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The relationship between insomnia and acute postoperative pain: a case-control study on laparoscopic cholecystectomy patients

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ABSTRACT

Aims: Psychological factors play a significant role in predicting postoperative pain. However, the impact of insomnia on acute postoperative pain is little known. The aim of this study was to investigate the relationship between insomnia and acute postoperative pain.

Methods: We performed a case-control study in patients undergoing elective laparoscopic cholecystectomy. Patients with an Insomnia Severity Index (ISI) score >14 were allocated to an insomnia group (n=35) and those with an ISI score <7 to a control group (n=35). All patients were asked to rate their current level of pain on a numeric rating scale (NRS) at 1, 2, 4, 8, 12, and 18 hours postoperatively.

Results: There was no between-group differences in age, gender, body mass index, American Society of Anesthesiologists score, or operating time. The patients in the insomnia group had higher NRS scores and requested significantly greater amounts of tramadol (269.4±33 mg vs. 235.0±36 mg; p<0.001) and rescue analgesia (paracetamol; 1.06±0.8 g vs. 0.40±0.7 g; p<0.001) postoperatively than did the controls. Analysis of covariance revealed a significant interaction between insomnia and the preoperative experience of pain (F=6.62; p=0.013) and significant impact of insomnia on the mean NRS score (F=15.47; p<0.001).

Conclusion: Patients who experienced preoperative insomnia and underwent elective cholecystectomy have a reduced threshold for postoperative pain, which increases the need for analgesics.

Keywords: Insomnia, sleep disorder, postoperative pain, pain threshold predictor, cholecystectomy

INTRODUCTION

More than 230 million patients undergo surgery each year worldwide.[1] Surgical procedures are often followed by acute postoperative pain, which should be relieved to promote healing and prevent complications.[2] However, despite efforts to improve the management of acute postoperative pain, a high number of patients experience moderate to severe pain during the immediate postoperative period.[3]

Insomnia is a common chronic disorder, defined as a subjective report of difficulty with initiation, duration, consolidation, or quality of sleep that occurs despite adequate opportunity for sleep and causes substantial distress and impairment of daytime functioning.[4,5] Psychiatric and medical comorbidities commonly present with insomnia.[6,7] Chronic pain is one of the most important of these comorbidities and may increase the burden on health care. There is strong evidence that sleep disturbances and chronic pain have a reciprocal relationship.[8-10] Symptoms of insomnia not only increase the risk of developing pain in the future but also increase the severity of existing pain. However, the severity of pain may also predict the severity of subsequent insomnia.[11-14]

Acute postoperative pain differs from chronic pain in its etiology, mechanism, and treatment.[15] Beyond incisional pain, hyperalgesia, the mechanism of ischemic pain, and central neuronal sensitization, and psychologic factors

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can be associated with the experience of postsurgical pain.[16] We hypothesized if patients with insomnia experienced increased postoperative pain. Therefore, we performed a case-control study to investigate the experience of postoperative pain in patients with insomnia undergoing elective laparoscopic cholecystectomy.

METHODS

After approval by İstanbul Training and Research Hospital Clinical Researches Ethics Committee (Date: 01.03.2019, Decision No: 1731), and obtaining informed consent from all enrolled subjects, we performed this prospective observational case-control study in patients scheduled for elective laparoscopic cholecystectomy between January 2017 and January 2020 at the İstanbul Training and Research Hospital. All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. Patients with renal failure, thyroid dysfunction, morbid obesity, obstructive sleep apnea, neurologic dysfunction, or alcoholism were excluded, as were patients receiving antidepressant therapy, those scheduled for urgent surgery, and those taking anticonvulsants or opioids.

To assess the nature, severity, and impact of insomnia, the patients completed the Turkish version of the 7 item Insomnia Severity Index (ISI) questionnaire.[17,18] The dimensions evaluated were as follows: severity of sleep onset, sleep maintenance, early morning awakening problems, sleep dissatisfaction, interference of sleep difficulties with daytime functioning, noticeability of sleep problems by others, and distress caused by sleep difficulties. A 5-point Likert scale was used to rate each item (0, no problems; 4, very severe problems) and yielded a total score ranging from 0 to 28. The total score was interpreted as follows: absence of insomnia (0-7); sub-threshold insomnia (8-14); moderate insomnia (15-21); or severe insomnia (22-28). The patients were divided into two groups according to the results of the ISI questionnaire. Thirty-five patients with moderate to severe insomnia (ISI >14) and sleep problems lasting for more than 3 months were allocated to an insomnia group and 35 with an ISI score ≤7 were allocated to a control group.

To assess the preoperative experience of pain, the patients were asked if they have experienced any pain lasting for 1 day or more in the previous month. If pain was reported, the patient was asked to describe the pain on a two-sided blank body manikin (2 front and back) before surgery. Pain that was located on both sides of the body above and below the waistline and in the axial skeleton was defined as ''widespread pain''. Pain experiences that did not meet all the criteria for widespread pain were defined as ''some pain''.

Postoperative pain was assessed by a different anesthesiologist who was blinded to group allocation. To evaluate the postoperative pain, the patients were asked to rate their current level of abdominal pain using a numeric rating scale (NRS; 0, no pain; 10, the worst imaginable pain) at 1, 2, 4, 8, 12, and 18 hours after surgery. Patients with a mean NRS score ≥4 were considered to have moderate to severe pain.

None of the patients received a premedication agent. Propofol 2 mg/kg, fentanyl 1 μg/kg, and rocuronium 0.5 mg/kg were used for the induction of anesthesia in all patients. No further fentanyl was administered intraoperatively. Anesthesia was maintained using sevoflurane in a mixture of oxygen 2 L/min and N_2O_2 L/min. The anesthesia technique during the operations was standardized.

An intravenous patient-controlled analgesia (PCA) device (CADD-Legacy Patient Control Analgesia Device Model 6300; Ambulatory Infusion Pump Smith Medical ASD, Dublin, OH, USA) was used in all patients for postoperative pain management. All patients were informed about how to use the device and how to control the pump before and after the operation. Each pump contained 300 mg tramadol diluted in 100 mL of 0.9% saline solution. The PCA device was set to deliver a continuous infusion rate of 10 mg per hour, with a bolus dose of 10 mg and a lock-out interval of 15 minutes. During treatment with PCA, when analgesia was inadequate, rescue analgesia (paracetamol 1 g) was provided.

Statistical Analysis

The power analysis was performed using the difference in NRS scores between the 2 groups and calculation was based on a findings of a previous study (19). We assumed that the mean NRS scores in the insomnia group and control group would be 3.6 and 2.0, with a standard deviation (SD) of ± 2.0 and calculated sample size for each group of 32 (α =0.05, β= 0.8). Therefore, 35 subjects were included in each group to allow for a dropout rate of 10%. Normality of distributions was tested with the Shapiro-Wilk test. Numerical data are expressed as the mean ± SD, and the categorical data as the number (percentage). The parametric data (age, body mass index [BMI]) were analyzed using the Student's t-test, nonparametric data (operating time, postoperative tramadol and paracetamol doses, postoperative NRS scores) with the Mann-Whitney U test, and categorical data (sex, preoperative experience of pain, American Society of Anesthesiologists (ASA) score, mean NRS score) with the chi-square test. We

also performed an analysis of covariance to assess the main effects of insomnia, age, sex, BMI, and preoperative experience of pain and their interaction with regard to the postoperative mean NRS score. The statistical analysis was performed using SPSS for Windows software (version 21; IBM Corp., Armonk, NY, USA). A P-value <0.05 was considered statistically significant.

RESULTS

The inclusion criteria were met by 110 of the 470 patients operated on by the same surgeon. (**Figure 1**) Due to technical problems with the device and drug inadequacy during the study, 40 of the 110 participants were eliminated from the study. The patients' descriptive data are summarized in **Table 1**. There was no statistically significant between-group difference in sex, age, BMI, operating time, or ASA physical classification. The preoperative experience of pain was more common in the insomnia group than in the control group (p=0.04). Nine patients in the insomnia group had some pain and 4 had widespread pain whereas 2 patients in the control group had some pain and 1 had widespread pain. The postoperative NRS scores at 1, 2, 4, 8, 12, and 18 hours after surgery was significantly higher in the insomnia group (**Table 2**). Tramadol consumption was also significantly higher in the insomnia group (269.4 ± 33 mg) than in the control group (235.0 ± 36 mg; p<0.001, **Table 3**). A rescue dose of paracetamol 1 g was required in 26 patients in the insomnia group and 12 in the control group (p=0.001). The mean NRS score was also calculated according to the results checked after surgery. Twenty-seven patients in the insomnia group (77.1%) and 4 in the control group (11.4%) experienced moderate or severe postoperative pain (p<0.001; **Table 3**).

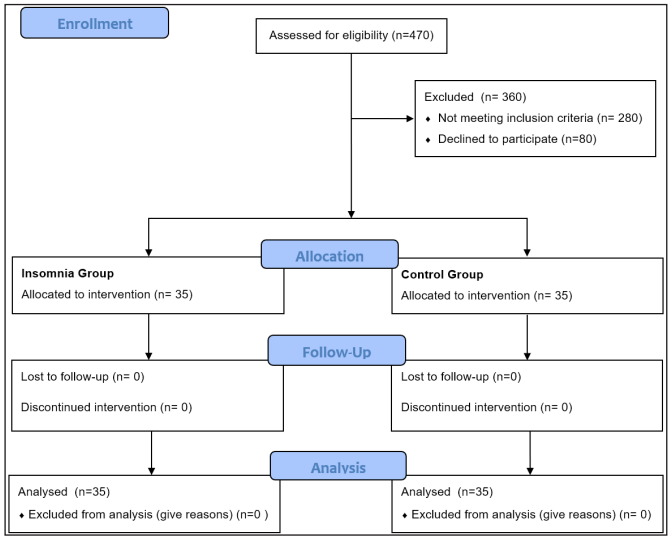

Figure 1. Flow Diagram of the Patient Selection

Table 1. Baseline descriptive and clinical characteristics

	Insomnia group	Control group	p
Age (years)	49.5±9	49.5±9	0.968
Gender (f/m)	27/8	24/11	0.420
BMI (kg/m²)	28.7 ±4	29.8 ±5	0.286
Duration of surgery (minute)	45.6±12	49.4 ±12	0.102
Preoperative pain experience (y/n)	13/22	3/32	0.04
ASA 1/ASA 2	18/17	18/17	1.0

f/m=female/male; BMI=Body mass index; y/n=yes/no ; ASA: American Society of Anesthesiologists, Data are presented as mean ±SD and number.

Table 2. Postoperative NRS Scores

	1h	2h	4h	8h	12h	18h
Insomnia group	8.37±2.1	7.43±2.2	6.00±2.1	4.49±1.9	3.09±1.6	2.34±1.6
Control group	7.06±2.3	5.57±2.1	3.29±2.1	1.63±2.0	0.54±1.3	0.43±1.3
P	0.02	<0.001	<0.001	<0.001	<0.001	<0.001

h=hour (Time after operation); Data are presented as mean ± SD

Table 3. Postoperative analgesic consumption and mean NRS scores

	Insomnia group	Control group	p
Tramadol consumption dose(mg)*	269.4 ±33	235.0±36	<0.001
Rescue dose of paracetamol (gr)*	1.06±0.8	0.40±0.7	<0.001
Mean NRS score ≥4**	27(77.1)	4(11.4)	<0.001

*Data are presented as mean ±SD; ** Data are presented as number (%)

To elucidate the interplay between demographic factors, insomnia, preoperative experience of pain, and mean NRS score, we performed an analysis of covariance (with the mean NRS score as the dependent variable, insomnia, preoperative experience of pain, and sex as independent variables, and age, BMI, and operating time as co-variables). We found a significant association between insomnia and preoperative experience of pain (F=6.62; p=0.013) and a significant impact of insomnia on the mean postoperative NRS score (F=15.47; p<0.001).

DISCUSSION

A number of experimental and clinical studies have documented the relationship between sleep disruption and hyperalgesia.[20-24] Sleep disruption is a stressor, and preoperative stressors may contribute to postsurgical hypersensitivity. In animal models, brief sleep deprivation before surgery has been shown to significantly worsen the severity of subsequent pain.[25] However, the relationship between insomnia disorder and acute postoperative pain is poorly understood.[26]

The results of this case-control study show that there is an impact of insomnia on the acute postsurgical experience of pain; 77.1% of our patients suffering from insomnia experienced moderate to severe pain

after elective cholecystectomy. We found that patients suffering from chronic insomnia reported higher pain scores than the controls at 1, 2, 4, 8, 12, and 18 hours postoperatively. There was an association between insomnia and postoperative analgesic consumption in patients with insomnia who requested more tramadol and rescue analgesics than by the controls.

Sleep and pain are inter-related. Sleep disturbances may exacerbate existing pain and predict new-onset pain.[27-29] Overlapping mechanisms may be involved in this complex relationship. Symptoms of insomnia may trigger a cascade of neuronal changes leading to central sensitization, which in turn may contribute to hyperalgesia.[30-32] A dysfunction in the mesolimbic dopaminergic system may underlie the comorbidity of insomnia and pain.[33] Furthermore, sleep deprivation has been shown to affect the serotoninergic system, which also plays a central role in the descending pain inhibitory control system.[34-37] The interplay of psychological factors, such as stress, anxiety, depression, and insomnia, may also contribute to hyperalgesia.[8] There is evidence suggesting that deregulation of the hypothalamic-pituitary-adrenal system may play a central role in this complex relationship.[40,41]

Acute pain also serves the important function of signaling harm to the body's integrity. In rats, acute sleep disruption preoperatively has been shown to worsen postoperative pain.[23] However, there is an important distinction between acute sleep disturbance and insomnia disorder in terms of their courses and trajectories.[42,43] Previous research showed that up to 30% of patients who underwent surgery had pain scores >3 on a visual analog scale of 10.[3] The fact that 77.1% of patients in our insomnia group and only 11.4% of those in the control group had moderate to severe postoperative pain underscores the strong impact of severity of insomnia on acute postoperative pain.

Early studies identified preoperative experience of pain as an independent factor in predicting acute postsurgical pain; however, experimental pain assessment studies could not identify patients at risk for acute postsurgical pain.[44,-46] Our study revealed an interaction between insomnia and preoperative pain, but we did not find any association between preoperative experience of pain and acute postsurgical pain. Overlapping complex mechanisms in the central nervous system rather than preoperative experience of pain in itself might play a significant role in predicting acute postsurgical pain.

ISI is a valuable and valid instrument that can not only be used as a screening tool for insomnia disorder but can also be an effective instrument in identifying patients with significant insomnia disorder.[25,26-47] We did not simply compare patients and controls by diagnosis but investigated the severity of insomnia in all subjects.

The duration, intensity, and location of postoperative pain differs between surgical procedures. To limit the potential impact of heterogeneity in surgical pathophysiology and procedures on the effects of insomnia on acute postsurgical pain, we selected patients with a history of cholelithiasis who were undergoing elective laparoscopic cholecystectomy.

To avoid confounding results, psychological factors other than insomnia are not considered in this paper. The aim of our study was to evaluate the ability of chronic insomnia to predict postoperative pain rather than the role of other mostly interrelated psychological factors.

Although our study included a homogenous sample, it is limited by its cross-sectional design. Pain following a single operation type was assessed because the study's participants were all homogeneous. After various operations, further studies with larger patient populations are required. Another limitation of the study is that it was not double-blind; only the pain assessor was not aware of group allocation.

CONCLUSION

The data presented here show that the severity of insomnia prior to surgery may worsen the experience of acute postoperative pain. Our results emphasize the relevance of preoperative sleep management in clinical care. Efforts to prevent and treat acute postoperative pain may be well served to target insomnia as a point of intervention.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of İstanbul Training and Research Hospital Clinical Researches Ethics Committee (Date: 01.03.2019, Decision No: 1731).

Informed Consent: Written consent was obtained from the patient participating in this study.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper and that they have approved the final version.

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