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RESEARCH

Insomnia and wake up and recovery from anesthesia: a prospective observational study

Uykusuzluk ve anesteziden uyanma ve derlenme: prospektif gözlemsel çalışma

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Abstract

Purpose: The aim of this study was to investigate whether wake up and recovery from anesthesia is earlier or later in patients with insomnia.

Material and Methods: This study included adult patients who were scheduled for elective ureteroscopy under general anesthesia. Using the Jenkins-Sleep Questionnaire (JSQ), the patients were separated into two groups: Insomnia Group and Control Group. Anaesthesia was standardized. After anesthesia induction, 4-6 % desflurane in nitrous oxide/oxygen (60-40%) concentration at flow of 3 L min^{-1} was administered. The parameters recorded were noninvasive arterial blood pressure, heart rate, peripheral oxygen saturation, end-tidal carbon dioxide values, inspiratory and expiratory concentrations of desflurane, anesthesia time, surgery time, time of eye opening, time of transfer to the recovery room. Pain was assessed with a Visual Analogue Scale (VAS) and recovery with the Modified Aldrete Recovery Score (MARS).

Results: Evaluation was made of 80 patients, comprising 25 females and, 55 males, grouped as 42 patients in the insomnia group and 38 in the control group. The demographic and hemodynamic data were not significantly different between the groups. The time of eye opening, transfer to the recovery room, VAS and MARS values were similar in both groups. When operation times were classified as < 30 min. and ≥ 30 min, no significant differences were determined between the groups in respect of wake up, recovery and pain parameters.

Conclusion: Compared with normal sleepers, patients with insomnia showed no differences in respect of wake up and recovery from anesthesia.

Keywords:. Anesthesia, insomnia, sleep, perioperative care, postoperative pain

Öz

Amaç: Bu çalışmanın amacı uykusuzluk çeken hastaların anesteziden uyanma ve derlenmesinin daha erken mi geç mi olduğunu araştırmak

Gereç ve Yöntem: Bu çalışma genel anestezi altında elektif üreteroskopi planlanan erişkin hastaları kapsamaktadır. Jenkins- Uyku Anketi (JSQ) kullanılarak hastalar iki gruba ayrıldı: Uykusuzluk Grubu ve Kontrol Grubu. Anestezi standardize edildi. Anestezi indüksiyonu sonrası desfluran 4-6 konsantrasyonda, nitröz oksit/oksijen (%40/60) konsantrasyonda ve akım 3 L dk^{-1}olarak uygulandı. Noninvaziv kan basıncı, kalp hızı, periferal oksijen satürasyonu, end- tidal karbondioksit değerleri, inspire ve ekshale edilen desfluran konsantrasyonları, anestezi süresi, cerrahi süresi, göz açma zamanı, derlenme odasına transfer zamanı kaydedildi. Görsel Ağrı Skalası (VAS) ağrıyı değerlendirmek, Modifiye Aldrete Derlenme Skoru (MARS) derlenmeyi değerlendirmek için kullanıldı.

Bulgular: Değerlendirme 25'i kadın, 55'i erkek olmak üzere 80 hasta ile yapıldı; Uykusuzluk grubunda 42, kontrol grubunda 38 hasta vardı. Demografik ve hemodinamik veriler gruplar arasında anlamlı farklılık göstermedi. Göz açma zamanı, derlenme odasına transfer zamanı, VAS ve MARS değerleri her iki grupta benzerdi. Operasyon süreleri 30 dakikanın altında ve 30 dakika ve üzeri olarak sınıflandırıldığında; uyanma, derlenme ve ağrı parametrelerinin karşılaştırılması açısından gruplar arası önemli farklılık görülmedi.

Sonuç: Normal uyuyanlarla karşılaştırıldığında, uykusuzluk çeken hastaların anesteziden uyanma ve derlenme açısından farkları olmadığı sonucuna varıldı.

Anahtar kelimeler: Anestezi, uykusuzluk, uyku, perioperatif bakım, postoperatif ağrı

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INTRODUCTION

Sleep is essential for the maintenance of health and is defined as a state of decreased arousal that is actively generated by nuclei in the hypothalamus, brainstem and basal forebrain[1,2]. Sleep is a nonhomogeneous state and has two major phases. Rapid eye movement (REM) sleep is associated with high brain activity and vivid dreaming. Non- REM (NREM) sleep is characterized by waxing and waning muscle tone, decreased heart rate, and decreased body temperature[3].

"Now, you're going to sleep" is a phrase often used by anesthesiologists to patients. General anesthesia is a reversible condition induced by drugs, which consist of amnesia, analgesia, unconsciousness, and akinesia[4]. The question to be answered for both states is what the mechanisms are regulating the control of consciousness.

Insomnia is a sleep disorder observed in approximately 10-30% of the adult population. Difficulty falling asleep, staying asleep and early awakening are the symptoms experienced in insomnia[5]. Risk factors of insomnia have been reported to be female gender, advanced age, depressive mood, snoring, comorbid medical conditions, high levels of perceived stress, nocturnal micturition, and regular hypnotic use[6]. Insomnia is associated with comorbid psychiatric and medical conditions[7]. Studies have shown that anxiety, depression, suicide and substance abuse can be triggered by insomnia[8]. The pathophysiology of insomnia is not well known, and generally, insomnia is believed to arise from a disorder of hyperarousal. An increased level of alertness throughout the day and night can lead to difficulty in sleeping[9].

Surgical intervention can be applied to patients suffering from insomnia. Early wake up and recovery from anesthesia is desired by anesthesiologists, and this is also true for patients with insomnia. However, there are few studies in the literature on the effects of anesthesia in these patients. In this context, the primary endpoint of this study was to investigate whether wake up and recovery from anesthesia is earlier or later in patients with insomnia. The secondary endpoints were the postoperative pain levels of the patients and inhalation agent consumption in the intraoperative period.

MATERIALS AND METHODS

The study was conducted in Adana City Training and Research Hospital by the Ethics Committee of Health Sciences University Adana Numune Training and Research Hospital (approval no.112, dated: September 13, 2017) and was registered at ClinicalTrials.gov. The study was conducted in Health Sciences University Adana City Hospital. Explanations about the study protocol were given to each participant and written informed consent was obtained.

Sample

A total of 80 patients, aged 18-55 years, with American Society of Anesthesiology (ASA) physical status I-II, who were scheduled for elective ureteroscopy were invited to participate in the study. Patients were excluded from the study if they had obstructive sleep apnea syndrome, thyroid disfunction, any neurological or psychiatric disorder, renal failure, morbid obesity, or if they were using anxiolytic, antidepressant, or anticonvulsant drugs. All 80 patients who were asked to participate and met the study criteria agreed and so, were included in the study.

Preoperative assessment

The patients were given no premedication. In the preoperative room the 4-item Jenkins-Sleep Questionnaire (JSQ) was applied to the patients by the preoperative anesthesia technician[10]. The JSQ is a well- known scale which is used to estimate sleep disturbances. The reliability and validity of this sleep scale has allowed it to be translated into different languages and used in clinical studies[11,12]. The JSQ evaluates sleep during the previous 4 weeks with 4 items of: "having trouble in falling asleep, trouble staying asleep, waking up several times per night, and waking up feeling tired and worn-out after the usual amount of sleep". The responses to the items were: not at all (1), 1 to 3 days (2), 4 to 7 days (3), 8 to 14 days (4), 15 to 21 days (5), 22 to 28 days (6). Based on the responses to the questionnaire, the patients were separated into two groups as the Insomnia Group and the Control Group. The Insomnia Group consisted of patients who reported sleep problems 4 to 7 days in the previous month for at least 1 item. Those with any sleep problem for 1 to 3 days in the previous month for 1 item or more were not included in the insomnia group. The patients giving responses

of "not at all" to all the items formed the control group.

Anesthetic management

Standardized general anesthesia was performed by an anesthetist blinded to the study groups. After the induction of anesthesia with propofol 2 mg kg^{-1} intravenously (iv), rocuronium 0.6 mg kg^{-1} iv was administered for muscle relaxation, then the patients were intubated and mechanically ventilated. Anesthesia maintenance was provided with 4-6 % desflurane in a gas mixture of 60% nitrous oxide and 40% oxygen at flow rate of 3 L min^{-1}. Patients were given tramadol 1 mg kg^{-1} and metoclopramide 10 mg iv after endotracheal intubation. Hemodynamic parameters were monitored and recorded, including systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), peripheral oxygen saturation (SPO2) values, and the concentrations of inspired and exhaled desflurane and end-tidal carbon dioxide (ET-CO2) values. Records were taken from the anesthesia machine screen at the start of surgery and at the 5th, 15th, 25th, 35th, 45th, and 60th minutes of surgery. Anesthesia depth was based on maintaining the hemodynamic parameters within 20% of the pre-induction baseline values. Clinical parameters such as tears, sweating, and pupil size were also used. Neuromuscular blockage was reversed with neostigmine 0.05 mg kg^{-1} and atropine sulphate 0.015 mg kg^{-1} iv at the end of surgery. While still in the operating room, the duration of anesthesia, surgery time, time of eye opening, and time of transfer to the recovery room were recorded. In the recovery room, pain was evaluated with a Visual Analogue Scale (VAS), and recovery with the Modified Aldrete Recovery Score (MARS).

Statistical analysis

As there are no similar studies in the literature, the large effect size (0,8) standardized by Cohen was used. Sample size calculated using G*Power 3.1.9.7 software (Franz Foul, Universitat Kiel, Germany). For 90% power, a minimum total of 68 patients (34 in each group) was found to be sufficient to provide Effect Size d=0.8, α=0.05. Considering potential later exclusions during the study period, the sample size was increased by 15% and 80 patients were included in the study. Data obtained in the study were analyzed statistically using IBM SPSS vn. 25.0 software (IBM Corpn., Armonk. NY, USA). Conformity of the data to normal distribution was assessed using the Kolmogorov-Smirnov, skewness-kurtosis, and graphical methods (histogram, Q-Q Plot, Stem and Leaf, Boxplot). The descriptive statistics of categorical data were expressed as frequency (n) and percentage (%) and were compared using the Chi-square test. Continuous variables were stated as mean ±, standard deviation (SD), median, minimum and - maximum values. In the comparison of quantitative data between groups, the Independent Samples t-test was used when distribution was normal, and the Mann-Whitney U test when distribution was not normal. The p value for the level of statistical significance level was accepted as α=0,05.

RESULTS

Evaluation was made of a total of 80 patients, comprising 25 females, and 55 males. According to the JSQ responses, 42 patients with insomnia were defined as the insomnia group and 38 patients as the control group. The age, gender, and ASA values of the patients were similar in both groups (Table 1).

No statistically significant difference was found between the groups in respect of hemodynamic parameters (SBP, DBP, HR and SPO2), ET-CO2, desflurane and ET-desflurane concentrations. The ET-desflurane concentrations of the groups are shown in Table 3.

The mean operation time was 32.02 ± 11.61 min in the insomnia group and 33.32 ± 11.92 min in the control group ($p = 0.62$). The mean anesthesia time was 37.24±11.66 min. in the insomnia group and 38.55 ± 11.81 min. in the control group ($p = 0.61$). The VAS and MARS values were similar in both groups. No significant difference was determined between the groups in respect of the time of eye opening, or the time of transfer to the recovery room ($p > 0.05$).

To evaluate the effect of the length of operation time on wake up, recovery and pain, the operation time was classified as < 30 min, and ≥ 30 min, with 34 surgical procedures having been completed in < 30 min and 46 operations in ≥ 30 min. The comparisons of wake up, recovery and pain parameters for both groups according to the operation times are shown in Table 2. There were no statistically significant differences between the groups.

Table 1. Baseline demographic characteristics

	Insomnia Group (n=42)	Control Group (n=38)	P value
Age (years)	37.19±8.38	36.13±9.74	0.603[a]
Gender (F* /M**)	12/30	13/25	0.763[b]
ASA*** (I/II)	10/32	11/27	0.789[b]

Data are presented as mean ± SD and number; *F: Female; **M: Male; ***ASA: American Society of Anesthesiologists
a: Independent Samples t- test, b: Chi-Square Test

Table 2. Comparisons between the groups of wake up, recovery and pain parameters according to the duration of the operation.

	Operation time < 30 min			Operation time ≥ 30 min		
	Insomnia Group (n=19)	Control Group (n=15)	P a value	Insomnia Group (n=23)	Control Group (n=23)	P a value
Time of eye opening	6.0 (4.0 – 8.0)	5.0 (3.0 – 8.0)	0.986	5.0 (3.0 – 10.0)	6.0 (2.0 – 10.0)	0.973
Time of transfer to the recovery room	9.0 (6.0 – 12.0)	9.0 (5.0 – 12.0)	0.595	10.0 (5.0 – 13.0)	9.0 (5.0 – 14.0)	0.524
VAS *	2.0 (1.0 – 4.0)	2.0 (1.0 – 8.0)	0.350	2.0 (1.0 – 8.0)	2.0 (1.0 – 8.0)	0.923
MARS**	10.0 (10.0 – 10.0)	10.0 (9.0 – 10.0)	0.260	10.0 (9.0 – 10.0)	10.0 (10.0 – 10.0)	0.076

Data are presented as median (min-max) values; *VAS: Visual Analogue Scale; **MARS: Modified Aldrete Recovery Score
a: Mann-Whitney U- test

Table 3. End-tidal concentrations of desflurane of the groups

	Insomnia Group (n=42)	Control Group (n=38)	P value*
Surgery start time	5.21±0.28	4.98±0.53	0.104
5 min	5.11±0.36	5.02±0.40	0.493
15 min	4.85±0.50	4.47±0.84	0.122
25 min	4.15±1.17	4.18±0.52	0.952
35 min	4.66±0.75	4.73±0.55	0.754
45min	4.35±0.79	4.72±0.88	0.383
60 min	4.20±0.00	4.85±0.35	0.371

Data are presented as mean ± SD values.; *: Independent Samples t- test

DISCUSSION

The results of this study demonstrated that the presence of insomnia had no effects on wake up and recovery from anesthesia. The level of pain experience was also similar in patients with and without insomnia.

Recovering from anesthesia is similar to waking from physiological sleep[13]. The result in both is a return to normal wakefulness. Multiple neurochemical systems including noradrenergic, cholinergic, serotonergic and hypocretin systems induce waking. These waking systems are assumed to be inhibited possibly by gamma- aminobutyric acid (GABA) during sleep. The activation of waking systems leads to the transition to the wakefulness state[14]. An increase of adrenocorticotropin (ACTH) release and typical EEG changes including increased activity in the alpha frequency band and decreased activity of delta and theta bands are the adaptive mechanisms which occur during the transition from sleep to wakefulness[15]. Emergence from anesthesia includes brain stem recovery, the return of spontaneous respiration, return of gag and corneal reflexes, swallowing, grimacing and the ability to follow commands[16]. Sleep shows spontaneous generation and termination, but the reversal of anesthesia requires anesthetic drug elimination[17]. In the timing of wakefulness, the duration of anesthesia and agent elimination are important, whereas the duration of sleep, environment and circadian rhythm are crucial in physiological sleep[18].

The idea for this study emerged with the question of whether patient's recovery from general anesthesia is like their recovery from physiological sleep. Sleep deprivation and insomnia are different terminologies. However, although the etiologies are different, the apparent effect is the problem of lack of sleep. Tung et al. evaluated the effect of anesthesia on sleep homeostasis in rats. Rats on which electroencephalographic/electromyographic electrodes were placed deprived of sleep for 24 hours with the disc over-water method, and then 6-hour propofol anesthesia was administered to the rats or ad libitum sleep was achieved with intralipid solution. It was concluded from the study that sleep recovery behavior in rats with 6 h of ad libitum sleep was similar to that of rats administered 6 h propofol anaesthesia[19]. This raises the question of whether insomnia would affect wake up and recovery from anesthesia. The results of this study emphasize that insomnia has no effect on wake up and recovery.

In the literature, age and gender are among the stated risk factors for insomnia, and insomnia has been reported to be more common in females and older adults[20]. In this study, age and gender were similar in the groups, but this finding was not compatible with the literature, and 28 % of the patients in the insomnia group were female. The small study population and inclusion of only patients with ASA I-II may have influenced this finding.

There are studies in literature that have presented different results on the anesthetic requirements of patients with sleep disorders. Erden et al. investigated the effect of insomnia on anesthetic requirement in a study of 50 patients who underwent elective laparoscopic cholecystectomy. The results showed that the end-tidal concentration of sevoflurane increased during anesthesia maintenance in patients with insomnia[21]. In contrast to those results, other studies have shown that the notion that higher doses of anesthesia would be required by patients with insomnia than by people with normal sleep may not be valid. Mirkheshti et al. compared patients with and without sleep quality disorder in respect of propofol dose requirements to achieve the same depth of anesthesia. The doses of propofol administered for general anesthesia induction and maintenance were found to be significantly lower in patients with a sleep quality disorder than in patients with a normal sleep pattern[22]. Similarly, Ho et al. investigated patients with different sleep quality in respect of the change in autonomic nervous system activity and the nociceptive/anti-nociceptive balance during different stages of surgery. It was reported that patients with poor sleep quality did not require a higher opioid dosage or higher concentration of inhalation anesthetics than those with normal sleep during general anaesthesia[23]. In the current study, a higher desflurane concentration was not needed in patients with insomnia.

Previous studies have indicated that pain tolerance may be reduced by sleep disorders[24,25]. In a prospective cohort study of patients undergoing total join arthroplasty, it was reported that poor sleep quality in the preoperative period was correlated with postoperative pain[26]. Similarly, Lin et al. stated that the level of postoperative pain and need for additional analgesia was increased in patients with insomnia undergoing non-cardiac surgery[27].However, unlike those studies, the current study results showed that the postoperative pain experiences of the patients were similar in both groups. This difference may be due to the smaller patient population in the current study compared to other studies. Moreover, there was no difference between the groups in respect of the length of the operations.

The JSQ was used for the subjective assessment of sleep in this study, so not using objective measurements of sleep such as polysomnography can be considered a limitation. Another limitation was that pain was only evaluated in the postoperative room. Pain assessment before surgery and at 6, 12, and 18-hours postoperatively with determination of the need for additional analgesia would have been more meaningful. It was not possible to perform EEG/BIS monitoring to reflect the depth of anesthesia in this study.

In conclusion, compared with normal sleepers, patients with insomnia show no differences in respect of wake up and recovery from anesthesia. This study can be considered preliminary to further studies which are needed to assess insomnia and anesthesia with additional assessment tools such as EEG/BIS monitoring and polysomnography.

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