Spinal Cord (2005) 43, 85–95

www.nature.com/sc

Original Article

Quality of sleep in individuals with spinal cord injury: a comparison between patients with and without pain

C Norrbrink Budh[1,2], C Hultling[1,2] and T Lundeberg[1,3]

[1]*Spinalis SCI unit, Karolinska University Hospital, Stockholm, Sweden;* [2]*Department of Public Health Sciences, Karolinska Institutet, Stockholm; Sweden;* [3]*Rehabilitation Medicine Clinic, Karolinska University Hospital, Stockholm, Sweden*

Study design: A cross-sectional descriptive study of self-reported quality of sleep in individuals with a spinal cord injury (SCI).
Objectives: To assess and describe subjective quality of sleep in patients with SCI, with and without pain.
Setting: Spinalis SCI unit, Stockholm, Sweden.
Methods: A total of 230 patients with an SCI were mailed a questionnaire containing queries about pain intensities, pain unpleasantness, mood, and sleep quality (Basic Nordic Sleep Questionnaire) to assess quality of sleep in patients with SCI with and without pain.
Results: Of the 192 questionnaires that were returned (response rate 83.4%), 191 were analysed. Patients were divided into three groups: (1) those who reported no pain ($n = 50$), (2) those who reported intermittent pain ($n = 42$), and (3) those who suffered from continuous pain ($n = 99$). Patients suffering from continuous pain rated pain intensity and unpleasantness significantly higher than those who only suffered from intermittent pain. The group with continuous pain also reported the poorest quality of sleep and the highest ratings of anxiety and depression of the three groups. Anxiety, together with pain intensity and depression, were the main predictors for poor sleep quality.
Conclusions: Poor subjective sleep quality was associated with higher ratings of pain intensity, anxiety, and depression. It is possible that melatonin serves as a modulator of these different aspects.
Sponsorship: This study was made possible by grants from Spinalis Foundation.
Spinal Cord (2005) **43,** 85–95. doi:10.1038/sj.sc.3101680; Published online 30 November 2004

Keywords: Basic Nordic Sleep Questionnaire; depression; anxiety; pain intensity; pain unpleasantness; sleeping pills

Introduction

Awareness of the importance of pain in individuals with a spinal cord injury (SCI) has been rising in recent years. As one of the major consequences of SCI, pain has been found to affect quality of life,[1–6] leisure time activities,[5,7] vocational status,[7,8] and sexuality.[9]

In non-SCI populations, poor sleep quality has been found in patients suffering from different health conditions such as obstructive pulmonary diseases, diabetes, rheumatic diseases,[10] and chronic pain conditions[11–14] as well as in patients suffering from affective disorders.[15]

Few studies, however, have focused on the quality of sleep in SCI populations. In Finland,[15] quality of sleep was assessed in (among others) patients with paraplegia. In this group, sleep quality was worse than in the control group, regarding insomnia, sleep latency, maintaining sleep, morning irritability, and willingness to go to bed.

In a study of Biering-Sörensen,[16] differences in sleep quality between patients with an SCI and individuals from the general population were assessed with the Nordic Sleep Questionnaire. They found that patients with SCI had poorer sleep quality, for example, reported more difficulties falling asleep, awakened more often at night, slept subjectively less well, were more often prescribed sleeping pills, slept more hours, took more and longer naps, and snored more. Spasms, pain and paresthesia, and troubles with voiding were found to be associated with poor sleep quality. Regarding the interference of pain with sleep disturbances in the spinal cord injured, Widerström-Noga *et al*[17] found that higher

Correspondence: C Norrbrink Budh, Spinalis SCI unit, Karolinska University Hospital, SE-169 89 Stockholm, Sweden

pain intensity was associated with poorer subjective sleep quality, that is, falling asleep and staying asleep. Rintala *et al*[8] also found chronic pain to interfere with sleep in individuals with an SCI.

In this study, we wanted to assess whether patients with SCI and pain differed from those without pain regarding subjective quality of sleep.

Methods and patients

Patients

This study was conducted at the Spinalis SCI unit at Karolinska University Hospital in Stockholm, Sweden, an outpatient clinic for patients with an SCI. Spinalis has the responsibility for lifetime follow-up in the greater Stockholm area, an area consisting of 1.8 million inhabitants. The estimated drop-out rate, that is, patients that do not receive their rehabilitation and their follow-up at Spinalis, is only a couple of percent.

In 1999, 456 SCI patients (76.5% of the total population of SCI patients in the Spinalis database at that time) were assessed in a yearly health control.[18] Besides the regular health control, they were interviewed and asked to fill in pain questionnaires. From this sample, we aimed at matching all female subjects to corresponding male subjects for age (± 3 years), ASIA (American Spinal Injury Association) impairment grade and level of lesion (cervical, thoracic, lumbar/sacral) in order to assess gender differences.[19] A total of 65 women were successfully matched and thus 130 SCI individuals were enrolled in this study. The reason behind matching for gender is that the gender ratio in patients with SCI is 3:1 for male subjects and due to this fact, studies on individuals with SCI often comprises few female subjects.

After 3 years, in 2002, a follow-up was carried out using mail. At this time, seven of the 130 patients were deceased. The remaining 123 patients were again asked questions about their pain and medication[20] as well as questions regarding the quality of sleep. Of the 123 questionnaires, 101 (82.1%) were returned. Parallel to this, 107 patients having reported *no pain* in their latest annual assessment were selected from patients in the Spinalis database. In this sample, a stratified randomization was used aiming at an equal distribution between the sexes. The sample of 107 patients received questionnaires containing queries regarding both quality of sleep and pain. In total, 230 patients with SCI were sent questionnaires. Those who had not returned the questionnaire within 1 month were sent a reminder. One patient was reported as deceased.

Of the 192 questionnaires (83.8%) that were returned, one had to be excluded because it had not been completely filled in. Of these 191 questionnaires (83.4%), 103 were from men and 88 from women, mean age 51.9 years, standard deviation (SD) 14.4, range 20–83 years. The mean age for the men was 51.2 years. SD 31.3 and for the women 52.5 years, SD 26.5. Distribution of age was normal. The mean time since injury was 15.6 years, SD 11.3, range 1–47 years. The distribution of paraplegia *versus* tetraplegia was 50.8:49.2%. In all, 129 of the patients were classified as having an incomplete lesion (ASIA impairment grades B–E) and 57 as having a complete lesion (ASIA grade A) (information on five patients was missing). By returning the questionnaires, the patients gave their informed consent to participate in our study.

Patients with pain could chose between two definitions: (1) pain present at least for the last 2 weeks or recurrent during at least four 2-week periods during the last year[21] (classified by the authors as intermittent pain) or (2) continuous/chronic pain during the last 6 months (classified by the authors as continuous pain). From the patients responses patients were classified into one of three groups as follows:

Category	*n*	*Mean age years (SD)*	*Men/women (%)*
No pain	50	47.5 (27.7)	56/44
Intermittent pain	42	51.5 (29.2)	52/48
Continuous pain	99	56.0 (28.4)	53.5/46.5

Surprisingly, few patients reported not having any pain at this occasion as compared to what was registered in the patient's computer files.

Measures

The pain questionnaire contained queries about pain intensity, pain unpleasantness (affective component of pain), mood (anxiety and depression), and sleep quality.

Pain intensity and pain unpleasantness

The scoring of pain intensity consisted of rating the mildest, the general, and the worst intensity on a 100-mm visual analogue scale (VAS), marked from 0 to 100 with the end points 'no pain' and 'unbearable pain'. The affective component was rated on a 100-mm VAS with the end points 'no unpleasantness' and 'worst imaginable unpleasantness'.

Mood

The Hospital Anxiety and Depression (HAD) Scale,[22] which is used for scoring mood, is a self-rating instrument for anxiety and depression consisting of 14 items, seven on anxiety and seven on depression. Each item has answers that have an assigned value between 0 and 3 points. When calculating mood from the HAD scale, patients are classified as sufferers from anxiety, depression, or both based on the sum score: 'cases', 11–21 points; 'doubtful cases', 8–10 points; and 'non-cases', 0–7 points.

Quality of sleep

Sleep quality was rated with the Basic Nordic Sleep Questionnaire (BNSQ),[23] which is a qualitative and

Table 1 Rating scales in the Basic Nordic Sleep questionnaire

Answer	*Question*		
	1, 3, 5, 7, 8, 8, 10, 11, 15a, 16, 18	*4*	*6*
1	Never or less than once per month	Usually I don't wake up at night	Well
2	Less than once per week	Once per night	Rather well
3	On 1–2 days per week	Two times	Neither well nor badly
4	On 3–5 days per week	3–4 times	Rather badly
5	Daily or almost daily	At least 5 times per night	Badly

quantitative instrument comprising 21 questions on sleep quality during the last 3 months (Table 1). This instrument has been developed by a task group from the Scandinavian Sleep Research Society in order to create a standardized questionnaire. The reproducibility has been assessed in a group of spinal cord injured individuals in Denmark[24] as well as in individuals from the general population and was found to be satisfactorily reproducible.

Three questions were excluded from the questionnaire due to the fact that patients might need assistance from another person which not everyone has: In what way do you snore (ask other people about the quality of snoring) (Q17)? If you snore at least 1–2 times per week, how many years have you been snoring (ask other people if you do not know) (Q19a)? and Age when you started to snore (Q19b)? Two other questions were not analysed due to the wide variations in the answers (eg answers like '10 pm–1 am' or 'it depends'): Q13 and Q14 on bedtimes and waking-up times.

Data on age, level of injury, and ASIA impairment grade were collected from the computer files.

The study was approved by the Ethics committee of Karolinska Institutet in Stockholm, Sweden.

Statistical methods

Calculations were made with individuals divided into the three groups: (1) no pain, (2) intermittent pain, and (3) continuous pain. Calculations were made with the nonparametric Mann–Whitney *U*-test and the Kruskal–Wallis analysis of variance (ANOVA), as the data obtained were either ordinal data (ratings of pain, unpleasantness, anxiety, depression, and sleep) or interval data lacking a normal distribution (sleep questions Q2, 12, 15b and 20). Multiple comparisons between the different categories within each variable were made using rank sums.[25] Correlations between poor sleep quality and general pain intensity, worst pain intensity, unpleasantness, anxiety, and depression were made with Spearman's rank invariant analysis. Factors associated with poorer quality of sleep were analysed with the SAS logistic regression analysis for an ordinal response variable (SAS®, Release 8.2, SAS Institute Inc., USA). The six different sleeping items were classified into three response categories, no (1), mild (2–3), and severe (4–5). Six logistic regression models were then performed with sleeping item as an ordinal response and pain (general and worst intensity, unpleasantness, intermittent, continuous), depression, and anxiety as covariates. Anxiety and depression were dichotomised (non-cases and doubtful cases/cases) and pain intensities and unpleasantness classified into groups of three categories (0–39, 40–69, and 70–100). Differences between patients with tetra- and paraplegia; between patients with incomplete and complete injuries; and between the genders *versus* quality of sleep, mood, and VAS ratings of pain intensity and unpleasantness were assessed with the Mann–Whitney *U*-test. Differences regarding prevalence of pain between patients with complete and incomplete injuries were analysed using the χ^2 test. The *t*-test for independent samples was used to analyse differences in age between patients with incomplete and complete injuries. The level of significance was set to 0.05.

Results

Sleep variables

The result of rating the sleep variables in the BNSQ are presented in Table 2 (categorical data) and Table 3 (numerical data). Differences were seen in the following sleep variables (Figure 1): difficulties to fall asleep (Q1), awakening during the night (Q3), overall sleeping quality (Q6), sleepiness in the morning (Q8), and during the day (Q9). In all of these variables, differences in quality of sleep were seen between patients *without pain* and patients who had *continuous pain*. No differences were seen between patients *without pain* and those with *intermittent pain*. In all but one of the variables (Q3), differences between the two groups of patients with pain were seen. A strong tendency towards significance was also seen in the answers to Q5 and Q15a. Those with continuous pain tended to wake up too early in the morning (Q5) ($P = 0.052$) while those without pain did not. Patients with continuous pain also tended to take more naps during the day (Q15a) ($P = 0.058$) than patients with intermittent pain.

Several patients found the questions on snoring (Q16) and sleep apnoea (Q18) difficult to answer (9 and 8% drop-outs, respectively) since they lived on their own for the most part and thus did not know if or how often they snored or had sleep apnoea.

Few individuals used prescribed sleeping pills (Q7) on a regular basis. The median value in all three groups

Table 2 Distribution of the answers to the questions on the Basic Nordic Sleep Questionnaire with a 5-point ordinal scale. The questionnaire was answered by three groups of patients: patients with no pain (NP), patients with intermittent pain (IP) and patients with continuous pain (CP)

Question		*n/group*	*1*	*2*	*3*	*4*	*5*	*P-value*
Q1	Have you had difficulties in falling asleep?	NP 48	52.1	27.1	8.3	10.4	2.1	0.009
		IP 42	52.4	19.0	14.3	7.1	7.1	
		CP 96	34.4	22.9	14.0	9.4	18.8	
Q3	How often have you awakened at night?	NP 46	15.2	13.0	17.4	19.0	34.8	0.019
		IP 42	7.1	11.9	14.3	21.4	45.2	
		CP 98	7.1	8.2	13.3	11.2	60.2	
Q4	How many times do you usually wake up during one night?	NP 47	14.9	44.7	21.3	19.1	0.0	0.071
		IP 40	7.5	42.5	37.5	10.0	2.5	
		CP 98	14.3	22.4	33.7	24.5	5.1	
Q5	How often have you awakened too early in the morning without being able to fall asleep again?	NP 49	46.9	32.7	10.2	6.1	4.1	0.052
		IP 42	42.9	31.0	14.3	2.4	9.5	
		CP 98	37.8	17.3	19.4	6.1	19.4	
Q6	How well have you been sleeping?	NP 50	46.0	32.0	14.0	8.0	0.0	<0.001
		IP 42	28.6	40.5	21.4	7.1	2.4	
		CP 99	19.2	29.3	25.3	16.2	10.1	
Q7	Have you used sleeping pills (by prescription)?	NP 48	89.6	2.1	2.1	0.0	6.3	0.12
		IP 42	85.7	0.0	2.4	0.0	11.9	
		CP 97	77.1	4.2	3.1	2.1	13.5	
Q8	Do you feel excessively sleepy in the morning after awakening?	NP 50	44.0	20.0	16.0	6.0	14.0	0.019
		IP 41	41.5	29.3	17.1	7.3	4.9	
		CP 97	28.6	21.4	18.4	11.2	20.4	
Q9	Do you feel excessively sleepy during the daytime?	NP 49	44.9	22.4	18.4	8.2	6.1	<0.001
		IP 40	33.3	33.3	15.4	5.1	12.8	
		CP 96	15.6	20.8	26.0	10.4	27.1	
Q10	Have you suffered from irresistible tendency to fall asleep while at work?	NP 39	84.6	7.7	2.6	5.1	0.0	0.41
		IP 34	88.2	2.9	8.8	0.0	0.0	
		CP 36	78.8	7.6	6.1	1.5	6.1	
Q11	Have you suffered from irresistible tendency to fall asleep during free time (leisure time)?	NP 45	53.3	22.2	13.3	8.9	2.2	0.098
		IP 39	48.7	30.8	5.1	10.3	5.1	
		CP 86	42.4	11.8	24.7	3.5	17.6	
Q15a	How often do you have a nap during the day?	NP 49	53.1	16.3	12.2	10.2	8.2	0.058
		IP 40	61.5	5.1	25.6	0.0	7.7	
		CP 99	41.4	16.2	18.2	4.0	20.2	
Q16	Do you snore while sleeping?	NP 45	37.8	17.8	20.0	11.1	13.3	0.95
		IP 35	42.9	14.3	22.9	2.9	17.1	
		CP 88	44.3	13.6	9.1	10.2	22.7	
Q18	Have you had breathing pauses (sleep apnoea) during sleep	NP 45	93.3	0.0	2.2	2.2	2.2	0.20
		IP 34	88.2	0.0	0.0	5.9	5.9	
		CP 77	81.8	3.9	2.6	3.9	7.8	

was 1 (never or less than once per month) with interquartile ranges (IQR) 1;1 in all groups. Of the 191 patients who answered this question, 37 (19%) used prescribed sleeping pills. In the nonpain group, eight patients (16%) used sleeping pills compared to six (14%) in the intermittent pain group and 23 (23%) in the continuous pain group. These differences were non-significant.

No significant differences were detected between the groups in their answers to the quantitative questions (Q2, 12, 15b, and 20) (Table 3). Patients without pain took 18 min on average to fall asleep compared with

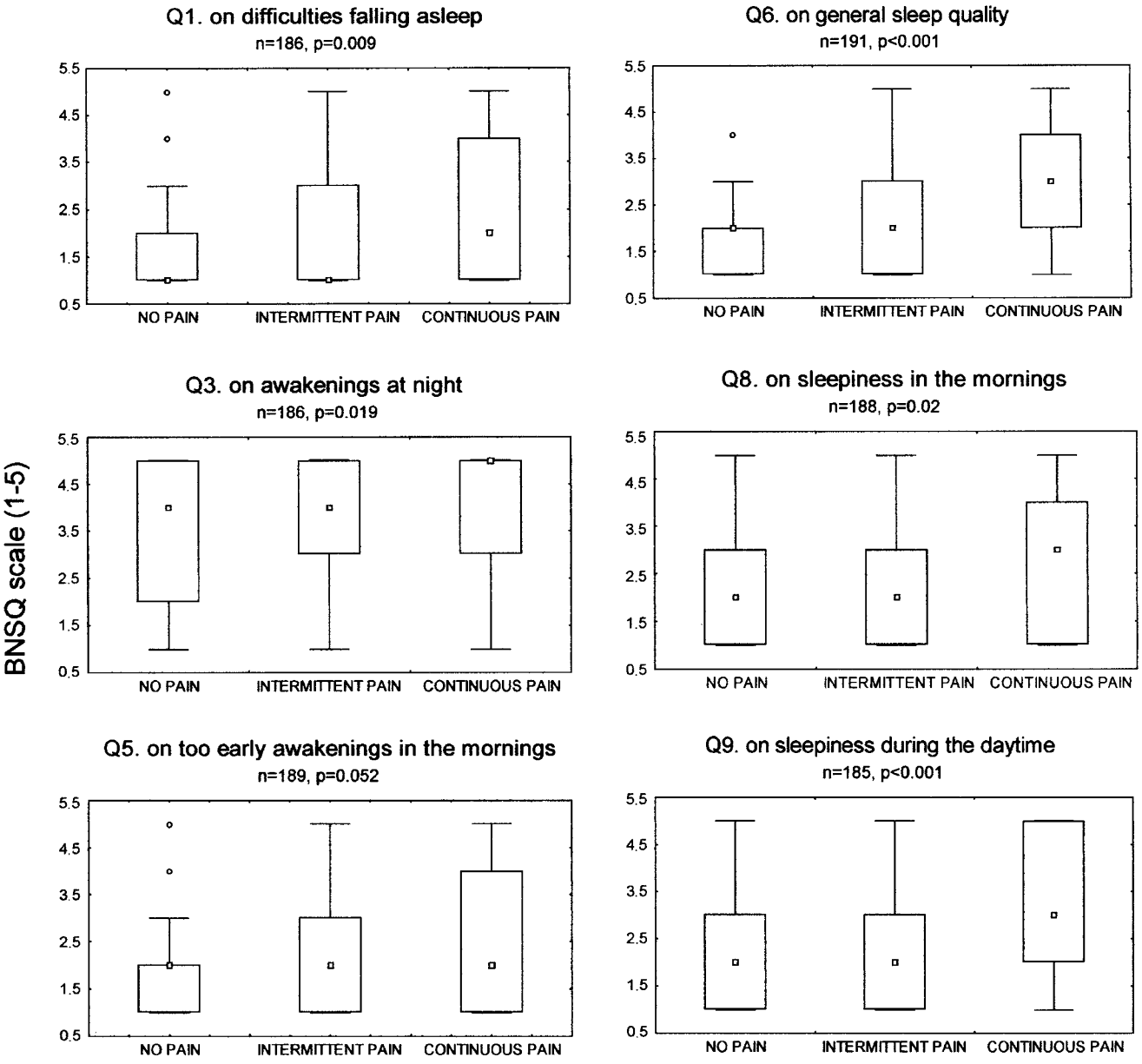

Figure 1 Box and whisker plots of sleeping variables in the Basic Nordic Sleep Questionnaire. Box plots of the sleep variables where differences between the three groups of patients (no pain, intermittent pain, and continuous pain) were found. The boxes represent a 25–75% range of the results and the whiskers represent the nonoutlier minimum and maximum values. The median values are marked with a square in the boxes and outliers with a round circle

those with continuous pain, who took an average of 31 min to fall asleep (Q2). Estimations of time spent sleeping at night (Q12) were slightly lower in the continuous pain group (6 h and 49 min) compared with those without pain or with only intermittent pain (7 h and 4 min in both groups). Time asleep differed little from the time the patients actually wished they had slept (Q20): those without pain wished they had slept on average another 35 min, those with intermittent pain another 36 min, and those with continuous pain another 61 min.

In Q21, an open question, patients were asked to describe what caused their disturbed sleep; 19 patients stated pain, 15 bladder management, 11 emotional distress, 10 spasms/spasticity, four sleep apnoea/snoring, three turning in bed, two dreams/nightmares, two sweating/warm, and two paresthesia.

Pain intensities and pain unpleasantness

Ratings of pain intensities (general, mildest, and worst) as well as of pain unpleasantness differed significantly

Table 3 Distribution of the quantitative questions in the Basic Nordic Sleep Questionnaire. The questionnaire was answered by three groups of patients: patients with no pain (NP), patients with intermittent pain (IP) and patients with continuous pain (CP)

Question	*n/group*	*Mean (min)*	*SD*	*Range*	*P-value*
Q2. How long time (how many minutes as an average) do you stay awake in bed before you fall asleep?					
(a) during working days	NP 40	18	17	1–60	0.16
	IP 39	23	30	2–120	
	CP 80	31	43	1–240	
(b) during freetime	NP 40	18	16	2–60	0.20
	IP 39	21	26	2–120	
	CP 80	33	46	1–240	
Q12. How many hours do you usually sleep per night?	NP 47	7 h 04	62	220–540	0.45
	IP 42	7 h 04	57	300–540	
	CP 96	6 h 49	88	210–660	
Q15b. If you take a nap, how long does it usually last (minutes)?	NP 27	43	20	10–90	0.16
	IP 69	69	54	25–240	
	CP 58	58	37	5–180	
Q20. How many hours of sleep do you need per night (how many hours would you sleep if you had the possibility to sleep as long as you need to)?	NP 47	7 h 39	1 h 14 min	3.5–12.0	0.89
	IP 38	7 h 40	0 h 51 min	5.0–9.0	
	CP 90	7 h 50	1 h 20 min	4.5–14.0	

NP = no pain; IP = intermittent pain; CP = continuous pain

between the two groups of individuals reporting pain (Figure 2). All ratings by individuals with continuous pain were significantly higher than those by patients reporting intermittent pain. The median values of the ratings of general pain in the two groups of intermittent *versus* continuous pain were 24.5 (IQR 17;46) and 51.5 (IQR 39;70), respectively, ($P<0.001$). The median value of the mildest pain was 4 (IQR 0;14) in the group classified as having intermittent pain and 30 (IQR 14;51) in the group with continuous pain, ($P<0.001$). Ratings of the worst pain followed a similar pattern – the median value in the group with intermittent pain was 58 (IQR 41;78) and in the group with continuous pain 80 (IQR 65;89), ($P<0.001$).

Regarding ratings of the affective component of pain, that is, pain unpleasantness, the group of individuals with intermittent pain had a median of 45 (IQR 21.5;66), while the continuous pain group had with a median of 64 (IQR 47;80), ($P=0.0011$). These values are not only statistically significant but most likely clinically significant as well.

Mood

Anxiety Ratings of anxiety on the HAD scale differed in the same way as ratings of pain intensity and unpleasantness, that is, individuals with continuous pain rated their anxiety as significantly higher ($P=0.0014$) than those with intermittent pain and those without pain (Figure 3). Patients without pain had a median value of 3 (IQR 1;4.5) as did those with intermittent pain (IQR 1.5;7), while patients with continuous pain had a median of 5 (IQR 2;9). Median values were low in all three groups, but when patients were classified as non-cases, doubtful cases, and cases according to the HAD scale, more patients suffering from continuous pain (33%) could be classified as doubtful cases and cases than could patients with intermittent pain (21%) and no pain (6%).

Depression The depression scores of patients with continuous pain were higher ($P<0.001$) than the scores of both patients with intermittent pain and those without pain on the HAD scale (Figure 3). The median value for patients with continuous pain was 4 (IQR 2;6.5) compared with those suffering from intermittent pain and those who were pain free, where the median values were 2 (IQR 1;4). When patients were classified as doubtful cases or cases, the highest number was found among patients suffering from continuous pain (19%) followed by those with intermittent pain (14%) and patients who were pain free (0%).

Level of lesion, completeness of injury, and gender

In our study, almost half of the respondents were patients with tetraplegia. There were no differences in ratings of general ($P=0.65$) or worst pain intensity ($P=0.21$), nor in pain unpleasantness ($P=0.45$) between patients with para- and tetraplegia. Neither were there any differences in ratings of anxiety ($P=0.55$) or depression ($P=0.55$) between the two groups.

Regarding the reported quality of sleep, tetraplegics rated general sleep quality (Q6) to be poorer than paraplegics ($P=0.051$). Both patients with tetra- and

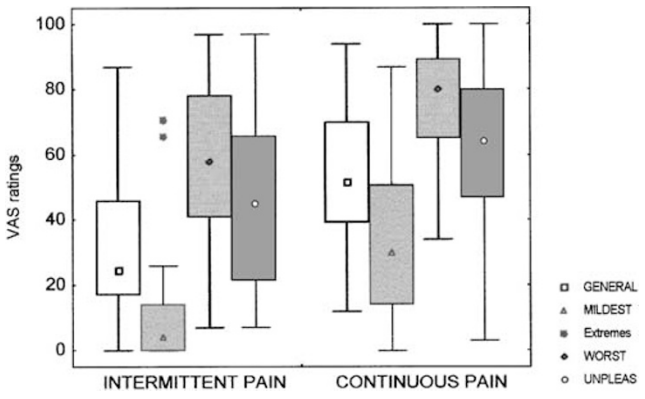

Figure 2 Ratings of pain intensities and pain unpleasantness. Differences between patients with intermittent pain and those with continuous pain in ratings of pain intensities and unpleasantness on a visual analogue scale (VAS). The boxes represent a 25–75% range of the results and the whiskers represent the nonoutlier minimum and maximum values. The median values are marked with a square in the boxes and outliers with a round circle

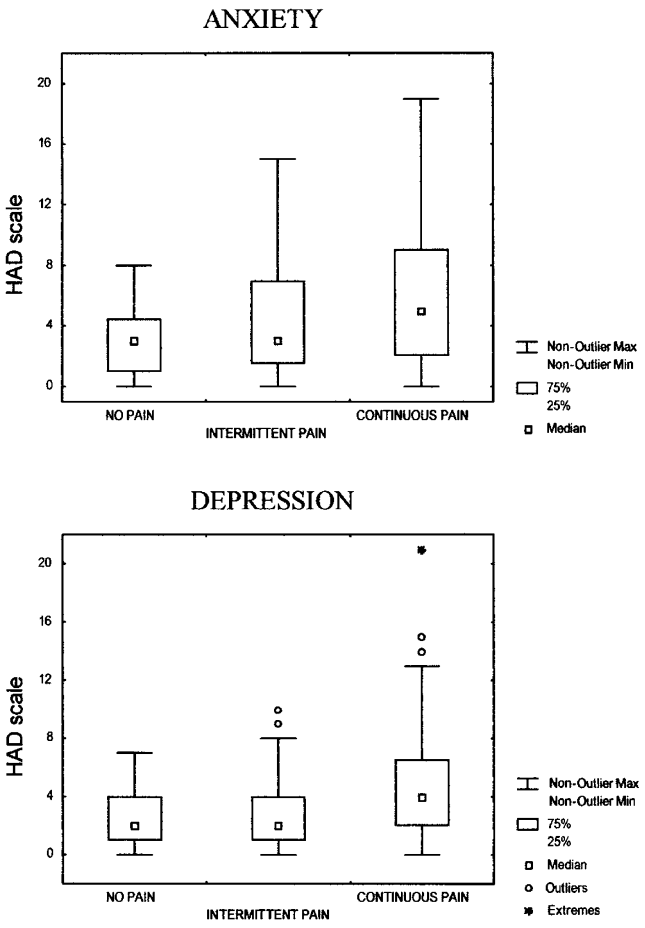

Figure 3 Box and whisker plots of ratings of anxiety and depression according to Hospital Anxiety and Depression (HAD) Scale in the three groups of patients

patients with paralegia had a median value of 2, but the IQRs were higher among tetraplegics [2;3] than paraplegics [1;3]. No other differences were found regarding the other qualitative variables between patients with tetra- or paraplegia.

There were no differences in ratings of general ($P=0.82$) or worst pain intensity ($P=0.20$), nor in pain unpleasantness ($P=0.51$) between patients with incomplete and complete injuries. Likewise, there were no differences regarding scoring of anxiety ($P=0.36$) or depression ($P=0.20$). However, patients with incomplete injuries rated quality of sleep to be poorer than patients with complete injuries regarding difficulties in falling asleep (Q1) ($P=0.044$), awakening during the night (Q3) ($P=0.005$), awakening too early in the morning (Q5) ($P=0.020$), overall sleep quality (Q6) ($P=0.045$), use of sleeping pills (Q7) ($P=0.024$), and sleepiness during leisure time (Q11) ($P=0.012$).

No gender differences were seen regarding ratings of general pain intensity ($P=0.92$), worst pain intensity ($P=0.52$), or unplesantness ($P=0.90$). Neither could we detect any differences between the genders regarding ratings of anxiety ($P=0.67$) or depression ($P=0.99$) or in analyses of quality of sleep and sex.

Correlations and predictors

In analyses with the Spearman rank invariant analysis of correlations between poor sleep and pain intensities (general and worst pain intensities), pain unplesantness and mood (anxiety and depression) correlations were found to be low (Table 4). Only the variable – Do you feel excessively sleepy during daytime (Q9)? had a moderate correlation coefficient of $r=0.44$ between poor sleep and depression.

In the logistic regression analysis, we assessed sleeping variables (dependent variables) that were found to be significant (Q1, 3, 6, 8, and 9), or very close to significant (Q5), in the univariate analyses. We chose to include independent variables that can be affected by treatment (presence of pain, pain intensities, pain unpleasantness, anxiety, and depression).

Anxiety was found to be the main predictor of poorer sleep quality in three of the six sleep variables assessed. In Q6, *'How well have you been sleeping the last 3 months?'*, ratings of the worst pain intensity was the main predictor and in Q5, *'How often have you awakened too early in the morning'*, and Q8, *'Do you feel excessively sleepy in the morning?'* depression was found to be the most predictive.

Discussion

Quality of sleep in individuals with spinal cord injury

In our study, we found the subjective quality of sleep to be poorer in patients with SCI and continuous pain than in patients with intermittent pain and patients without pain. This inferior quality of sleep in patients with SCI

Table 4 Statistical analysis of correlations and predictors for poor sleep quality

Sleep question	*Q1*			*Q3*			*Q5*		
	Predictors	*OR+CI*	*P*	*Predictors*	*OR+CI*	*P*	*Predictors*	*OR+CI*	*P*
Logistic regression analysis	1. anxiety 2. continuous pain	2.9 (1.4–5.8) 2.1 (1.0–4.4)	0.003 0.03	1. anxiety	2.4 (1.0–5.6)	0.04	1. depression 2. anxiety	3.3 (1.3–8.7) 3.0 (1.4–6.2)	0.01 0.005
	Variable	*r*		*Variable*	*r*		*Variable*	*r*	
Spearman's rank correlations	1. depression 2. anxiety 3. unpleasantness	0.27 0.25 0.24		1. general pain intensity 2. depression	0.13 0.12		1. anxiety 2. depression 3. unpleasantness	0.34 0.32 0.27	
Sleep question	*Q6*			*Q8*			*Q9*		
	Predictors	*OR+CI*	*P*	*Predictors*	*OR+CI*	*P*	*Predictors*	*OR+CI*	*P*
Logistic regression analysis	1. worst pain intensity (ratings between 70 and 100)	4.2 (1.9–9.1)	<0.001	1. depression	3.4 (1.4–8.3)	0.008	1. anxiety	3.5 (1.7–7.2)	<0.001
	2. worst pain intensity (ratings between 40 and 69)	2.7 (1.2–6.1)	0.02	2. continuous pain	1.8 (0.9–3.6)	0.09	2. continuous pain	3.0 (1.5–6.1)	0.003
	3. anxiety	2.3 (1.1–4.8)	0.03						
	Variable	*r*		*Variable*	*r*		*Variable*	*r*	
Spearman's rank correlations	1. anxiety/depression 3. worst pain intensity	0.32 0.30		1. anxiety/depression 3. worst pain intensity	0.34 0.31		1. depression 2. anxiety 3. general pain intensity	0.44 0.35 0.28	

CI = confidence interval, OR = odds ratio, *r* = Spearman's rank correlation coefficient

The data was first analysed with the Spearman's rank correlation coefficient; a univariate statistical test. Correlations with all variables assessed (depression, anxiety, general pain intensity, worst pain intensity, and unpleasantness) in all sleep variables were low except for Q9 where a modest correlation between depression and poor sleep quality was found. Thereafter, logistic regression analyses were carried out to detect predictors for the poor sleep quality. In three of the six variables, anxiety seemed to be the most important predictor for poor sleep quality (difficulties in falling asleep, awakenings at night, sleepiness during daytime). In two variables depression was the predictor (too early awakenings, sleepiness in the mornings) and in one the worst pain intensity was found to be the main predictor (how well have you been sleeping)

and continuous pain was observed in the variables overall sleep quality during the last 3 months, difficulties in falling asleep, number of awakenings at night, sleepiness in the mornings and during the day, and waking up too early in the mornings. Patients in the continuous pain group rated pain intensities (general, mildest, and worst) higher as well as pain unpleasantness, depression, and anxiety.

In the logistic regression analysis, anxiety was the main predictor for the worse quality of sleep. The poorer sleep quality that was found, however, was not associated with the *presence of pain* since no difference was found between patients with intermittent pain and patients without pain. Likewise, no differences were found between these two groups in ratings of anxiety and depression.

Comparisons with other studies on sleep quality

In Denmark, the sleep quality of patients with an SCI was compared with the sleep quality of the general population using the Nordic Sleep Questionnaire.[16] Danish researchers found quality to be poorer in the SCI population in most of the assessed variables. When comparing our results with those obtained from their SCI population (Tables 2 and 3), we can see that our patients with continuous pain seem the rate their quality of sleep poorer than the Danish SCI population rated their sleep in most questions, except for naps (Q15a), snoring (Q16), sleep apnoea (Q18), and the use of prescribed sleeping pills (Q7) where our results are very similar. Looking at our patients classified as suffering from intermittent pain and those without pain, their self-reported quality of sleep was similar to, or slightly better than the Danish SCI population in general. In the Danish study, patients reported that 'pain and paresthesia' was the greatest problem interfering with sleep (31.7%), followed by spasms (20.3%) and voiding (17.7%). In our study, pain was also the main problem reported to interfere with sleep quality, followed by bladder management emotional distress, and spasms/spasticity. Only two of our patients reported that paresthesia caused sleeping problems.

Difficulties in maintaining sleep has been reported to worsen with increasing age in patients with somatic diseases,[10] and in our study the patients were almost 10 years older than in the Danish study, which could also be a part of the explanation of the poorer sleep quality seen in our sample of patients with continuous pain. This group had a higher mean age (56.0 years) than the patients without pain (47.5 years) and those with intermittent pain (51.5 years). This is in accordance with our previous findings that pain prevalence in SCI seems to increase with age.[19]

Despite reporting troublesome sleep, relatively few of our patients reported the use of prescribed sleeping pills. A total at 23% of the patients with continuous pain used drugs to improve sleep now and then, as did 14% of those with intermittent pain, and 16% of those without pain.

No difference between the groups were found regarding snoring and sleep apnoeas, but these conditions can be difficult to detect if you sleep alone. In patients with tetraplegia, apnoeas – especially the obstructive kind – have been found to be a significant problem (prevalence between 15 and 48%), interfering negatively with the quality of sleep.[26–28] Unfortunately, apnoeas cannot be verified by subjective reports. Apnoeas can be associated with, among other things, obesity (a high body-mass index) and the use of antispastic medication. Data on weight and length, as well as on the use of antispastic medication, are missing in our study.

We did not find any differences between patients with tetra- and paraplegia regarding the prevalence of sleep apnoea. However, this might be because many of our patients were either not diagnosed as having sleep apnoea or were not aware of this problem. We did find, though, that patients with tetraplegia reported their general quality of sleep to be poorer than those with paraplegia. Patients with para- and tetraplegia did not differ regarding any other sleep variables. It is possible that part of the explanation may be attributed to sleep apnoea. Polysomnographic studies and/or measuring of nocturnal saturation (hypoxia is associated with apnoea) are necessary to diagnose these problems. Periodic leg/limb movements (PLM) may also cause sleep disturbances in patients with SCI.[29,30] In this study, PLM was not monitored.

We found that patients with incomplete injuries reported poorer sleep quality than patients with complete injuries. There is no obvious explanation for this difference as patients with incomplete injuries did not report either higher pain intensities/unpleasantness, or higher scores on anxiety or depression. Neither did patients with incomplete injuries have a higher prevalence of pain ($P = 0.14$). The mean age, however, was higher among patients with incomplete injuries, 55.7 *versus* 46.9 years and as mentioned before, higher age has in general been seen to be associated with poorer sleep.[10]

Predictors for poor sleep

In our group of patients suffering from continuous pain, ratings of pain intensities, unpleasantness, anxiety, and depression were all higher than in our other two groups of patients. To detect predictors of poor sleep quality, we used logistic regression analyses and found that ratings of the worst pain intensity were predictive for overall sleep quality and ratings of depression for waking up too early in the morning and for sleepiness in the mornings. Ratings of anxiety, however, were associated with most of the reported problems with sleep.

Findings of mood interfering with sleep are supported by other studies. In one study on patients with chronic pain,[31] higher ratings of both anxiety and depression were found, as compared with healthy controls, but only depression was found to be predictive for poorer sleep

quality. A study on patients with chronic low back pain[12] also found sleep disturbances to be mainly associated with a depressed mood. In general, pain severity does not seem to be predictive for poorer sleep as often as mood, but in most studies, sleep disturbances and high pain intensities coincide.[11–14,31]

However, pain severity was found to be predictive for *falling asleep* and for *staying asleep* in a study on patients with spinal cord injuries.[17]

Relation between pain and sleep

Several studies have reported that patients with pain report poorer sleep quality. Simply the presence of pain or its intensity is rarely predictive of this. Does this mean that pain is not the cause of the sleep disturbance? Is it even so that poor sleep quality can enhance or even result in pain if persisting for a longer period of time? In a study on pain and sleep in women with fibromyalgia,[32] the authors suggest that poor sleep precedes increased pain, rather than the opposite. On the other hand, in a study in patients with chronic pain conditions, other researchers reported that the onset of sleep disturbances coincided or followed the onset of pain,[13] which suggests that sleep disturbances are secondary to pain. The issue of poor sleep quality and pain bears a striking resemblance to the question of which came first, the hen or the egg.

Physiological connections

Neuromodulators such as serotonin, norepinephrine, and melatonin are involved in regulating anxiety, depression, pain, and sleep. The agents that are recommended in the treatment of anxiety are selective serotonin reuptake inhibitors (SSRIs). In depression, SSRIs together with tricyclic antidepressants (TCAs) are used and in neuropathic pain conditions, TCAs are considered one of the first treatment options. TCA is also used, alongside benzodiazepines in sleeping disorders. Monoamines seem to be a common denominator in the treatment strategies of these four conditions. The role of monoamines in sleep is to a large extent still unknown. It has been demonstrated that serotoninergic neurons play a key role in the timing of the REM (rapid eye movement) and non-REM sleep periods.[33] Interestingly, serotonin is also a precursor of melatonin,[34,35] and the secretion of melatonin has been found to increase with the use of norepinephrine reuptake inhibitors.[34] The regulation of melatonin synthesis and release appears to be dependent on intact neuronal cervical pathways and sympathetic innervation.[34,36–38] The concentration of melatonin (in serum and plasma respectively) in cervically complete spinal cord injured individuals was found to be decreased and lacking the diurnal rhythm.[37,38] The secretion of melatonin is important for the regulation of the diurnal rhythm and the induction of sleep. Lack of diurnal rhythm could be a contributing factor to the poorer sleep quality found in tetraplegics.

Low levels of melatonin have been found in depressed patients even to the extent that low nocturnal secretion has been proposed to be a 'trait marker for major depressive disorders'.[34]

Melatonin has also been found to have an antinociceptive effect on rats,[35,39] possibly by promoting the release of beta-endorphin.[35] We suggest that melatonin may be a common denominator in pain, depression, and sleep disturbances.

Conclusion

The subjective quality of sleep in patients with SCI and continuous pain was poorer than in patients who were pain free or who only had intermittent pain. Poor sleep quality was associated with higher ratings of pain intensity, anxiety, and depression. It is possible that melatonin serves as a modulator of these different aspects. This needs to be further explored and such studies are underway.

Acknowledgements

We thank The Spinalis Foundation for financial support and statistician Elisabeth Berg, LIME, Karolinska Institutet for valuable statistical advice and support.

References

1 Lundqvist C, Siösteen A, Blomstrand C, Lind B, Sullivan M. Spinal Cord Injuries. Clinical, functional and emotional status. *Spine* 1991; **50:** 41–50.
2 Wagner Anke AG, Stenhjem AE, Kvalvik Stanghelle J. Pain and life quality within 2 years of spinal cord injury. *Paraplegia* 1995; **33:** 555–559.
3 Westgren N, Levi R. Quality of life and traumatic spinal cord injury. *Arch Phys Med Rehabil* 1998; **79:** 1433–1439.
4 Putzke JD, Richards JS, Dowler RN. The impact of pain in spinal cord injury: a case–control study. *Rehabil Psych* 2000; **45:** 386–401.
5 Murphy D, Reid DB. Pain treatment satisfaction in spinal cord injury. *Spinal Cord* 2001; **39:** 44–46.
6 Putzke DP, Richards JS, Hicken BL, DeVivo MJ. Interference due to pain following spinal cord injury: important predictors and impact on quality of life. *Pain* 2002; **100:** 231–242.
7 Ravenscroft A, Ahmed YS, Burnside IG. Chronic pain after SCI. A patient survey. *Spinal Cord* 2000; **38:** 611–614.
8 Rintala DH, Loubser PG, Castro J, Hart KA, Fuhrer MJ. Chronic pain in a community-based sample of men with spinal cord injury: prevalence, severity, and relationship with impairment, disability, handicap, and subjective well being. *Arch Phys Med Rehabil* 1998; **79:** 604–614.
9 Westgren N, Hultling C, Levi R, Seiger Å, Westgren M. Sexuality in women with traumatic spinal cord injury. *Acta Obst Gynecol Scand* 1997; **76:** 977–983.
10 Gislason T, Almqvist M. Somatic diseases and sleep complaints. *Acta Med Scand* 1987; **221:** 475–481.
11 Pilowsky I, Crettenden I, Townley M. Sleep disturbances in pain clinic patients. *Pain* 1985; **23:** 27–33.

12 Atkinson JH, Ancoli-Israel S, Slater MA, Garfin SR, Gillin JC. Subjective sleep disturbance in chronic back pain. *Clin J Pain* 1988; **4:** 225–232.
13 Morin CM, Gibson D, Wade J. Self-reported sleep and mood disturbance in chronic pain patients. *Clin J Pain* 1998; **14:** 311–314.
14 Wilson KG, Watson ST, Currie SR. Daily diary and ambulatory activity monitoring of sleep in patients with insomnia associated with chronic musculoskeletal pain. *Pain* 1998; **75:** 75–84.
15 Hyyppä MT, Kronholm E. Quality of sleep and chronic illness. *J Clin Epidemiol* 1989; **42:** 633–638.
16 Biering-Sörensen F, Biering-Sörensen M. Sleep disturbances in the spinal cord injured: an epidemiological questionnaire investigation, including a normal population. *Spinal Cord* 2001; **39:** 505–513.
17 Widerstrom-Noga EG, Felipe-Cuervo E, Yezierski RP. Chronic pain after spinal injury: interference with sleep and daily activities. *Arch Phys Med Rahabil* 2001; **82:** 1571–1577.
18 Norrbrink Budh C *et al*. Pain in a Swedish spinal cord injury population. *Clin Rehabil* 2003; **17:** 685–690.
19 Norrbrink Budh C *et al*. Gender related differences in pain in spinal cord injured individuals. *Spinal Cord* 2003; **41:** 122–128.
20 Norrbrink Budh C, Lundeberg T. Use of analgesic drugs in individuals with spinal cord injury. *J Rehabil Med* (in press).
21 Levi R, Ertzgaard P. Quality indicators in spinal cord injury care: a Swedish collaborative project. The Swedish Spinal Cord Injury Council 1998. *Scand J Rehabil Med Suppl* 1998; **38:** 1–80.
22 Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. *Acta Psychiatr Scand* 1983; **67:** 361–370.
23 Partinen M, Gislason T. Basic Nordic Sleep Questionnaire (BNSQ): a quantitated measure of subjective sleep complaints. *J Sleep Res* 1995; **4**(Suppl 1)**:** 150–155.
24 Biering-Sörensen F, Biering-Sörensen M, Hilden J. Reproducibility of Nordic Sleep Questionnaire in spinal cord injured. *Paraplegia* 1994; **32:** 780–786.
25 Siegal S, Castellan NJ. *Nonparametric Statistics for the Behavioural Sciences, 2nd edn*. McGraw-Hill international editions. McGraw-Hill: New York 1988 pp 213–214.
26 Klefbeck B, Sternhag M, Weinberg J, Levi R, Hultling C, Borg J. Obstructive sleep apneas in relation to severity of cervical spinal cord injury. *Spinal Cord* 1998; **36:** 621–628.
27 Burns SP, Kapur V, Yin KS, Buhrer R. Factors associated with sleep apnea in men with spinal cord injury: a population-based case–control study. *Spinal Cord* 2001; **39:** 15–22.
28 Stockhammer E *et al*. Characteristics of sleep apnea syndrome in tetraplegic patients. *Spinal Cord* 2002; **40:** 286–294.
29 Dickel MJ, Renfrow SD, Moore PT, Berry RB. Rapid eye movement sleep periodic leg movements in patients with spinal cord injury. *Sleep* 1994; **17:** 733–738.
30 De Mello NT, Silva AC, Esteves AM, Tufik S. Reduction of periodic leg movement in individuals with paraplegia following acerobic physical exercise. *Spinal Cord* 2002; **40:** 646–649.
31 Sayar K, Arikan M, Yontem T. Sleep quality in chronic pain patients. *Can J Psychiatry* 2002; **47:** 844–848.
32 Affleck G, Urrows S, Tennen H, Higgins P, Abeles M. Sequential daily relations of sleep, pain intensity, and attention to pain among women with fibromyalgia. *Pain* 1996; **68:** 363–368.
33 Aldrich MS (ed). In: *Sleep Medicine*. Oxford University Press: Oxford 1999 pp 27–38.
34 Webb S, Puig-Domingo M. Role of melatonin in health and disease. *Clin Endocrinol* 1995; **42:** 221–234.
35 Yu CX, Zhu CB, Xu SF, Cao XD, Wu GC. The analgesic effects of peripheral and central administration of melatonin in rats. *Eur J Pharmacol* 2000; **403:** 49–53.
36 Kneisley LW, Moskowitz MA, Lynch HJ. Cervical spinal cord lesions disrupt the rhythm in human melatonin excretion. *J Neural Transm Suppl* 1978; **13:** 311–323.
37 Li Y, Jiang DH, Wang ML, Jiao DR, Pang SF. Rhythms of serum melatonin in patients with spinal lesions at the cervical, thoracic or lumbar region. *Clin Endocrin* 1989; **30:** 47–56.
38 Zeitzer JM, Ayas NT, Shea SA, Brown R, Czeisler CA. Absence of detectable melatonin and preservation of cortisol and thyrotropin rhythms in tetrapelgia. *J Clin Endocrinol Metabol* 2000; **85:** 2189–2196.
39 Naguib M *et al*. Pharmacological effects of intravenous melatonin: comparative studies with thiopental and propofol. *Br J Anaesth* 2002; **4:** 504–507.