Br J clin Pharmac 1994; **37**: 539–543

Effects of zolpidem on sleep architecture, night time ventilation, daytime vigilance and performance in heavy snorers

M. A. QUERA-SALVA[1], CROWE McCANN[1], J. BOUDET[2], M. FRISK[2], P. BORDERIES[3] & Ph. MEYER[2]
[1]Unité de Sommeil, Service de Réanimation, Hôpital Raymond Poincaré, Garches, [2]Service de Pharmacologie Clinique, Hôpital Necker-Enfants-Malades, Paris and [3]Synthélabo, Division SNC, Meudon-la-Forêt, France

1 In a double-blind, crossover, placebo controlled trial, zolpidem 10 mg, a new imidazopyridine hypnotic drug, was administered in a single dose to 10 healthy non-obese heavy snorers.
2 Nocturnal polysomnography showed that zolpidem increased total sleep time, sleep efficiency and the percentage of stage 2.
3 Respiratory monitoring showed that zolpidem did not modify the percentage of total sleep time spent snoring. The percentages of total sleep time with a SaO_2 < 4% of the baseline value and with a SaO_2 < 90% and the mean SaO_2 were also unchanged with zolpidem. The respiratory disturbance index was modestly increased by zolpidem although in all but one subject it remained < 5 with both treatments.
4 Zolpidem intake did not impair daytime vigilance and performance evaluated the day after.

Keywords zolpidem hypnotic sleep snorer nocturnal ventilation vigilance performance tests

Introduction

Heavy snoring affects 19% of the general population: 24.1% of men and 13.8% of women [1]. Insomnia is a common problem; in a recent survey, 6.2% of a representative sample of the French population were taking hypnotics on a regular basis [2]. In addition, snorers frequently complain of disturbed nocturnal sleep with sleep fragmentation. Consequently, they are often sleepy during the day [3] and may be prescribed hypnotics to reduce their complaints.

Benzodiazepines, especially those with long acting effects are known to depress the central control of ventilation [4, 5] and have a myorelaxant effect: this may favour upper airway collapse in a snoring population whose upper airway resistance is already increased [6].

Zolpidem is a new imidazopyridine hypnotic which has been shown to be an effective sleep inducer [7–10]. It binds selectively at omega 1 (BZD 1) receptors and has specific hypnotic properties [11]. Zolpidem has less myorelaxant action than benzodiazepines [12–14]. It may thus be less likely to induce sleep related ventilatory disturbances (apnoeas, hypopnoeas and oxygen desaturations) than benzodiazepines in a snoring population.

The aim of the present study was to document the effects of a single dose of zolpidem 10 mg in comparison with placebo on nocturnal ventilation and daytime vigilance in heavy, non-obese, heavy snorers.

Methods

The study was performed under double-blind conditions according to a crossover design. The protocol had been approved by the Necker-Enfants Malades Hospital Ethics Committee. Healthy male snorers aged 35–50 years, with a body mass index (BMI = weight in kg/body surface in cm^2) ≤ 28 [15] gave their written informed consent for the study. Subjects were considered as healthy following a normal physical examination, laboratory tests (creatinine, glucose, SGOT, SGPT,

Correspondence: Dr M. A. Quera-Salva, Unité de Sommeil, Service de Réanimation Médicale, Hôpital Raymond Poincaré, 104, Bd Raymond Poincaré, 92380 Garches, France

GGT), ECG and normal vital capacity and FEV_1/FVC on spirometry.

Heavy snorers were defined as following: (1) to snore every night, but not necessarily throughout the night, (2) to snore loudly or very loudly, the noise being heard from other rooms and disturbing their bed-partners, (3) no history of apnoeas.

Patients were excluded if they had any history of current medical illness, serious psychiatric antecedents, current insomnia or abnormal scores on the SCL 90 R questionnaire [16]. All subjects taking medications known to affect sleep or vigilance were also excluded. In addition, they were required to drink habitually four or less caffeinated drinks per day and not to have a history of heavy alcohol intake. Drinks containing alcohol or caffeine were prohibited during the day of performance tests.

Nocturnal polysomnography was carried out in the standard way with electroencephalogram (C4-A1, O1-A2), electrooculogram (ROC-A1, LOC-A2) and electromyogram (submental). Nasal and buccal airflow were measured using thermistors and respiratory movements with abdominal and thoracic strain gauges. Oximetry was carried out using a Biox 3 (Ohmeda) oximeter. Duration of snoring was measured using an interphone connecting the subject's room to the technical control room. A diagnostic nocturnal polysomnographic study was carried out 1 week before the main study in order to exclude sleep pathology and to help subjects adapt to the procedures.

All sleep recordings were examined by one independent analyst. Sleep architecture was scored according to the criteria of Rechtschaffen & Kales [17]. Cessation of airflow for 10 s or more was scored as an apnoea. If abdominal and thoracic movements continued it was called obstructive. If all movements ceased it was categorised as being central. Hypopnoeas (reduction in airflow of at least 50% for at least 10 s) were only taken into account if there was an associated drop in SaO_2 of at least 4% of baseline. The number of apnoeas and hypopnoeas per hour of sleep was calculated (respiratory disturbance index: RDI). The RDI is considered abnormal when it is greater than 10 [18, 19].

The multiple sleep latency test (MSLT), a standardized method used in the assessment of daytime sleepiness [20], was carried out after the night-time polysomnography. The MSLT consists of five consecutive tests starting 2 h after awakening and is done at 2 hourly-intervals throughout the day. This test evaluates the propensity to fall asleep. In addition, three performance tests were realized just before each sleep latency test. The performance tests were the following:

- Critical flicker fusion (CCF) [21]. The threshold was determined using the psychophysiological method of limits, on ascending and descending scales. It was measured in hertz and the response taken into account was the average of 6 stimulus presentations.
- Choice reaction time (CRT) [22]. During this test, the subjects were required to extinguish 1 of 6 stimulus lights, illuminated at random, by touching the appropriate button. The CRT response measure was the mean latency of response to 20 stimulus presentations in milliseconds.
- Digit symbol substitution test (DSST) [23]. The subjects were asked to complete as many substitutions as possible in a 90 s period. The number correctly performed gave the measure taken. Different grills were given for each performance test battery to avoid a practice effect.

The two treatment nights were separated by an interval of 1 week. Medication (zolpidem or placebo) was administered at 22.45 h; sleep recordings were started at 23.00 h and terminated at 7.00 h. Every treatment night was followed by MSLT and performance tests throughout the day.

The Wilcoxon non-parametric test was used for comparisons between the two treatments and the two nights (night 1 and night 2).

Results

Ten patients aged between 33–51 (mean 42) years took part in the study. Their BMI was between 24–28 (mean 26.5). All patients completed the study.

Table 1 shows the sleep architecture data for the two treatment nights. The sleep continuity was significantly improved with zolpidem: total sleep time was longer ($P < 0.02$), wake after sleep onset was shorter ($P < 0.02$) and sleep efficiency index (total sleep time/total sleep period) was higher ($P < 0.01$). The time and the percentage of total sleep time spent in stage 2 was significantly greater on the zolpidem night ($P < 0.01$). No significant differences were found, in relation to the other sleep architecture parameters. The comparison between the sleep architecture variables on night 1 and

Table 1 Effects of treatments on various sleep measures, on percentages of total sleep time occupied by sleep stages over the whole night, and on respiratory variables (mean ± s.d. for 10 heavy snorers)

Measure	*Zolpidem 10 mg*	*Placebo*
Total sleep time (min)	434.0 ± 36.0*	379.0 ± 70.5
Sleep latency (min)	9.5 ± 8.0	12.5 ± 16.0
Number of awakenings	4.5 ± 3.5	7.5 ± 4.0
Wake after sleep onset (min)	34.5 ± 23*	91.5 ± 58.5
Sleep efficiency index†	90.5 ± 5.5**	78.5 ± 14.0
Stage 1	24.0 ± 12.0	25.0 ± 14.0
Stage 2	44.0 ± 8.0**	38.0 ± 9.0
Stages 3 + 4	13.5 ± 8.5	16.5 ± 5.5
REM	18.5 ± 5.5	20.5 ± 8.0
Respiratory disturbance index	3.0 ± 3.0*	1.5 ± 1.5
Minimum value of SaO_2	86.5 ± 3.5*	88.5 ± 3.0
Percentage of total sleep time spent with $SaO_2 < 90\%$	1.5 ± 2.5	0.5 ± 0.5
Percentage of total sleep time spent with $SaO_2 < 4\%$ of base line value	1.5 ± 2.5	0.0 ± 0.0
Mean SaO_2	94 ± 1.5	94.5 ± 1.0
Percentage of total sleep time spent snoring	35.0 ± 14.0	24.0 ± 14.0

Significance levels: *$P < 0.002$; **$P < 0.001$.
†Sleep efficiency index: total sleep time/time in bed.

night 2 indicated that the order of the treatment administration did not play a role.

Table 1 also shows the respiratory variables for the two treatment nights. A significant difference was found between the two treatments in relation to the number of apnoeas and hypopnoeas per sleep hour ($P < 0.02$). The mean RDI was 3.0 ± 3.0 (range: 0.5–10) for zolpidem and 1.5 ± 1.5 (range: 0–3) for placebo. The RDI did not exceed 5 on the zolpidem night, except for one subject with an RDI of 10 (3 on the placebo night). The minimum value for SaO_2 was significantly lower after zolpidem. For all subjects the minimum value of SaO_2 was 81% for the zolpidem night and 84% for the placebo night. With zolpidem, eight subjects had a minimum $SaO_2 < 90\%$ (range: 81–89) compared with seven subjects with placebo (range: 84–89). Looking at SaO_2 in further detail we did not find any differences between zolpidem and placebo for the percentage of TST spent with a $SaO_2 < 90\%$ or with a $SaO_2 < 4\%$ of baseline value (mean SaO_2 value after 20 min, the patient being awake and in a supine position). The mean SaO_2 value was also similar on both nights. The percentage of TST spent snoring did not differ significantly between zolpidem and placebo.

Table 2 shows the mean sleep latency values in the MSLT. They were lower with both treatments than those expected in a normal population [20]. Sleep latency values after zolpidem (9.8 ± 5 min, range: 3.5–17.5) did not differ from those after placebo (10.0 ± 5.0 min, range: 32.0–17.5). As expected, a diurnal variation occurred in both groups. The lowest point on the zolpidem day was at 13.00 h and at 15.00 h for the placebo.

Table 2 also shows the data of the performance tests. They also confirmed a lack of hangover effect with little difference between the two treatments. The CCF values were similar on both occasions except at 13.00 h where it was significantly higher with zolpidem (the subjects were more alert: 29.5 ± 2.5 *vs* 30.5 ± 3.5, $P = 0.007$). An obvious diurnal variation was not found on either day. The CRT and DSST results showed no significant differences between zolpidem and placebo. On both treatments a slower reaction time in CRT was noted at 13.00 h and no obvious fluctuations in DSST were seen throughout the day.

Table 2 Daytime vigilance evaluations at different hours of the day after zolpidem 10 mg or placebo medications administered at bedtime (mean ± s.d. for 10 heavy snorers)

	Zolpidem	*Placebo*
Multiple sleep latency test (min)		
09.30 h	11.5 ± 7.0	12.5 ± 7.0
11.30 h	10.0 ± 5.5	10.0 ± 6.0
13.30 h	8.0 ± 5.0	8.5 ± 5.0
15.30 h	8.5 ± 5.0	7.5 ± 5.0
17.30 h	11.0 ± 7.0	11.0 ± 7.0
Mean	9.5 ± 5.5	10.0 ± 5.0
Critical flicker fusion test (Hz)		
07.00 h	30.0 ± 2.5	30.0 ± 3.0
09.00 h	29.5 ± 3.0	29.5 ± 2.5
11.00 h	30.5 ± 2.5	30.5 ± 2.0
13.00 h	30.5 ± 3.0*	29.5 ± 2.5
15.00 h	30.5 ± 3.0	30.0 ± 3.0
17.00 h	30.5 ± 3.0	30.0 ± 3.0
Choice reaction time (ms)		
07.00 h	631.0 ± 68.0	628.5 ± 54.5
09.00 h	618.0 ± 65.5	615.0 ± 66.0
11.00 h	621.0 ± 82.0	589.5 ± 75.0
13.00 h	644.5 ± 93.5	642.5 ± 91.0
15.00 h	596.5 ± 75.5	594.0 ± 83.0
17.00 h	618.5 ± 106.0	583.0 ± 87.5
Digital symbol substitution test		
07.00 h	53.0 ± 10.5	56.0 ± 9.5
09.00 h	57.5 ± 12.0	56.0 ± 11.5
11.00 h	57.5 ± 11.5	58.5 ± 13.5
13.00 h	59.5 ± 9.5	58.0 ± 10.0
15.00 h	60.5 ± 11.5	56.5 ± 10.0
17.00 h	58.5 ± 11.0	60.5 ± 10.5

Significance level: *$P = 0.007$.

Discussion

Recent epidemiological data suggest a close association between heavy snoring and cardiovascular disorders [1, 24–27]. The sustained systemic hypertension in heavy snorers may be related to the repeated inspiratory efforts against a closed or partially closed airway [1] and/or to the repeated episodes of hypoxia. Snoring results from a narrowing of the upper airway, which increases the turbulence of the incoming air on inspiration, causing a noisy vibration of the soft tissues of the pharynx. Normally, on inspiration, the pharynx remains open because of the action of the airway opening muscles [28, 29]. However, alcohol intake, sleep deprivation and some medications, such as CNS depressants and myorelaxants, may produce greater degrees of airway obstruction resulting in a sleep apnoea syndrome [30]. In this way, hypnotic drugs may worsen or induce sleep apnoea [4], and their use may be associated with an increased mortality in the elderly [31]. As hypnotics are widely prescribed to the general population of whom 20% are snorers, it is important that these drugs have as little effect on respiration as possible.

This study shows that in heavy snorers, zolpidem 10 mg has a hypnotic action when compared with placebo. With zolpidem, we observed a significant increase in total sleep time and sleep efficiency, and a decrease in wake after sleep onset. Furthermore, slow wave sleep and REM sleep were not decreased by zolpidem. These results, using a single dose of zolpidem 10 mg, are comparable with the results of Cirignotta *et al.* [32] with a single dose of zolpidem 20 mg in middle aged sleep apnoea patients.

In the present study, except for one subject whose RDI was almost pathological with zolpidem (i.e. RDI = 10), all subjects' RDI were far from being abnormal with zolpidem (RDI < 5); the different indices of SaO_2 desaturation, except for the minimum SaO_2 and the time of snoring, were slightly but not statistically significantly higher with zolpidem for both nights. However, we consider that the % TST spent with $SaO_2 < 90\%$ and < 4% baseline are better measures of desaturation than the minimum value which may represent only a few seconds during a whole night. No studies have

reported the effect of other hypnotics in non-apnoeic snorers, a population at risk for sleep apnoea syndrome. Dolly & Block [4] reported that the ingestion of a single 30 mg tablet of flurazepam by asymptomatic volunteers caused an increase in frequency of apnoea and oxygen desaturation during sleep, but they questioned the clinical relevance of these findings. Theoretically a hypnotic drug may cause respiratory problems during sleep either because of its myorelaxant effect and/or by depressing the respiratory centre. Zolpidem has little myorelaxant effect [33]. In addition, it seems that zolpidem has no respiratory depressing properties. A study was carried out in awake patients with severe COPD looking at the effect of various hypnotics, including zolpidem, triazolam and flunitrazepam on respiratory centre function. The results demonstrated that neither zolpidem nor triazolam had any significant effects on arterial blood gases or control of breathing in contrast to flunitrazepam [5].

A study monitoring respiration with a simple inductance plethysmograph and oximetry was carried out in a group of 10 elderly female patients recovering from hip and knee replacement surgery, to evaluate the respiratory effects of zolpidem 10 mg taken over 4 nights [34]. The elderly are known to be a population with a higher risk of sleep related respiratory disturbances [35, 36]. The incidence of sleep related respiratory disturbances was not significantly increased compared with placebo on any night. However, on the zolpidem night the frequency of obstructive apnoeas leading to O_2 desaturations of < 90% was significantly greater on the first treatment night than on the last. This is similar to the findings of Kurtz *et al.* [37] who found a significant increase in the number of apnoeas in an elderly population after they took a single dose of zolpidem 10 mg for the first time; but apparently the number of apnoeas decreased after repeated intake. Cirignotta *et al.* [32] reported in middle aged sleep apnoea patients, a non-significant increase in the RDI after zolpidem 20 mg in comparison with placebo; nevertheless they observed on zolpidem a significant reduction in both the minimum level of SaO_2 during the apnoeas and hypopnoeas and the average level. However, the tested dose was twice that normally recommended for insomnia (20 mg).

In this study, no difference was found overall between zolpidem and placebo in relation to the different vigilance and performance tests. These results confirm those of previous studies carried out with zolpidem [7, 38, 39]. However, as heavy snorers are at risk to suffer from daytime somnolence [28] we felt that it was important to establish that zolpidem did not produce or increase pre-existing somnolence. Although no significant differences were found between zolpidem and placebo, six of the subjects had a mean MSLT value of less than 10 min after placebo and in six subjects the value improved after zolpidem. The CFF, a test which measures vigilance, was significantly improved at 13.00 h by zolpidem compared with placebo. In addition, the performances of the other tests were similar after both treatments. These results show that in this population, a single dose of zolpidem 10 mg improves sleep efficiency and respects sleep architecture as well as the level of daytime vigilance. A marked improvement would probably only occur after treating the cause of the snoring, since the daytime somnolence of snorers is directly related to the microarousals produced by the repeated efforts against partially occluded upper airways [3].

In conclusion, in comparison with placebo, a single dose zolpidem 10 mg has a significant hypnotic effect in healthy middle aged heavy snorers. Furthermore, zolpidem does not produce deterioration in daytime performance tests or vigilance the day after. Apnoea-hypopnoea index was modestly increased with zolpidem, as the RDI was almost pathological in one snorer with zolpidem. To confirm these results, we recommend that further studies be carried out looking at ventilation after repeated doses of zolpidem, in a larger sample of heavy snorers and in other populations at risk such as mild sleep apnoea syndrome or COPD patients.

This study was supported by a grant from Synthélabo, Division SNC, Meudon-la-Forêt, France.

References

1 Lugaresi E, Cirignotta F, Coccagna G, Piana C. Some epidemiological data on snoring and cardiocirculatory disturbances. *Sleep* 1980; **3**: 221–224.

2 Quera-Salva MA, Orluc A, Goldenberg F, Guilleminault C. Insomnia and use of hypnotics: study of a French population. *Sleep* 1991; **14**: 386–391.

3 Guilleminault C, Stoohs R, Duncan S. Daytime sleepiness in regular heavy snorers. *Chest* 1991; **99**: 40–48.

4 Dolly FR, Block AJ. Effect of flurazepam on sleep-disordered breathing and nocturnal oxygen desaturation in asymptomatic patients. *Am J Med* 1984; **73**: 239–243.

5 Murciano D, Aubier M, Palacios S, Pariente R. Comparison of zolpidem, triazolam and flunitrazepam effects on arterial blood gases and control of breathing in patients with severe chronic obstructive pulmonary disease. *Chest* 1990; **97**/3 (Suppl.): 51S–52S.

6 Mendelson WB, Garnett D, Gillin C. Flurazepam-induced sleep apnea syndrome in a patient with insomnia and mild sleep-related respiratory changes. *J Nerv Ment Dis* 1981; **4**: 261–264.

7 Bensimon G, Foret J, Warot D, Lacomblez L, Thiercelin JF, Simon P. Daytime wakefulness following a bedtime oral dose of zolpidem 20 mg. *Br J clin Pharmac* 1990; **30**: 463–469.

8 Herrmann WM, Kubicki S, Wober W. Zolpidem: a four-week pilot polysomnographic study in patients with chronic sleep disturbances. In *Imidazopyridines in sleep disorders. A novel experimental and therapeutic approach*, eds Sauvanet JP, Langer SZ, Morselli PL. New York: Raven Press, 1988; 261–278.

9 Nicholson AN, Pascoe PA. Hypnotic activity of an imidazopyridine (zolpidem). *Br J clin Pharmac* 1986; **21**: 205–211.

10 Merlotti L, Roehrs T, Koshorek G, Zorick F, Lamphere J, Roth T. The dose effects of zolpidem on the sleep of healthy normals. *J clin Psychopharmac* 1989; **9**: 9–14.

11 Zivkovic B, Perrault G, Morel E, Langer DJ. Comparative pharmacology of zolpidem and other hypnotics and sleep inducers. In *Imidazopyridines in sleep disorders. A novel experimental and therapeutic*

approach, eds Sauvanet JP, Langer SZ, Morselli, PL. New York: Raven Press, 1988; 97–109.

12 Langer SZ, Arbilla S. Imidazopyridines as a tool for the characterization of benzodiazepine receptors: a proposal for a pharmacological classification as omega receptor subtypes. *Pharmac Biochem Behav* 1988; **129**: 763–766.

13 Lloyd KG, Zivkovic B. Specificity within the GABA receptor supramolecular complex: a consideration of the new omega 1 receptor selective imidazopyridine hypnotic zolpidem. *Pharmac Biochem Behav* 1988; **129**: 781–783.

14 Sanger DJ, Perrault G, Morel E, Joly D, Zivkovic B. The behavioural profile of zolpidem. A novel drug of imidazopyridine structure. *Physiol Behav* 1987; **41**: 235–240.

15 Khosla T, Lowe FR. Indice of obesity derived from body weight and height. *Br J Prev Soc Med* 1967; **21**: 121–128.

16 Derogatis LR, Richels K, Roch AF. The SCL 90 and the MMPI, a step in the validation of a new self-report scale. *Br J Psychiat* 1976; **128**: 280–289.

17 Rechtschaffen A, Kales A. *A manual of standardised terminology, techniques and scoring system for sleep stages in human subjects*. National Institute of Public Health, Publ. No. 204, US Government Printing Office, Washington DC, 1986.

18 American Thoracic Society. Medical Section of the American Lung Association. Indications and standards for cardiopulmonary sleep studies. *Am Rev resp Dis* 1989; **139**: 559–568.

19 Berry R, Webb W, Block A. Sleep apnea syndrome: a critical review of the apnea index as a diagnostic criterion. *Chest* 1984; **85**: 529–531.

20 Carskadon MA, Dement WC, Mitler MM, Roth T, Westbrook PR, Keenan S. Guidelines for the multiple sleep latency test (MSLT): a standard measure of sleepiness. *Sleep* 1986; **9**: 519–524.

21 Hindmarch I. Critical flicker fusion frequency (CCF): the effects of psychotropic compounds. *Pharmacopsychiatria* 1982; **5**: 225–240.

22 Hindmarch I. Psychomotor function and psychoactive drugs. *Br J Pharmac* 1980; **10**: 189–209.

23 Wechsler D. *Manual for the Wechsler adult intelligence scale*. National Foundation for Education Research, London, 1955.

24 Koskenovo M, Kaprio J, Partinen ??, Longinyanio H, Sarna S, Heikkila F. Snoring as a risk factor for hypertension and angina pectoris. *Lancet* 1985; **i**: 893–895.

25 Koskenovo M, Kaprio J, Telakivi T, Partinen M, Heikkila F, Sarna S. Snoring as a risk factor for ischemic heart disease and stroke in men. *Br med J* 1987; **294**: 16–19.

26 Norton PG, Dunn EV. Snoring as a risk factor for disease; an epidemiological survey. *Br med J* 1985; **291**: 630–632.

27 Partinen M, Palomaki H. Snoring and cerebral infarction. *Lancet* 1985; **2**: 1325–1326.

28 Guilleminault C, Silvestri R, Mondini S, Coburn S. Aging and sleep apnea: action of a benzodiazepine, acetazolamide, alcohol and sleep deprivation in healthy elderly group. *J Gerontol* 1984; **39**: 655–661.

29 Issa FG, Sullivan CE. Upper airway closing pressure in snorers. *J appl Physiol* 1984; **57**: 528–553.

30 Onal E, Lopate M, O'Connor TD. Diaphragmatic and genioglossal electromyogram response to isocapnic hypoxia in humans. *Am Rev resp Dis* 1981; **124**: 215–217.

31 Fancourt G, Castleden M. Use of benzodiazepines with particular reference to the elderly. *Br J Hosp Med* 1986; **35**: 321–326.

32 Cirignotta F, Mondini S, Zucconi M, Gerardi R, Farolfi A, Lugaresi E. Zolpidem-polysomnographic study of the effect of a new hypnotic drug in sleep apnea syndrome. *Pharmac Biochem Behav* 1988; **29**: 807–809.

33 Depoortere H, Zivkovik B, Lloyd KG, Sanger DJ, Perrault G, Langer SZ, Bartholini G. Zolpidem, a novel non-benzodiazepine hypnotic. Neuropharmacological and behavioral effects. *J Pharmac Ther* 1986; **237**: 649–658.

34 Rhodes SP, Parry P, Hanning CD. A comparison of the effects of zolpidem and placebo on respiration and oxygen saturation during sleep in the healthy elderly. *Br J clin Pharmac* 1990; **30**: 817–824.

35 Ancoli-Israel S, Kripke D, Mason W. Characteristics of obstructive and central sleep apnea in the elderly. *Biol Psychiat* 1987; **22**: 741–750.

36 Bliwise, D., Feldman, D., Bliwise, N., Carskadon, M., Kraemer, H., North, C., Petta, D., Seidel, W. & Dement, W. (1987). Risk factors for sleep disordered breathing in heterogenous geriatric populations. *J Am Geriatr Soc* 1987; **35**: 132–141.

37 Kurtz D, Fillius B, Bonigen C. Effect of zolpidem on the sleep of healthy elderly subjects: polysomnographic recording assessments and pharmacokinetics. In *Imidazopyridines in sleep disorders. A novel experimental and therapeutic approach*, eds Sauvanet JP, Langer SZ, Morselli PL. New York: Raven Press, 1988; 382.

38 Besset A, Tafti M, Barthouil Ph, Rossi P, Billiard M. Effect of zolpidem 10 mg on sleep architecture and daytime psychomotor skills in poor sleepers. *Sleep Res* 1990; **19**: 54.

39 Dujardin K, Derambure P, Guieu JD, Borderies P, Leconte P. Effects of zolpidem 10 mg on cognitive performance: an extensive investigation. *J Sleep Res* 1992; **1**: 64.

(Received 19 July 1993, accepted 10 February 1994)