


Effect of Circadian Rhythm and Sleep Quality on Post-operative Pain in Patients with Spinal Anesthesia

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ABSTRACT

Objective: In our study, we aimed to investigate the effects of circadian rhythm and sleep quality on post-operative pain in patients who will undergo minor pelvic surgery under spinal anesthesia.

Methods: The prospective study includes 60 patients, aged 18–65, American Society of Anesthesiologists (ASA) I-III, whose operation was planned by general surgery and urology by applying spinal anesthesia, and divided into two groups, 30 in the morning and 30 in the afternoon, according to the time of surgery. Sleep quality with preoperative Pittsburgh Sleep Quality Index (PUKI), demographic data, preoperative and peroperative heart rate, systolic, diastolic blood pressure, peripheral oxygen saturation values, post-operative 0th, 6th, 12th, 24th h Visual Analog Scale (VAS) scores, the total amount of analgesic used in the first 24 h postoperatively, and time to first and second analgesic needs were recorded.

Results: It was determined that 24 (40%) of the patients had good sleep quality according to PUKI. When the patients were grouped as those who had surgery in the morning and afternoon, no significant difference was found between the groups in terms of age, gender, ASA, and sleep quality. When the correlation between PUKI scores and VAS scores was examined, no correlation was observed. In the morning group, VAS0 ($p=0.005$), VAS6 ($p<0.001$), and VAS24 ($p=0.04$) values were lower, post-operative analgesic requirement was less, and the time to first and second analgesic requirement was longer. It was found that there was no significant difference in terms of quality.

Conclusion: As a result, it was concluded that if the anesthetic agents we use are applied at selected times, the treatments can be more effective, the drugs can be arranged according to the application hours to optimize the effectiveness of the agents and perhaps reduce their toxic effects, and that more comprehensive studies, especially including night studies, should be done.

INTRODUCTION

Surgeries that cause both physical and psychological stress can have different effects on patients after the operation. The pain we observed after surgery is one of the most important of these effects, and since it affects the duration of discharge, post-operative morbidity, and quality of life, it is necessary to minimize it and prevent it if possible. The severity of pain becomes closely related to the individual's own characteristics when the stimulus is standardized. At the same time, the response to harmful stimuli is not constant throughout the entire 24-h period.

There are many rhythms that affect the characteristics of

the person in our daily life, the most important one is the circadian rhythm, which is defined as the biological clock of the organism, and expresses the psychological and behavioral cycle of living things that lasts approximately 24 h.^[1] The sleep-wake cycle is also the most fundamental and decisive circadian rhythm.^[2] The circadian rhythm plays an important role in taking the drugs at the right time. The correct intake of drugs through the circadian rhythm is important to ensure minimum toxicity and their maximum effectiveness.

The effect of circadian rhythm on the pharmacodynamics and pharmacokinetics of drugs is still not fully known. For anesthetics, especially local anesthetics and new analgesic

agents, information about circadian rhythms remains fragmentary.

Mammalian cells have a molecular clock that controls the timing of many biochemical reactions, including the cellular response to environmental stimuli. The circadian clock is the most important of the rhythms that affect our daily lives and has approximately 24 h and plays a role in the regulation of almost all hormones.^[3] Existing data show that signs and symptoms are not the same over time, and often have cyclical changes, but they also report temporal changes in the effects of many drugs including anesthetics in animals and humans.^[4] However, in our literature review, although studies showing the effectiveness of circadian rhythm on general anesthetics are common, there are limited studies showing its effectiveness in regional anesthesia.

Therefore, in this study, two different times in patients who underwent spinal anesthesia; the effects and side effects of circadian rhythm and sleep on post-operative pain were investigated by comparing morning and afternoon. In our study, we aimed to reveal the period in which patients who underwent surgery experienced more pain according to the circadian rhythm would help us in terms of predictability and preventability.

MATERIALS AND METHODS

Subjects

A prospective, single-center, observational clinical study was conducted between February 15, 2021, and April 30, 2021, Hospital of University and carried out on 60 patients who will undergo elective surgery under spinal anesthesia. Written informed consent was obtained from the patients after all explanations.

Ethical Approval

All procedures performed in the studies involving human participants were in accordance with the ethical standards of the institutional and with the 1964 Helsinki Declaration and its later amendments and comparable ethical standards. The study was approved by Hospital Ethics Committee approval (Decision no:2020/514/181/14, Date: July 08, 2020).

Participants

Our study included 60 patients, 30 men and 30 women, in the 18–75 age group, who were scheduled for elective surgery, in the American Society of Anesthesiologists (ASA) I-III, without neuropsychiatric disease, who underwent urological, pelvic, inguinal, and perineal general surgery lasting longer than 30 min with spinal anesthesia. Exclusion criteria were patients who have had any anesthetic except spinal anesthesia, inadequate post-operative analgesia follow-up records, other than ASA I-III, and operation end time after 12:00 and 16:00.

Groups

Patients who were admitted to the surgery were randomly

divided into 2 groups according to the time of the operation, 30 (15 females and 15 males) of the patients in the morning (08.00–12.00) and 30 (15 females and 15 males) of the patients in the afternoon (12.00–16.00).

Baseline Assessment

The sleep quality of all patients included in the study was evaluated with the Pittsburgh Sleep Quality Index (PSQI) (scale with questions what time do you usually go to bed, time taken to fall asleep, what time do you wake up in the morning, the average sleep time at night, your sleep quality in the last month, did you use medication to help you sleep last month, did you fall asleep during your social activity last month, how much trouble did this cause in your functioning last month?) considering the last month before surgery.

Procedure

When the patients were taken to the operating room, midazolam (0.03 mg/kg) was administered intravenously for premedication. After standard monitoring (Electrocardiogram, non-invasive arterial pressure, peripheral oxygen saturation [SpO₂]), demographic data (age, gender), systolic and diastolic blood pressures (SBP, DBP), and heart rate (HR) were measured and recorded. With a 25G spinal needle, 2.5 mL (12.5 mg) hyperbaric 0.5% bupivacaine (Marcaine 20 mg/4 mL, Sanofi, Türkiye) was administered by entering the subarachnoid space from the L3-L4 spinal space. The sensory block was checked every 30 s until reaching the T10 level. After the target anesthesia was achieved, the operation was started. Paracetamol 1000 mg (Parol 1000 mg/100 mL, Atabay, Türkiye) was administered as the first analgesic to patients with post-operative VAS>4, and dexametoprolfen 50 mg (Arveles 50 mg/2 mL, UFSA, Türkiye) was administered intravenously when the second analgesic was required. It was deemed appropriate to administer paracetamol to those who needed a third analgesic.

Measurements

HR, SBP, DBP, and SpO₂ values were recorded at 0, 5, 15, 25 min and every 15 min thereafter. The end of drug administration for spinal anesthesia was accepted as 0 min.

Patients who were grouped as patients who were operated in the morning and afternoon had post-operative Visual Analog Scale (VAS) values at 0, 6, 12, and 24 h, total analgesic amounts, time to first and second analgesic requirement, sleep quality (subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbance, use of sleeping pills, and daytime dysfunction) according to PSQI scoring, and side effects (headache, nausea-vomiting, hypotension, bradycardia, back pain, and urinary retention) were recorded.

The primary aim of this study is to investigate the effects of circadian rhythm and sleep quality on post-operative pain in patients undergoing minor pelvic surgery under spinal anesthesia. The secondary purpose is; is the comparison of hemodynamic response and side effects during

the operation.

Statistical Analysis

Data were entered into the Statistical Package for the Social Sciences (IBM®SPSS Statistics for Windows, Version 23.0, Armonk, NY, USA) software package. Quantitative variables were presented as mean, maximum (max) and minimum (min) values, and qualitative variables as percentage values. Normal distributions were reported as mean values. Student's t-test was used for comparisons between groups. Pearson's Chi-square test was used for the analysis of qualitative variables; however, Fisher's exact test was used if the sample size was small (≤ 5). Non-parametric continuous variables presented as median values were compared using the Mann-Whitney U test. The Kruskal-Wallis test was used to compare non-normal quantitative variables if there were more than two groups. A two-way ANOVA test was performed to examine the effect of two different categorical independent variables (those who had surgery in the morning and those who were operated in the afternoon in this study) on one continuous dependent variable (VAS in this study). In addition, to examine whether there is a correlation between subjective sleep, latency, sleep duration, sleep efficiency, sleep disturbance, sleep medication, dysfunction, and PUKI scores and VAS scores in all patients, regardless of morning-afternoon groups, it was assumed that the variables did not have a normal distribution and Spearman Rank correlation coefficient (ρ) was calculated. Thus, the relationship between sleep disorders and analgesia was investigated. A $p < 0.05$ was considered statistically significant. If the p value was between 0.05 and 0.099, this value was considered to be close to

statistical significance.

RESULTS

Of 60 patients with a mean age of 51.7 ± 14.5 (min=20, max=75) years, 30 (50%) were female and 30 (50%) were male. The majority of the patients were found to be ASA I ($n=49$, 81.7%). While sleep quality was good in 24 (40%) patients according to PSQI, it was determined that sleep quality was impaired in 36 (60.0%) patients.

When the patients were grouped as morning surgery ($n=30$) and afternoon surgery ($n=30$), it was found that there was no statistically significant difference between the groups in terms of age, gender, ASA, subjective sleep, sleep latency, sleep duration, sleep efficiency, sleep disorder, use of sleeping pills, sleep function disorder, PSQI score, and sleep quality according to PSQI (Table 1).

While preoperative and post-operative systolic and DBP values and peroperative DBP values did not differ statistically between the groups, it was observed that the SBP at 15th min was statistically lower in those who were operated in the afternoon than in those who were operated on in the morning (mean 125.1 mmHg vs. mean 117.0 mmHg, $p=0.04$). No difference was observed between the groups in terms of other hemodynamic parameters.

The comparison between the groups in terms of post-operative VAS results, post-operative analgesic requirements, and time required for analgesics according to the period of surgery are given in Table 2.

When the effect of the operated period (morning-after-

Table 1. Comparison of patients in terms of demographic and sleep status according to the time period of surgery

Variables	Morning (n=30)	Afternoon (n=30)	p-value
Age (year), mean \pm SD	53.7 \pm 14.8	49.8 \pm 14.2	0.344
Gender, n (%)			
Male	15 (50%)	15 (50%)	1.000
Female	15 (50%)	15 (50%)	
ASA n (%)			
I	2 (6.7%)	3 (10.0%)	
II	23 (76.7%)	26 (86.7%)	0.135
III	5 (16.7%)	1 (3.3%)	
Subjective sleep, mean \pm SD	1.1 \pm 0.7	1.1 \pm 0.9	0.807
Sleep latency, mean \pm SD	1.1 \pm 0.9	1.2 \pm 0.8	0.463
Sleep duration, mean \pm SD	1.0 \pm 0.9	1.1 \pm 1.0	0.889
Sleep efficiency, mean \pm SD	1.0 \pm 1.2	0.8 \pm 1.1	0.549
Sleep disorder, mean \pm SD	1.1 \pm 0.5	1.1 \pm 0.6	0.956
Sleeping pill, mean \pm SD	0.4 \pm 1.0	0.1 \pm 0.6	0.222
Sleep function disorder, mean \pm SD	0.2 \pm 0.5	0.3 \pm 0.7	0.826
PSQI score, mean \pm SD	6.0 \pm 3.7	6.1 \pm 4.1	0.894
Sleep quality according to PSQI, n (%)			
Good (<5)	10 (33.3%)	14 (46.7%)	0.292
Impaired (≥ 5)	20 (66.7%)	16 (53.3%)	

SD: Standard deviation; n: Number; PSQI: Pittsburgh sleep quality index; ASA: American society of anesthesiologists.

Table 2. Comparison between the groups in terms of postoperative Visual Analog Scale results, postoperative analgesic requirements and time required for analgesics according to the time period of surgery

	Morning (n=30)	Afternoon (n=30)	p-value
Postoperative VAS scores			
VAS 0	0.0±0.0	0.5±0.9	0.005
VAS 6	2.9±0.9	4.2±1.7	<0.001
VAS 12	2.9±1.0	3.0±1.2	0.963
VAS 24	1.6±0.9	2.0±0.7	0.048
Postoperative analgesic requirements			
No need for postoperative analgesics, n (%)	16 (53.3%)	9 (30.0%)	0.067
Those who need analgesics at least twice postoperatively, n (%)	7 (23.3%)	15 (50.0%)	0.032
Time required for analgesics			
Time for first analgesic * (min), mean±SD	279.2±101.8	146.4±104.6	<0.001
Time for second analgesic # (min), mean±SD	545.7±108.6	445.3±150.8	0.021

*Comparison was made over a total of 35 patients (14 in the morning group and 21 in the afternoon group). # Comparison was made over a total of 22 patients (7 in the morning group and 15 in the afternoon group). VAS: Visual analog scale; Min: Minute.

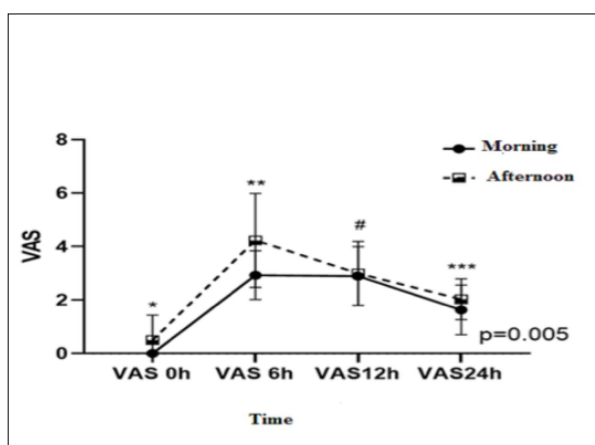


Figure 1. Evaluation of the effect of the operated time period (morning-afternoon) on the Visual Analog Scale variable with two-way ANOVA. * $p < 0.01$, ** $p < 0.001$, *** $p < 0.05$, # $p > 0.05$. VAS: Visual Analog Scale (cm); H: Hours.

noon) on the VAS variable was analyzed with two-way ANOVA, a statistically significant difference was found between the two groups ($p = 0.005$) (Figure 1).

When the correlation between subjective sleep, sleep latency, sleep duration, sleep efficiency, sleep disorder, sleeping pill, sleep function disorder, PSQI scores in patients, and VAS scores in time periods was examined, no significant correlation was found between any parameter and VAS values (Table 3).

When the patients who needed analgesics at least once postoperatively ($n = 35$) and those who did not need any analgesics ($n = 25$) were compared, no statistically significant difference was found between the groups in terms of age, gender, ASA, sleep latency, sleep duration, sleep efficiency, sleep disorder, sleeping pill, sleep function disorder, PSQI scores, and sleep quality according to PSQI (Table 4). However, there was a statistically significant difference be-

Table 3. Evaluation of the correlation between subjective sleep, sleep latency, sleep duration, sleep efficiency, sleep disorder, sleeping pill, sleep function disorder, Pittsburgh Sleep Quality Index scores and Visual Analog Scale in patients

	VAS 0		VAS 6		VAS 12		VAS 24	
	Rho	p-value	Rho	p-value	Rho	p-value	Rho	p-value
Subjective sleep	0.096	0.464	-0.120	0.363	-0.077	0.558	0.073	0.578
Sleep latency	0.149	0.257	-0.062	0.636	-0.075	0.568	-0.075	0.569
Sleep duration	0.047	0.722	-0.138	0.294	0.002	0.987	0.138	0.291
Sleep efficiency	0.054	0.683	-0.071	0.592	0.106	0.422	0.149	0.256
Sleep disorder	0.136	0.299	-0.166	0.205	-0.150	0.154	-0.021	0.873
Sleeping pill	0.034	0.797	-0.053	0.686	0.001	0.997	0.064	0.626
Sleep function disorder	0.141	0.283	-0.019	0.887	0.050	0.706	0.054	0.681
PSQI scores	0.082	0.532	-0.123	0.350	-0.005	0.970	0.141	0.282

Rho: Spearman correlation coefficient; PSQI: Pittsburgh sleep quality index; VAS: Visual analog scale.

Table 4. Comparison of patients who need analgesics at least once postoperatively and patients who do not need analgesics at all

Variables	No need for analgesics (n=25)	Needing analgesics (n=35)	p-value
Age (years), mean±SD	51.6±14.3	51.8±14.9	0.952
Gender, n (%)			
Male	14 (56.0%)	16 (45.7%)	0.432
Female	11 (44.0%)	19 (54.3%)	
ASA n (%)			0.723
I	2 (8.0%)	3 (8.6%)	
II	20 (80.0%)	29 (82.9%)	
III	3 (12.0%)	3 (8.6%)	
Subjective sleep, mean±SD	0.8±0.7	1.2±0.8	0.045
Sleep latency, mean±SD	1.1±0.9	1.2±0.8	0.871
Sleep duration, mean±SD	1.0±0.8	1.0±1.0	0.975
Sleep efficiency, mean±SD	0.6±1.1	1.1±1.2	0.177
Sleep disorder, mean±SD	1.1±0.4	1.0±0.6	0.533
Sleeping pill, mean±SD	0.2±0.8	0.3±0.9	0.968
Sleep function disorder, mean±SD	0.2±0.6	0.2±0.7	0.824
PSQI scores, mean±SD	5.4±3.3	6.5±4.2	0.292
Sleep quality according to PSQI, n (%)			
Good (<5)	11 (44.0%)	13 (37.1%)	0.593
Impaired (≥5)	14 (56.0%)	22 (62.9%)	

SD: Standard deviation; n: number; PSQI: Pittsburgh sleep quality index; ASA: American society of anesthesiologists.

tween these two groups in terms of subjective sleep quality. It was observed that the mean subjective sleep quality score was statistically lower in patients who did not need analgesics at all than in patients who needed analgesics at least once (mean 0.8 vs. 1.2, $p=0.04$).

When the patients were grouped as those with a PSQI score of <5 ($n=24$) and those with a PSQI of ≥5 ($n=36$), no statistically significant difference was found between the groups in terms of post-operative VAS results at all times, post-operative analgesic requirement and time required

for analgesic requirement (Table 5).

Postoperatively, at least one side effect was seen in 27 (45.0%) patients. The most common side effect was headache ($n=20$, 33.3%). Nausea was observed in 14 (23.3%) of the patients while vomiting developed in 8 (13.3%) patients.

No statistically significant correlation was observed between the development of side effects and the time of surgery (morning/afternoon), gender, and sleep quality according to PSQI. There was no significant difference be-

Table 5. Comparison of those with Pittsburgh Sleep Quality Index score <5 and ≥5 in terms of postoperative Visual Analog Scale results, postoperative analgesic requirement and time required for analgesic requirement

	PSQI<5 (n=24)	PSQI≥5 (n=36)	p-value
Postoperative VAS scores			
VAS 0	0.3±0.7	0.1±0.6	0.357
VAS 6	4.0±1.9	3.3±1.1	0.240
VAS 12	2.8±1.0	3.0±1.2	0.856
VAS 24	1.7±0.8	1.9±0.8	0.512
Postoperative analgesic requirement			
No need for postoperative analgesics, n (%)	11 (45.8%)	14 (38.9%)	0.593
Needing analgesics at least twice postoperatively, n (%)	9 (37.5%)	13 (36.1%)	0.913
Time required for analgesic requirement			
Time for first analgesic * (min), mean±SD	218.0±141.1	188.6±110.4	0.775
Time for second analgesic # (min), mean±SD	453.8±111.9	493.4±165.5	0.471

*Comparisons were made on a total of 35 patients. # Comparison was made over a total of 22 patients. PSQI: Pittsburgh sleep quality index; VAS: Visual analog scale; Min: Minute.

tween the side effects and the patients who needed and did not need analgesics.

DISCUSSION

In the study where we investigated the effects of circadian rhythm and sleep quality on post-operative pain in patients who were operated under spinal anesthesia, it was observed that pain scores in the first 24 h, analgesic needs were lower, and first analgesic requirements were later in patients who underwent morning surgery. When the effect of sleep quality is evaluated according to PSQI; it was determined that there was no significant difference in terms of VAS scores and analgesic needs between patients with good and impaired sleep quality in patients who had undergone surgery, but the “subjective sleep” score, one of the PSQI components, was found to be lower in those who did not receive any analgesics. When compared in terms of hemodynamic parameters, peroperative SBP was found to be significantly lower in patients who were operated only in the afternoon, compared to those who underwent surgery in the morning.

Existing data show that signs and symptoms are not the same over time, and often have cyclical changes, but they also report temporal changes in the effects of many drugs, including anesthetics, in animals and humans.^[4] However, in our literature review, although studies showing the effectiveness of circadian rhythm on general anesthetics are common, there are limited studies showing its effectiveness in regional anesthesia.

In the study of Anastasopoulou-Sampani et al. in which they investigated the total amount of fentanyl used in the intra-operative period in cases undergoing elective cholecystectomy operation under general anesthesia, they reported that less fentanyl was used in the group that was taken after 08:00 and finished before 10:30 Am compared to the group that underwent surgery between 11:00 and 15:00.^[5]

In the study conducted by Desai et al. in 1657 pregnant patients who underwent labor with combined spinal epidural anesthesia, they reported that analgesia requirements and pain scores were lower in the morning and afternoon group than in the evening and night groups, and there was no difference in terms of side effects.^[6]

In the study of Kılıçarslan et al., in which they divided the patients who will undergo inguinal hernia and anorectal surgery under spinal anesthesia as 06.00–12.00 (Group 1) and 12.00–18.00 (Group 2), according to the operation time, consistent with the results of our study, they determined that the post-operative first analgesic requirement time was longer in the morning group. They also found that there was no difference between the groups in terms of side effects, and the most common side effect was nausea and vomiting.^[7] We think that the hormone melatonin, which is thought to have a very good anesthetic effect with its anxiolytic, hypnotic, analgesic, sedative, and anticonvulsant effects, and showing a circadian release pat-

tern, may be effective in our results.^[8] Melatonin, which is synthesized in the pineal gland, is secreted during the night and its level reaches the highest point between 02.00 and 04.00 at night, decreases around 09.00 in the morning, and reaches its lowest level in the afternoon.^[9] Since the circadian rhythm of melatonin is genetically determined, its release is constant in each individual. However, its production decreases with age. In addition, although its oscillation does not change in individuals, there are great differences in the amplitude of rhythm among individuals.^[10]

Bruguerolle and Isnardon, on the other hand, reported that the highest lidocaine concentration was reached when it was applied at 15.30 in their study in which they applied a single dose of lidocaine infiltration at 09:30, 12:30, 15:30, and 18:30 h to four groups of men during dental surgery.^[11]

In the study of Bruguerolle et al. in which they evaluated pain scores by applying lidocaine cutaneously before venous cannulation, they found the plasma lidocaine concentration to be higher in the evening in children and the morning in mice.^[12]

Studies have shown that there are clearly contradictory or different results between the periods when pain is heard most, and that the most pain may occur in the morning and/or evening. We think that this may be due to the influence of many internal and external factors on the circadian rhythm. We think that the places where painful stimuli are applied in the body, the intensity of painful stimuli cannot be standardized and the pain threshold is different in all tissues are some of these factors and may cause differences in the results of the study. In addition, we believe that circadian changes in membrane permeability and access to channels may also cause changes in the efficacy of local anesthetics.

Morphine consumption is highest at 09:00 after abdominal surgery, at least at 15:00,^[13] lowest at night in gynecological patients,^[14] and highest at 08:00–12 o'clock in patients undergoing laparotomy for gynecological malignancies.^[15] Similarly, it was reported that morphine consumption was the highest in the morning hours in patients undergoing thoracic surgery, but a second peak of morphine consumption was observed between 16:00 and 20:00 h.^[16]

As a result of studies similar to all these studies, chronotherapy, which takes into account circadian rhythms by choosing the time of day for drug treatment, has gained importance in recent years. In this way, rug administration can be based on the circadian patterns of a disease or operation, optimizing drug effects and reducing side effects.

In terms of hemodynamic parameters, it was observed that peroperative SBP values were significantly lower in patients who were operated only in the afternoon, compared to those who underwent surgery in the morning. We attributed the development of perioperative hypotension in patients who underwent surgery in the afternoon to the fact that the preoperative fasting period of the patients was longer than those who underwent surgery in the morning, and therefore, the intravascular volumes

decreased further in the period until the beginning of the surgery.

One of the factors affecting the circadian rhythm is; is the sleep-activity cycle. Wright et al. reported a correlation between sleep disruption (low sleep efficiency) the night before surgery and pain in the first 7 days postoperatively in their study of 24 patients who would undergo elective breast-conserving surgery under sedation.^[17]

Kundermann et al., in their study investigating the effects of sleep deprivation on thermal pain thresholds in 20 healthy volunteers, found that there was a decrease in both hot and cold pain thresholds in the group who was deprived of sleep for two nights, and sleep deprivation caused hyperalgesic changes in somatosensory functions.^[18]

In the study of Zor in which they collected sleep-related data of 30 female patients who will undergo breast surgery for 12 days with actigraphy, they also evaluated PSQI in line with our study and stated that there was no correlation between post-operative pain and PSQI.^[19] In their study, unlike us, they compared the “reduced sleep efficiency,” one of the components of PSQI, by asking only the total time spent in bed, the time of going to bed, and getting up. In our study, no relationship was found between this component and post-operative pain, but a relationship was observed between post-operative pain and “subjective sleep quality,” one of the components of PSQI. We think that the reason why the need for analgesics is less in patients with low “subjective sleep quality” in our study may be due to the objective response of other sleep quality assessment components and the fact that the “subjective sleep quality” component is mostly based on the subjective response of the patient. Thus, we can conclude that the mechanisms of pain formation are closely related to the patient’s mood, apart from some physiological and pharmacological pathways.

Although different results were observed on this subject in our literature review, no difference was found in terms of side effects in the morning and afternoon groups in our study, and we determined that gender was not effective in post-operative pain.

Limitations

Since our study was performed on elective surgeries and only elective cases were taken during the daytime in our hospital, morning and afternoon groups were compared. However, we think that the comparison of the evening and/or night groups will add more meaning to the results of our study and there is a need for studies in this direction. In addition, melatonin levels of the patients could not be determined, since melatonin levels could not be measured in the laboratories of our hospital. We think that these are the limitations of our study.

Conclusion

In this study, which was conducted to investigate the level of post-operative pain according to circadian rhythm and sleep quality in patients with spinal anesthesia, patients

who underwent surgery in the morning had lower post-operative pain levels, less post-operative analgesic needs, and later than those who underwent surgery in the afternoon, but there was no significant relationship between PSQI and VAS scores. It was observed that only the “subjective sleep quality” score of the PSQI components was lower in those who did not need post-operative painkillers.

Since the severity of post-operative pain varies between individuals, there is a need to investigate the effects of modifiable risk factors in analgesic requirements and circadian rhythms on clinical anesthesia. It was concluded that administration of general and regional anesthetic agents in our practice according to the application hours with chronotherapy may be beneficial to increase drug efficacy and reduce toxic effects, however, more comprehensive new studies including day and night comparisons are needed.

Ethics Committee Approval

This study approved by the Kartal Dr Lütfi Kırdar City Hospital Clinical Research Ethics Committee (Date: 08.07.2020, Decision No: 2020/514/181/14).

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: D.Ç.; Design: D.Ç., G.A., B.Ç.; Supervision: D.Ç., G.A., K.T.S.; Materials: D.Ç., G.A.; Data: D.Ç., G.A.; Analysis: D.Ç., G.A., B.Ç., K.T.S.; Literature search: D.Ç., G.A., B.Ç., K.T.S.; Writing: D.Ç., G.A., B.Ç., K.T.S.; Critical revision: G.A., B.Ç., K.T.S.

Conflict of Interest

None declared.

REFERENCES

1. Memiş Ö, Ekren N. Human centric lighting. *Int Per of Recent Tech in App Eng* 2019;1:30–5. [\[CrossRef\]](#)
2. Zee PC, Manthena P. The brain’s master circadian clock: Implications and opportunities for therapy of sleep disorders. *Sleep Med Rev* 2007;11:59–70. [\[CrossRef\]](#)
3. Meléndez-Fernández OH, Liu JA, Nelson RJ. Circadian Rhythms Disrupted by Light at Night and Mistimed Food Intake Alter Hormonal Rhythms and Metabolism. *Int J Mol Sci* 2023;24:3392.
4. Belanger PM, Bruguerolle B, Labrecque G. Rhythms in pharmacokinetics: absorption, distribution, metabolism, and excretion. In: Redfern PH, Lemmer B, editors. *Physiology and pharmacology of biological rhythms*. Heidelberg: Springer-Verlag; 1997. p. 177–204.
5. Anastasopoulou-Sampani D, Sampanis E, Karagiris G. The need for analgesia in elective cholecystectomies influenced by the time of day the operation is performed. *Acta Anaesthesiol Scand* 1996;40:955.
6. Desai S, Leong SB, Yvonne L, Sia A. Chronobiology of parturients receiving neuraxial labour analgesia with ropivacaine and fentanyl: a prospective cohort study. *Int J Obstet Anesth* 2009;18:43–7.
7. Kiliçarslan G, Alkan M, Kurtipek Ö, Unal Y, Şivgin V, Dikmen K, et al. The effect of circadian rhythm in patients undergoing spinal anesthesia. *Agri* 2021;33:168–75.

8. Marseglia L, D'Angelo G, Mantri S, Aversa S, Arrigo T, Reiter RJ, et al. Analgesic, anxiolytic and anaesthetic effects of melatonin: new potential uses in pediatrics. *Int J Mol Sci* 2015;16:1209–20. [CrossRef]
9. Yağar S, Çavuş MA, Dönmez A, Karadeniz Ü, Açık G, Saydam GS, et al. Does the time of anesthesia effect serum cortisol and melatonin levels and outcome in cardiac surgery? *JCV* 2015;21:77–81.
10. Arendt J. Melatonin. *Clin Endocrinol* 1988;29:205–29. [CrossRef]
11. Bruguerolle B, Isnardon R. Daily variations in plasma levels of lidocaine during local anaesthesia in dental practice. *Ther Drug Monit* 1985;7:369–70. [CrossRef]
12. Bruguerolle B, Giaufre E, Prat M: Temporal variations in transcutaneous passage of drugs: The example of lidocaine in children and in rats. *Chronobiol Int* 1991;8:277–82. [CrossRef]
13. Graves DA, Batenhorst RL, Bennett RL, Wettstein JG, Griffen WO, Wright BD, et al. Morphine requirements using patient-controlled analgesia: influence of diurnal variation and morbid obesity. *Clin Pharm* 1983;2:49–53.
14. Auvil-Novak SE, Novak RD, Smolensky MH, Kavanagh JJ. Twenty-four hour variation in self-administration of morphine sulfate (MS) and hydromorphone (H) by post-surgical gynecologic cancer patients. *Ann Rev Chronopharmacol* 1988;5:343–6.
15. Auvil-Novak SE, Novak R, Smolensky MH, Morris MM, Kwan JV. Temporal variation in the self-administration of morphine sulfate via patient-controlled analgesia in postoperative gynecologic cancer patient. *Annu Rev Chronopharmacol* 1990;7:253–6.
16. Labrecque G, Lepage-Savary D, Poulin E. Time-dependent variation in morphine-induced analgesia. *Annu Rev Chronopharmacol* 1988;5:135–8.
17. Wright CE, Bovbjerg DH, Montgomery GH, Weltz C, Goldfarb A, Pace B, et al. Disrupted sleep the night before breast surgery is associated with increased postoperative pain. *J Pain Symptom Manage* 2009;37:352–62. [CrossRef]
18. Kundermann B, Sernal J, Huber MT, Krieg JC, Lautenbacher S. Sleep deprivation affects thermal pain thresholds but not somatosensory thresholds in healthy volunteers. *Psychosom Med* 2004;66:932–7. [CrossRef]
19. Zor S. Evaluation of sleep characteristics of patients in the first 24 hours after breast surgery by actigraphy method. Master's thesis, Bülent Ecevit University, Institute of Health Sciences, Department of Nursing, Surgical Diseases Nursing Program; 2017.

Spinal Anestezi Uygulanan Hastalarda Sirkadiyen Ritim ve Uyku Kalitesinin Postoperatif Ağrı Üzerine Etkisi

Amaç: Çalışmamızda spinal anestezi altında minör pelvik cerrahi geçirecek hastalarda sirkadiyen ritim ve uyku kalitesinin postoperatif ağrı üzerine etkisini araştırmayı amaçladık.

Gereç ve Yöntem: Prospektif çalışmaya genel cerrahi ve üroloji tarafından spinal anestezi uygulanarak operasyonu planlanan 18-65 yaş arası ASA I-III 60 hasta dahil edildi ve cerrahi zamanına göre sabah 30, öğleden sonra 30 hasta olmak üzere iki gruba ayrıldı. Preoperatif Pittsburgh Uyku Kalitesi İndeksi (PUKİ) ile uyku kalitesi, demografik veriler, ameliyat öncesi ve ameliyat sırasında kalp hızı, sistolik, diyastolik kan basıncı, periferik oksijen saturasyon değerleri, ameliyat sonrası 0., 6., 12., 24. saat Vizüel Analog Skala (VAS), postoperatif ilk 24 saatte kullanılan toplam analjezik miktarı, birinci ve ikinci analjezik ihtiyacına kadar geçen süre kaydedildi.

Bulgular: Hastaların 24'ünün (%40) PUKİ'ye göre uyku kalitesinin iyi olduğu belirlendi. Hastalar sabah ve öğleden sonra ameliyat olanlar olarak gruplandırıldığında gruplar arasında yaş, cinsiyet, ASA ve uyku kalitesi açısından anlamlı fark bulunmadı. PUKİ skorları ile VAS skorları arasındaki korelasyon incelendiğinde herhangi bir korelasyon gözlenmedi. Sabah grubunda VAS0 (p=0.005), VAS6 (p<0.001) ve VAS24 (p=0.04) değerleri daha düşük, postoperatif analjezik ihtiyacı daha az, birinci ve ikinci analjezik ihtiyacına kadar geçen süre daha uzun bulundu. Kalite açısından anlamlı bir fark olmadığı belirlendi.

Sonuç: Sonuç olarak, kullandığımız anestezi ajanlarının seçilen zamanlarda uygulanması durumunda tedavilerin daha etkili olabileceği, ajanların etkinliğini optimize etmek ve belki de etkilerini toksik etkilerini azaltmak için ilaçların uygulama saatlerine göre düzenlenebileceği ve özellikle gece çalışmalarını içeren daha kapsamlı çalışmaların yapılması gerektiği kanısına varıldı.

Anahtar Sözcükler: Görsel analog skala; Pittsburgh uyku kalitesi indeksi; postoperatif ağrı; sirkadiyen ritim; uyku kalitesi; spinal anestezi.