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Does Pain Following Laparoscopic Cholecystectomy Differ in Diabetics?

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ABSTRACT

Introduction: Individuals with diabetes differently respond to painful stimuli in the postoperative period than non-diabetic patients. This variation causes a scorching, tingling, numbness, or even hyperalgesic sensation due to a change in sensory perception. During routines sometimes we donot remember how patients' pain differ in some situations. Diabetes mellitus is an important disease that we must remember when we plan our postoperative pain relief plan. This study aimed to assess the pain levels and analgesic requirements of individuals with diabetes following laparoscopic cholecystectomy (LC).

Methods: Patients with symptomatic gallstones and cholecystitis underwent elective LC between April 2019 and April 2020. Patients' records were prospectively registered and retrospectively received from the patients' record system on the postoperative course. A total of 70 cases were evaluated within the scope of the study, 35 (50%) of whom were diagnosed with diabetes and 35 (50%) were control subjects.

Results: When the results were examined, it was determined that there was a difference between the two groups that were statistically significant at the 5th and 10th minutes of the bispectral index ($p<0.05$). When the two groups were compared, patients in the control group had more pain on the postoperative course and mean score of 8 ($p=0.049$), 7 ($p=0.016$), 5 ($p=0.02$), 4 ($p=0.032$), 2 ($p=0.014$) respectively 1, 2, 4, 8, 12, 24 hours on the numeric rating scale, $p<0.001$). In the multivariable analysis, the group with diabetes was shown to be strongly related with a significantly lower dosage of tramadol consumption compared to the control group.

Conclusion: According to our findings, the patient with diabetes who underwent LC experienced less postoperative discomfort than those without diabetes. In contrast to the previous studies, our findings show that patients with diabetes have less post-operative pain and require fewer analgesics.

Keywords: Diabetes mellitus, cholecystectomy, postoperative pain

Introduction

Laparoscopic cholecystectomy (LC) is the gold standard method for symptomatic patients; it has several benefits over the open approach, including reduced pain and quicker recovery (particularly in the first 24 hours), as well as a shorter length of hospital stay (1,2).

Although one of the most common surgical procedures, research on postoperative pain management for cholecystectomy is still underway (3).

When adequate postoperative pain management is not achieved, it poses a serious risk for patients (4). Inadequate pain management delays oral intake and mobilization and increases the likelihood of persistent postoperative pain (5,6).

A higher [American Society of Anesthesiologists (ASA) classification] score, younger age, preoperative discomfort, female gender, and the anatomic site of surgery are some published risk variables that indicate a higher likelihood of postoperative pain (7,8).

Individuals with diabetes differently respond to painful stimuli in the postoperative period than non-diabetic patients. This variation causes a scorching, tingling, numbness, or even hyperalgesic sensation due to a change in sensory perception. An altered perception of pain results in a longer recovery time, which typically requires multimodal and long-term pain management (9-11).

We used a numeric rating scale (NRS) to evaluate the degree of postoperative pain. NRS is a system that scores pain from 0 to 10. A tolerable pain threshold is assessed to be NRS=3, while individuals score

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NRS >4 are considered to be in moderate to severe pain and hence in need of further analgesics (12,13).

Enhanced Recovery After Surgery (ERAS) colorectal surgery guidelines recommend opioid-sparing multimodal analgesia, including paracetamol in conjunction with epidural analgesia, after open surgery (14,15).

After undergoing LC in patients with diabetes, this study aimed to assess their levels of pain and assess their need for analgesic medication.

Methods

Study Design

Patients with symptomatic gallstones and cholecystitis underwent elective LC at University of Health Sciences Turkey, İstanbul Training and Research Hospital, between April 2019 and April 2020. Patients' records were prospectively registered and retrospectively received from the patient records system in the postoperative course.

The study enrolled patients scheduled for elective LC between the ages of 23 and 69, with an ASA class of I-II. The study included 70 patients, including 35 with controlled diabetes and 35 without diabetes. The patients were excluded from the study with liver cirrhosis, concurrent common bile duct stones, acute pancreatitis, past medical history of analgesic allergy, and conversion to open cholecystectomy. Before beginning the operation, all the participants were given information on the procedure, and their written consent was obtained. Ethical committee approval was obtained from the Local Ethics Committee of University of Health Sciences Turkey, İstanbul Training and Research Hospital (approval number: 188, date: 17.06.2022). All patients were discharged from the hospital the day following the operation as part of the standard procedure, and they were followed up at an outpatient clinic one week and two months after surgery.

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.

The primary outcome of the study was the cumulative dosage of tramadol, whereas the secondary outcome was the mean pain intensity 24 h after surgery. Pain intensity was assessed with the NRS by participants 0, 1, 2, 4, 8, 12, 16, and 24 h after surgery. On a scale from 0 to 10, with 0 signifying no pain at all and 10 reflecting the greatest suffering possible, patients were asked to assess their pain severity. The postoperative pain scores were assessed and recorded by the researchers. The target for postoperative analgesia management was an NRS score of 3 or less. On the day of surgery, the pain management protocol called for administrating opioids intravenously through a PCA device. During treatment with the PCA device, rescue analgesia in the form of 1 gram of paracetamol was administered when analgesia was insufficient.

Age, sex, body mass index (BMI), a diagnosis of diabetes mellitus (DM), and ASA class were the clinical factors that were considered to be baseline variables. The postoperative course, the preoperative treatment plan, the length of hospital stay, and any complications that arose were all recorded.

Statistical Analysis

The patient data gathered for the study were analyzed using the IBM Statistical Package for the Social Sciences (SPSS 23.0-IBM, NY, USA) for Windows 23.0 software. For categorical data, frequency and percentage were provided; for continuous data, median, minimum, and maximum descriptive values were provided. Using the Kolmogorov-Smirnov test, the compatibility of the data with the Gaussian distribution was determined. The "Mann-Whitney U test" was employed to compare groups, while the "chi-square or Fisher's exact test" was used to compare categorical variables. When the p-value was less than 0.05, the results were considered statistically significant.

Results

A total of 70 cases were evaluated within the scope of the study, 35 (50%) of whom were diagnosed with diabetes and 35 (50%) were control subjects. Table 1 shows the distribution of the demographic characteristics of the cases included in the evaluation. As shown in Table 1, there was a statistically significant difference between the age of the two groups ($p<0.05$). Patients in the diabetes group were older than the control group. There was no statistically significant difference between the two groups in terms of gender, BMI, and operation time ($p>0.05$).

Table 2 shows the distribution of the participants' bispectral index and oxygen saturation values at the start of the operation and every five minutes. When the table was examined, a statistically significant difference between the two groups was observed at the 5th and 10th minutes of the bispectral index ($p<0.05$). The bispectral index of the

Table 1. Demographic variables of patients

	Total	Diabetes group, (n=35)	Control group, (n=35)	p-value
	Median (min.-max.) or n (%)	Median (min.-max.) or n (%)	Median (min.-max.) or n (%)	
Age, year	**52 (23-69)**	**55 (35-68)**	**47 (23-69)**	**0.016**
Gender				0.332
Woman	41 (58.6)	23 (65.7)	18 (51.4)	
Man	29 (41.4)	12 (34.3)	17 (48.6)	
BMI, kg/m^2	29.3 (22.3-39.4)	29.3 (23-39.4)	29.2 (22.3-37.7)	0.888

min.: Minimum, max.: Maximum, BMI: Body mass index

control group was higher than that of the diabetes group. In terms of oxygen saturation, there was a difference between the two groups at the start and the 20-minute, with the control group having higher values than the diabetes group. There was no statistically significant difference between the two groups in the measurements of all other parameters (End-tidal CO_2, heart rate, blood pressure) every five minutes ($p>0.05$).

Table 3 shows the participants' post-operative medication dosages and pain severity distribution. The table revealed no statistically significant difference between the two groups in terms of pain or vomiting ($p>0.05$). When the two groups were compared, the control group's patients experienced more pain during the postoperative period, scoring a mean of 8 ($p=0.049$), 7 ($p=0.016$), 5 ($p=0.02$), 4 ($p=0.032$), and 2 ($p=0.014$) on the NRS, respectively, at 1, 2, 4, 8, 12, and 24 h. This difference was significant ($p<0.001$) (Table 3).

While there was a statistically significant difference in pain intensity over time and additional analgesic dosage between the two groups, the control group's pain severity was higher than the diabetes group in NRS scores ($p>0.05$).

The intensity of pain was the highest immediately following surgery and gradually decreased. In multivariable analysis, the group with diabetes was found to be strongly related to a much lower tramadol dose than the control group. In terms of additional analgesic dosage, while the control group used more than the diabetes group, the difference was not statistically significant ($p>0.05$).

In this study, the control group's age was statistically significantly lower and the NRS score was higher than the group with diabetes's. Covariance analysis was used to see if there was any difference in pain severity between the groups in terms of the effect of age and diabetes on pain severity. It was discovered that diabetics had lower NRS scores and

Table 2. Perioperative BIS and SpO_2 parameters

Characteristics (n=70)	Total	Diabetes group, (n=35)	Control group, (n=35)	p-value
	Median (min.-max.) or n (%)	Median (min.-max.) or n (%)	Median (min.-max.) or n (%)	
BIS (0. minute)	98 (90-99)	98 (90-98)	98 (92-99)	0.322
BIS (5. minute)	**47.5 (38-70)**	**44 (38-62)**	**48 (39-70)**	**0.021**
BIS (10. minute)	**46 (39-58)**	**45 (39-55)**	**48 (40-58)**	**0.044**
BIS (15. minute)	47 (39-60)	46 (40-60)	48 (39-58)	0.258
BIS (20. minute)	46 (40-61)	45 (40-61)	48 (40-60)	0.364
BIS (25. minute)	48 (40-60)	48 (40-59)	50 (40-60)	0.676
BIS (30. minute)	48 (40-60)	46 (40-59)	48 (40-60)	0.279
BIS (35. minute)	50 (40-60)	48 (40-60)	50.5 (40-56)	0.186
BIS (40. minute)	48 (40-70)	47 (41-70)	50 (40-58)	0.266
BIS (45. minute)	47 (40-67)	46 (40-67)	47.5 (40-59)	0.308
BIS (50. minute)	47 (39-55)	46 (40-55)	48 (39-55)	0.341
BIS (55. minute)	47 (40-54)	46 (41-50)	49 (40-54)	0.060
BIS (60. minute)	47.5 (40-55)	46 (41-55)	49 (40-52)	0.737
SpO_2 (0. minute)	**99 (95-100)**	**98 (95-100)**	**99 (96-100)**	**0.020**
SpO_2 (20. minute)	**99 (96-100)**	**99 (96-100)**	**99 (98-100)**	**0.021**

min.: Minimum, max.: Maximum, BIS: Bispectral index

Table 3. Postoperative pain scores and analgesic consumption amounts

Characteristics (n=70)	Total	Diabetes group (n=35)	Control group, (n=35)	p-value
	Median (min.-max.) or n (%)	Medyan (min.-max.) or n (%)	Medyan (min.-max.) or n (%)	
Total tramadol dose (mg)	**241 (135-300)**	**225 (160-300)**	**260 (135-300)**	**0.002**
Rescue analgesic consumption (n, %)				
1. hour	24 (34,3)	8 (22,9)	16 (45,7)	0.078
2. hour	10 (14,3)	2 (5,7)	8 (22,9)	0.084
8. hour	1 (1,4)	1 (2,9)	0 (0,0)	1,000
NRS 1. hour	**8 (0-10)**	**8 (0-10)**	**8 (4-10)**	**0.049**
NRS 2. hour	**6 (0-10)**	**5 (0-10)**	**7 (4-10)**	**0.016**
NRS 4. hour	**4 (0-10)**	**4 (0-9)**	**5 (0-10)**	**0.002**
NRS 8. hour	**2 (0-9)**	**2 (0-9)**	**4 (0-8)**	**0.032**
NRS 12. hour	**0 (0-7)**	**0 (0-7)**	**2 (0-6)**	**0.014**

min.: Minimum, max.: Maximum, NRS: Numeric rating scale

analgesic requirements regardless of age. Univariate analysis found no link between gender, BMI, or ASA class and postoperative pain.

Discussion

According to the findings, the patient with diabetes who underwent LC experienced less postoperative discomfort than those without diabetes. It was discovered that in both groups, the analgesic required was significant in the first 12 hours and that there was no further analgesic requirement after 12 hours.

Multimodal analgesia, particularly in the first 12 h, and then further analgesic medication as needed can be used to address post-operative pain in these patients when the ERAS protocol is used. Thus, the best balance in terms of cost-effectiveness is reached with the use of fewer analgesics, further decreasing postoperative problems and facilitating early recovery.

Despite the administration of the same analgesic regimen, there was considerable inter-individual heterogeneity in pain severity following each surgical method. Patients with diabetes' responses to painful stimuli differed from normal patients in the postoperative period. There are various findings regarding the level of postoperative pain after various surgical procedures performed in patients with diabetes. Berglund et al. (9) found that patients with diabetes had more pain (as measured by the visual analog scale for pain) and poorer functional outcomes 6 months and 1 year after arthroscopic rotator cuff surgery. Rajamäki et al. (16) identified DM as an independent predictor of persistent pain following hip or knee replacement. Another study by Reinstatler et al. (11) on patients with diabetes who had received inflatable penile prosthesis surgery due to erectile dysfunction has revealed that significant postoperative penile pain was more common in patients with hemoglobin A1c levels greater than 8% and resulted in more unplanned visits after discharge period.

Some medical conditions, such as diabetes, have been linked to increased narcotic dosage due to changes in pain perception compared to patients without such conditions.

Furthermore, up to one-fourth of patients with diabetes have co-occurring health problems such as cardiovascular disease, major depression, rheumatoid arthritis, and peripheral neuropathy (17). Neuropathy alters sensory perception and can cause sensations such as burning, tingling, numbness, and even hyperalgesia (18).

In contrast to the previous studies, our findings show that patients with diabetes have less post-operative pain and require fewer analgesics. This finding supports the hypothesis that postoperative pain levels may differ depending on the anatomical location, as stated in the literature (8). High ASA score, preoperative discomfort, young age, female gender, and anatomic site of surgery are all characteristics linked to higher postoperative pain and have been the subject of published research (7,8).

There are reports with findings consistent with our research. Lindberg et al. (19) observed, for example, that DM was related to decreased postoperative pain. Patients with diabetes experienced less postoperative pain than those without diabetes, which was linked to reduced sensation brought on by diabetic peripheral neuropathy, according to previous studies of patients undergoing heart surgery (20). Several factors, such as organ-specific surgery, may explain the variations in results. Approximately 30% of diabetics suffer from neuropathic pain (21). Nevertheless, diabetic neuropathy is associated with diminished sensory input, which may explain why our patients with diabetes experienced less postoperative pain (22).

After surgery, younger patients reported increased pain. According to a systematic review, there is a negative relationship between age and pain intensity, and postoperative analgesic use (7). Tighe et al. (8) observed that younger age was related to higher postoperative pain, on average by a half NRS unit every 10 years, when they retrospectively analyzed postoperative pain in various surgeries within the first 24 h following surgery. Lautenbacher et al. (23) discovered in a meta-analysis of the relationship between age, pain perception, and pain tolerance that mental pain perception does not change with age, but that older adults lose pain sensitivity due to an increase in pain thresholds. Opioid renal clearance reduced with age, which may lead to decreased pain in elderly people (24).

According to the current findings, there is already a need for greater analgesics to be administered to young patients on the day of surgery. Recent research indicated that older patients require a lower dosage of tramadol for postoperative pain management than younger patients do. These findings are in line with the findings of a study that showed postoperative pain ratings reduced with increasing age (25).

According to our findings, the mean age of those in the control group was significantly younger than those in the diabetes group, and mean-NRS-scores were also significantly higher, as reported in previous studies. When a statistical analysis was performed, it sufficiently said that the group with diabetes's NRS scores and analgesic requirements were lower, regardless of age.

The latest ERAS guidelines for postoperative analgesia following colorectal surgery state that the aim is to avoid opioids and use multimodal analgesia in conjunction with epidural analgesia (in open surgery) where needed (15). We would like to add to the ERAS recommendations that young patients require greater analgesia, and analgesia should be tailored because it is difficult to predict the intensity of postoperative pain..

Female sex and a high ASA class have been highlighted in various articles as reasons for postoperative pain (8,26,27).

Study Limitations

Our study had some limitations. It is single-center, and a relatively small number of patients are included in each cohort. Another limitation is that the patient's emotional states such as depression and anxiety, which may affect their pain thresholds, were not evaluated (26,27).

Conclusion

In this study, neither the presence of the ASA class nor the presence of female gender was connected with pain. As a consequence of this,

the notion that gender and ASA class affect post-LC pain levels is not supported by our data.

Ethics Committee Approval: Ethical committee approval was obtained from the Local Ethics Committee of University of Health Sciences Turkey, İstanbul Training and Research Hospital (approval number: 188, date: 17.06.2022).

Informed Consent: Their written consent was obtained.

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