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ORIGINAL ARTICLE

The effect of pre-operative sleep quality on post-operative pain and emergence agitation: prospective and cohort study

El efecto de la calidad del sueño preoperatorio sobre el dolor posoperatorio y la agitación de emergencia: estudio de cohorte prospectivo

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Abstract

Objective: *Our study aimed to investigate the effect of pre-operative sleep quality on post-operative pain and emergence agitation.* **Materials and methods:** *Our study was performed 80 patients with American Society of Anesthesiologists I-II and 18-65 years of age. The patients were divided into poor (Group A, n = 40) and good sleep quality (Group B, n = 40). All patients were operated on under standard general anesthesia. The emergence agitation and pain status of all groups were evaluated in the recovery room and post-operative period. Results: There was no significant difference between the groups regarding demographic data. Post-operative numeric rating scale scores and analgesic consumption were significantly higher in Group A than in Group B (p < 0.05). There was no significant difference between the groups regarding post-operative emergence agitation and extubation quality (p > 0.05).* **Conclusion:** *In our study, poor pre-operative sleep quality increases post-operative pain and analgesic consumption; however, emergence agitation is not associated with sleep quality in the pre-operative period.*

Keywords: *Emergence agitation. Post-operative pain. Sleep quality.*

Resumen

Objetivo: *Nuestro estudio tuvo como objetivo investigar el efecto de la calidad del sueño preoperatorio sobre el dolor posoperatorio y la agitación de emergencia.* **Materiales y métodos:** *Nuestro estudio se realizó en 80 pacientes con ASA I-II y de 18 a 65 años de edad. Los pacientes se dividieron en mala (grupo A, n = 40) y buena calidad del sueño (grupo B, n = 40). Todos los pacientes fueron operados bajo anestesia general estándar. La agitación de emergencia y el estado del dolor de todos los grupos se evaluaron en la sala de recuperación y en el período postoperatorio.* **Resultados:** *No hubo diferencia significativa entre los grupos con respecto a los datos demográficos. Las puntuaciones NRS postoperatorias y el consumo de analgésicos fueron significativamente más altos en el Grupo A que en el Grupo B (p < 0.05). No hubo diferencia significativa entre los grupos con respecto a la agitación de emergencia postoperatoria y la calidad de la extubación (p > 0.05).* **Conclusión:** *En nuestro estudio, la mala calidad del sueño preoperatorio aumenta el dolor posoperatorio y el consumo de analgésicos; sin embargo, la agitación de emergencia no se asocia con la calidad del sueño en el período preoperatorio.*

Palabras clave: *Agitación de emergencia. Dolor postoperatorio. Calidad del sueño.*

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Introduction

Sleep is a temporary period of unconsciousness that can become conscious again with internal and external stimuli[1]. Besides being a basic need, sleep is also an important part of the recovery process in the post-operative period. Sleep quality is a measure of a person's well-being. This concept includes parameters such as sleep duration, sleep time, number of night awakenings, and sleep depth[1]. Sleep quality is affected by various factors such as environmental factors, work, lifestyle, social life, general health, and stress[2].

Impaired sleep quality was found to be associated with a weakened immune system, susceptibility to infection, increased risk of post-operative cardiovascular and cerebrovascular events, and prolonged hospital stay. In addition, it has been shown that poor sleep quality lowers the pain threshold and causes hyperalgesia[3].

Post-operative pain is one of the factors that closely affect the healing process of the patient. Therefore, determining the etiological causes is an important step in pain management. Recent studies have shown that sleep quality is a triggering factor for acute pain and has an important role in exacerbating chronic pain. Therefore, poor sleep quality is a predictor of post-operative pain[4]. Considering all these, it should not be forgotten that poor sleep quality in the pre-operative period is an important risk factor for post-operative sleep disturbance and pain.

Agitation during recovery from general anesthesia is an important recovery problem. There are studies investigating the relationship between pre-operative sleep disorder and post-operative pain[4-6]. However, studies investigating the relationship between pre-operative sleep disturbance and post-operative emergence agitation have not been found. For this reason, we determined our hypothesis in this study: sleep quality in the pre-operative period may reduce post-operative pain and emergence agitation.

Materials and methods

Our study was planned as a prospective clinical study between January 2021 and September 2021 after the approval of the local ethics committee (Karadeniz Technical University Faculty of Medicine Ethics Committee, 2020/376).

A total of 96 patients were scheduled to undergo elective open cholecystectomy and thyroidectomy in the general surgery operating room of our hospital. Sixteen patients were excluded from this study since 10 patients were American Society of Anesthesiologists (ASA) III, four patients were > 65 years old, and two patients had serious systemic illnesses. The study was carried out on 80 patients with ASA risk classification I, II, and 18-65 years of age, whose written and verbal consents were obtained, who were scheduled for open cholecystectomy and thyroidectomy in the general surgery operating room of our hospital.

Patients with a body mass index (BMI) of more than 30 kg/m^2, who have obstructive sleep apnea syndrome, who use induction agent(s), drugs related to opioid allergy, psychiatric disorder, chronic pain, and chronic sleep disorder, who have an active infection, who need follow-up in the post-operative intensive care unit, who were uncooperative, and were unable to compare physical and verbal performance were excluded from the study. During the examination performed in the pre-operative anesthesia outpatient clinic 1 day before the operation, patients who met the appropriate criteria were informed about the study, and their written and verbal informed consent was obtained.

The pre-operative sleep quality of the patients to be included in the study was evaluated with the Pittsburgh Sleep Quality Index (PSQI). Patients with a PSQI score above 5 were classified as poor sleep quality (Group A, n = 40), and patients with a PSQI score below 5 were classified as good sleep quality (Group B, n = 40). A consort flow diagram of the study is shown in figure 1. Pre-operative PSQI and age, gender, weight, BMI, and ASA risk scores of all patients were recorded.

State-Trait Anxiety Inventory (STAI) was used to evaluate the pre-operative anxiety levels of all patients. STAI-I and II are two different forms consisting of 20 questions, STAI-I indicates situational anxiety level, and STAI-II indicates trait anxiety level. Scoring varies between 20 and 80. Patients who were informed about STAI were asked to fill in the STAI-I and STAI-II forms. As a result of the STAI I-II evaluation, it was evaluated as 0-19 points as absent, 20-39 points as mild, 40-59 points as moderate, 60-79 points as severe, 80 points, and above as panic (very severe).

In standard anesthesia monitoring of patients taken to the operating room, non-invasive mean arterial pressure (MAP), heart rate (HR), peripheral oxygen saturation (SpO_2), electrocardiograph, end-tidal carbon dioxide ($EtCO_2$), and bispectral index (BIS) (Aspect) Medical Systems, Norwood, MA, USA) were applied.

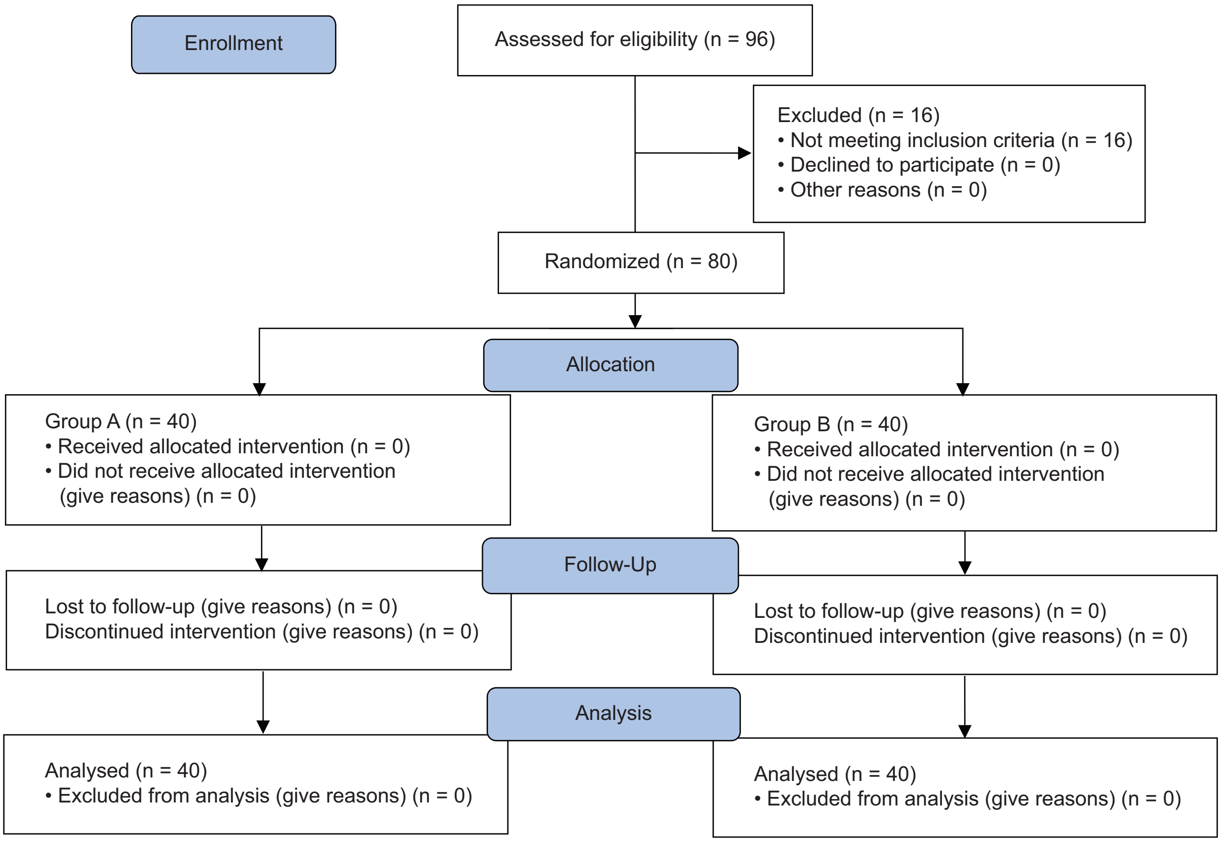

Figure 1. *Consort flow diagram of the study.*

In the induction of anesthesia, intravenous (iv) 1 μg/kg fentanyl, 5-7 mg/kg pentothal, and 0.6 mg/kg rocuronium were administered, and endotracheal intubation was performed after sufficient time for muscle relaxation. Mechanical ventilation was applied with a tidal volume of 6-8 ml/kg, a respiratory frequency of 12/min, and $EtCO_2$ of 32-35 mmHg. Anesthesia was maintained at a BIS of 40-60 with 50% O_2/air, 2% of sevoflurane, and an iv infusion of 0.1 mcg/kg/h remifentanil. Additional doses of rocuronium were administered to the patients when necessary. MAP, HR, SpO_2, and $EtCO_2$ values of all patients were recorded at baseline, intubation, 20-min intervals after intubation, and just before extubation.

At the end of the operation, all patients were extubated after removing oropharyngeal secretions when it was observed that the depth and number of respirations were adequate, the cardiovascular findings were stable, and the BIS value was above 80. The extubation quality levels of the extubated patients were evaluated with the "Extubation Quality Scale" of 5 (1 = no coughing, comfortable breathing, 2 = quite soft, mild coughing (1-2 times), 3 = moderate coughing (3-4 times), 4 = severe coughing, and labored breathing (5-10 times), and 5 = laryngospasm, severe coughing and labored breathing)[7].

Post-operative agitation scoring was done in the recovery room using the Richmond Agitation-Sedation Scale (RASS)[8]. The highest agitation score of the patients in this period was recorded, and it was accepted that emergence agitation developed in patients with a RASS score of ≥ 2. In the first stage, verbal suggestions were made to patients who developed emergence agitation, and iv 10-20 μg dexmedetomidine was administered to those who did not respond. Patients with sufficient muscle strength (ability to raise their head and move their extremities in response to commands) and airway safety were taken from the operating room to the post-anesthesia care unit (PACU). Patients with an Aldrete score ≥ 9 were sent to the service from the PACU.

The pain status of all patients was evaluated with the numeric rating scale (NRS) at the 2nd, 12th, and 24th h postoperatively. Patients with NRS > 3 were administered iv 50 mg dexketoprofen as an additional analgesic. In addition, iv 4 mg ondansetron was administered to

Table 1. Demographic data and clinical characteristic

Parameters	Group A (n = 40)	Group B (n = 40)	p
Age (year)	47.0 ± 11.5	46.4 ± 12.2	0.799*
Weight (kg)	71.1 ± 8.8	73.5 ± 10.4	0.276*
Height (cm)	165.2 ± 7.1	167.0 ± 6.6	0.198†
BMI (kg/m²)	26.2 ± 2.9	25.8 ± 3.0	0.530†
ASA (I/II)	13/27	20/20	0.173‡
Sex (F/M)	32/8	30/10	0.88‡
Operation time (min)	73.5 ± 24.0	70.1 ± 29.5	0.260†
Anesthesia time (min)	85.0 ± 24.8	80.5 ± 28.6	0.336†
STAI-I Scor	43.0 ± 6.5	41.6 ± 5.1	0.461†
STAI-II Scor	47.8 ± 6.6	45.2 ± 7.9	0.053†
Type of surgery			
Thyroidectomy	2	9	0.655‡
Cholecystectomy	8	1	
Length of stay in hospital (day)	2.04 ± 0.82	1.75 ± 0.67	0.121†

*t-test.
†Mann–Whitney U-test.
‡Ki-kare test.
Statistics presented as Mean ± SD or N. Group A: worse sleep quality group, Group B: good sleep quality group. BMI: body mass index; ASA: American Society of Anesthesiologists Classification; STAI I-II: State-Trait Anxiety Inventory.

patients who developed nausea and vomiting. Additional analgesic and antiemetic use were recorded in the service follow-ups in the post-operative 24-h period.

Statistical analysis

IBM SPSS 23.0 statistical package program was used to analyze the data. Descriptive statistics of the evaluation results are given as numbers, percentages for categorical variables, and mean and standard deviation for numerical variables. The conformity of the variables to the normal distribution was examined with the Kolmogorov–Smirnov test. In comparing the mean values of the measurement variables between the groups, the t-test was used when the variable was suitable for normal distribution, and the Mann–Whitney U-test was used when it was not. The Chi-square test was used to compare categorical data. The statistical significance level was accepted as $p < 0.05$.

Within the scope of the study, it was aimed to reach the maximum number that can be reached in the included surgeries and during the data collection period. The power analysis results using the mean and standard deviation values of the groups for sleep quality, which is the study's main hypothesis, showed that while the power was 100% for the NRS 2nd h and 12th h, it was 99.67% for the 24th h. In this context, a total of 80 patients, including 40 with poor and 40 with good sleep quality, were included in the study.

Results

The patients' demographic data, including age, gender, weight, height, BMI, ASA risk scores, operation and anesthesia times, and pre-operative STAI-I and STAI-II scores, are shown in table 1. There was no statistically significant difference between the groups ($p > 0.05$). Intraoperative variables such as MAP, HR, peripheral oxygen pressure, and $EtCO_2$ of the patients are shown in figure 2. There was no statistically significant difference between the groups during the follow-up periods ($p > 0.05$).

NRS changes and analgesic consumption of the patients at the post-operative 2nd, 12th, and 24th h are shown in table 2, and it was found to be statistically significantly higher in Group A compared to Group B in all follow-up periods (respectively, for all NRS; $p < 0.001$, $p = 0.048$).

The extubation quality scores, post-operative agitation scores, and dexmedetomidine consumption of the patients are shown in table 3, and there was no statistically significant difference between the groups ($p > 0.05$).

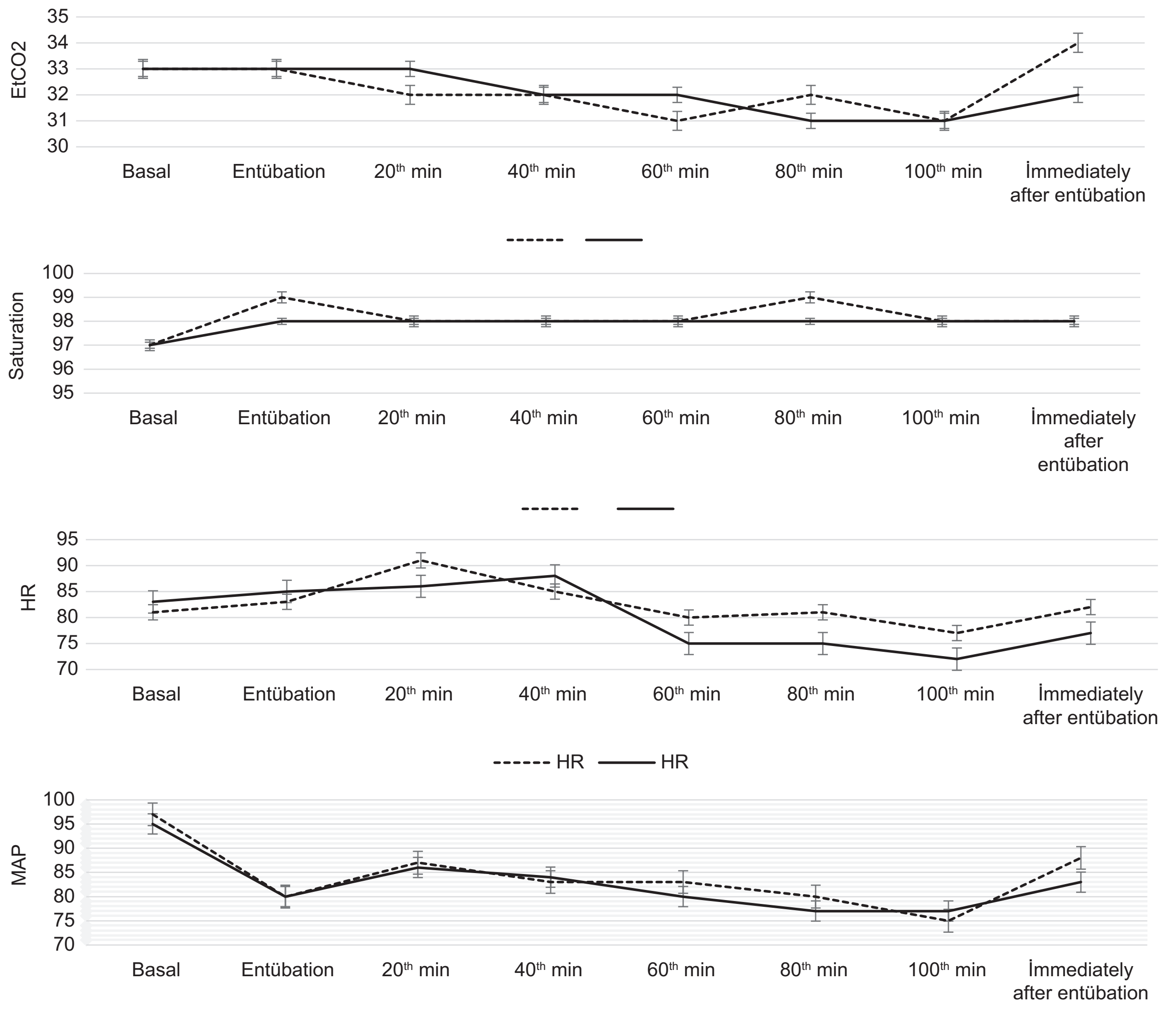

Figure 2. *Intraoperative variables.*

Discussion

Our study observed that patients with poor sleep quality in the pre-operative period had high pain scores and increased additional analgesic consumption in the post-operative period. However, there was no difference between patients with poor and good sleep quality regarding emergence agitation.

Sleep, one of the basic components of a healthy life, plays a key role in many biological activities. In addition to being a basic need, sleep is also an important part of the recovery process in the post-operative period[1]. Impairment in sleep quality can lead to deterioration in both physical and cognitive functions. It can also cause changes in many systems, including endocrine, cardiovascular, neurological, and immune systems[3].

Table 2. NRS and analgesic consumption change of groups

Parameters	Group A (n = 40)	Group B (n = 40)	p
NRS 2^{th} h	5.05 ± 1.57	2.45 ± 1.09	< 0.001*
NRS 12^{th} h	3.28 ± 1.40	1.20 ± 0.82	< 0.001*
NRS 24^{th} h	1.30 ± 0.56	0.75 ± 0.49	< 0,001*
Analgesic Consumption (deksketoprofen) (mg)	26.43 ± 10.40	16.67 ± 12.91	0.048*

*Mann–Whitney U-test.
Statistics presented as mean ± SD. Group A: worse sleep quality group, Group B: good sleep quality group. NRS: numbering rating scale.

Table 3. Comparison of recovery period

Parameters	Group A (n = 40)	Group B (n = 40)	p
RASS score ≥ 2	7 (77.8)	2 (22.2)	0.154*
RASS score < 2	33 (46.5)	8 (53.5)	
Extubation quality score	1.9 ± 1.1	1.7 ± 1.1	0.379†
Deksmedetomidine consumption (mg)	0.017 ± 0.005	0.015 ± 0.007	0.593†

*Ki-kare test.
†Mann–Whitney U-test.
Statistics presented as Mean ± SD or N (%).Group A: worse sleep quality group, Group B: good sleep quality group. RASS: Richmond Ajitasyon Sedasyon Skalası.

Many physiological, psychological, and environmental factors can affect the quality and quantity of sleep. Among these, age, gender, anxiety, and surgical stress are important factors[9,10].

Pain, one of the complications developing in the post-operative period, may cause a prolongation of hospital stay. On the other hand, impairment in sleep quality can also prolong hospital stays by lowering the post-operative pain threshold. Wang et al., in their study on breast cancer cases, reported that patients in the poor sleep group had higher pain levels and, as a result, a longer hospital stay[5]. Luo et al. concluded that the decrease in pre-operative sleep times in patients who underwent joint arthroplasty might reduce the post-operative pain threshold, and the patients need more time to recover from post-operative surgical trauma, resulting in a longer hospital stay[6]. When our study was evaluated in terms of hospital stay, no statistically significant difference was found between the good and poor sleep groups. In our study, patients in the group with poor sleep quality had higher post-operative pain levels and post-operative additional analgesic consumption, which can be explained by the fact that post-operative pain levels were controlled as a result of close follow-up and early intervention.

Pain is a sensory, unpleasant emotional sensation, a behavior pattern that originates from a specific part of the body due to severe tissue damage or not, related to the subjective, primitive protective experiences of the person in the past[11]. Determining the etiological causes is an important step in managing pain, which is one of the most critical recovery problems of the post-operative period. It is known that sleep quality affects pain[12]. There is a bidirectional relationship between pain and sleep quality. While severe pain may impair sleep quality, a decrease in sleep quality may cause hyperalgesia by lowering the pain threshold[12]. Thus, sleep disorders are an important modifiable risk factor for pain. Many studies compare sleep quality and post-operative pain levels[4-6]. Wang et al. investigated the effect of sleep quality on post-operative pain in breast surgery cases. The patients were divided into two groups, good and poor sleep quality, by pre-operative PSQI test. They concluded that the pain levels and the need for post-operative analgesics were higher in the group with poor sleep quality at the post-operative 2nd, 12th, and 24th h, and as a result, the hospital stay was longer[5]. In the study of Zinger et al., in which they examined the cases who underwent cesarean section, it was observed that the pain level was higher in the first 24 h postoperatively in patients with poor pre-operative sleep quality, and the consumption of analgesics was less in the group with good sleep quality. As a result of the study, it was concluded that impairment of sleep quality during pregnancy is an expected situation, and pain management should be handled carefully by predicting the increase in post-operative pain levels due to poor sleep quality[4]. In the study of Luo et al., in patients who underwent total joint arthroplasty, it was observed that post-operative pain scores were higher, additional analgesic needs were higher, and the length of hospital stay was longer in patients with high PSQI scores. As a result, they concluded that pre-operative sleep quality is directly related to clinical parameters and that poor pre-operative sleep quality should be detected and treated[6]. In the study of Büyükyılmaz et al., in which knee-hip arthroplasty was performed, and sleep quality was evaluated with PSQI, it was observed that patients with poor sleep quality had higher pain scores, and similarly, those who had more pain had a decrease in sleep quality. It was concluded that there is a vicious cycle between pain and sleep quality[13]. In our study, in which we investigated the relationship between sleep quality and post-operative pain, we observed that post-operative pain levels and analgesic consumption were higher in patients with poor pre-operative sleep quality, in line with the literature.

Complications such as hypertension, tachycardia, laryngeal edema, bronchospasm, aspiration, bronchopneumonia, and atelectasis can be seen in patients after extubation, which reveals the importance of extubation quality in post-operative complications[14]. There is no study evaluating the relationship between extubation quality and sleep quality. In our study, no significant difference was found between patients with poor and good sleep quality in terms of extubation quality.

Recovery problems such as agitation, disorientation, and violence observed in the early post-operative period are defined as emergence agitation, and its incidence in adults is between 4.7% and 21.3%[15]. Various factors, such as the patient, surgery, or anesthesia method, may be effective in the emergence of emergence agitation. Although pre-operative anxiety and post-operative pain are known risk factors for emergence agitation, we could not find any study investigating the relationship between pre-operative sleep quality and emergence agitation. Although we expected emergence agitation to be higher in the poor sleep group compared to the good sleep group, which was the hypothesis of our study, and the number of patients with emergence agitation was higher in the poor sleep group, no statistically significant difference was found between the two groups.

In studies investigating the relationship between anesthesia method and emergence agitation in the literature, it is known that it is more common, especially in the pediatric age group, due to sevoflurane used in the maintenance of anesthesia. However, it has been found that the use of remifentanil as an analgesic in addition to sevoflurane reduces emergence agitation[16-18]. In the study of Sun et al. on patients who underwent lobectomy, they were divided into two groups: those using sevoflurane and sevoflurane/remifentanil in the maintenance of anesthesia. Emergence agitation was found to be significantly less in the post-operative period in the group that used remifentanil in addition to sevoflurane in the maintenance of anesthesia[16]. In the study of Dong et al., the pediatric patient group who had adenotonsillectomy was discussed. The patients were divided into two groups, those using sevoflurane and sevoflurane/remifentanil. In terms of emergence agitation in the post-operative period, emergence agitation was found to be significantly less in the group in which remifentanil was used in addition to sevoflurane[17]. In a meta-analysis by Wang et al., it was observed that using remifentanil as an adjuvant with sevoflurane reduced emergence agitation[18]. In all these studies, it can be concluded that the use of remifentanil in addition to sevoflurane in the maintenance of anesthesia reduces emergence agitation.

Remifentanil is an opioid derivative with an ester bond and is generally used as a continuous infusion intraoperatively due to its faster onset and end of action than other opioids[19]. However, due to its faster elimination feature, pain and hyperalgesia in the early post-operative period, which also cause emergence agitation due to remifentanil use, is a common concern[20,21]. Although it is more common, especially in high doses and long-term use, it has been reported that the frequency of hyperalgesia is lower in infusions up to 0.2 μg/kg/min[22]. It is not clear why remifentanil used with sevoflurane reduces EA. Possible mechanisms include remifentanil's increased analgesic properties due to the combined use of both drugs in reducing EA, despite its short half-life, deep inhibition of pharyngeal and laryngeal reflexes after head and neck surgeries specific to the surgery to be performed, direct or indirect inhibition of the paradoxical excitatory effects of sevoflurane due to the current excitatory activity in the locus coeruleus region of the central nervous system by μ-opioid agonists[17,22-24].

In our study, remifentanil infusion was used in addition to sevoflurane in anesthesia maintenance. The lack of significant difference in emergence agitation in the poor sleep group is due to remifentanil used in the maintenance of anesthesia due to possible mechanisms described in the literature.

Many pharmacological agents have been used to prevent emergence agitation. These include opioids, benzodiazepines, alpha-2 agonists, ketamine, non-steroidal anti-inflammatory drugs, N2O, and propofol[25,26]. Many studies have reported that dexmedetomidine, an alpha-2 agonist, prevents emergence agitation. Garg et al. investigated the effect of dexmedetomidine on emergence agitation in patients undergoing nasal surgery under general anesthesia and reported that dexmedetomidine reduced the incidence of emergence agitation by 89.5%[27]. In our study, we preferred dexmedetomidine in patients who developed emergence agitation in the post-operative period. We did not detect a significant difference between the groups regarding dexmedetomidine consumption.

Limitations

First, the sleep parameters of our study were evaluated with subjective scales. Second, methods such as polysomnography can provide more objective results. However, subjective assessment methods assess sleep parameters closer to patients' true feelings. Finally, remifentanil infusion is frequently used as an analgesic in the maintenance of anesthesia to reduce the concentration of sevoflurane used to prevent EA due to sevoflurane use. Although we used sevoflurane and remifentanil infusions as standard in both groups in our study, we could not follow the sevoflurane use of the groups to determine how much they reduced the use of sevoflurane. The literature on the relationship between emergence agitation and sleep quality is limited, and there is a need for a study with a larger case series on this subject.

Conclusion

Poor sleep quality may have undesirable effects in the post-operative period. Therefore, evaluating patients in terms of sleep quality in the pre-operative period will help determine the method of post-operative pain and analgesia. In addition, emergence agitation seen in the post-operative period is not associated with good or poor sleep quality in the pre-operative period but can be prevented due to sevoflurane and remifentanil used in the maintenance of anesthesia.

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Conflicts of interest

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Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained approval from the Ethics Committee for analysis and publication of routinely acquired clinical data and informed consent was not required for this retrospective observational study.

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