current study, temazepam was administered preemptively in patients with potential problematic sleep (i.e. a reported history of difficulty achieving or maintaining sleep in the sleep laboratory or unfamiliar environments), or during the course of the study if they were unable to establish sleep. Of the patients who were administered temazepam for these purposes, 29% were diagnosed with moderate OSA and 44% with severe OSA. This information would not have been available if sleep had not been achieved.

In conclusion, this retrospective analysis identified no significant systematic effects of 10 mg of temazepam on assessment of the severity of OSA by PSG, either within the first 3 h following its administration or over the entire study duration. These findings suggest that it is reasonable to use temazepam to facilitate sleep in patients being investigated for suspected OSA in monitored environments such as a sleep laboratory. They also suggest that it is a reasonable short-term therapeutic option for OSA patients with comorbid insomnia or who are having difficulty achieving sleep during implementation of PAP therapy to facilitate its introduction [30]. However, individual sensitivities must always be taken into account where temazepam use is being contemplated in unmonitored environments and further prospective research into the phenotypic characteristics that define such vulnerabilities is warranted.

Financial Support This study was supported by a National Health and Medical Research Council project grant (No. 572647) and Sir Charles Gairdner Hospital Research Advisory Committee grant (2016-043). PRE was supported by a National Health and Medical Research Council Senior Research Fellowship (No 513704). CV received a Dr. Margaret Loman-Hall Honours Scholarship.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All patients had provided written consent to have information obtained in association with their PSG study used for research purposes but formal consent by the patients for this particular study was not required. The study was approved by the Human Research Ethics Committee at Sir Charles Gairdner Hospital (Ref 2011-027) and was performed in accordance with the ethical standards of the institution and the 1964 Declaration of Helsinki and its later amendments.

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