Comparison of the Effects of Propofol and Dexmedetomidine Infusion on Sedation in the Recovery Room in Patients Undergoing Cholecystectomy

ABSTRACT
Aims: This study aimed to compare the effects of propofol and dexmedetomidine infusion on sedation in the Recovery Room in Patients Undergoing Cholecystectomy.
Methods: This randomized clinical trial was conducted on 71 patients scheduled for laparoscopic cholecystectomy in Yasuj in 2023-2024. Patients were randomly assigned to two groups: 35 received propofol and 36 received dexmedetomidine. The level of agitation was assessed using the Richmond Agitation-Sedation Scale (RASS) at (.) and 40 minutes after surgery by the researcher. Data analysis was performed using SPSS (version 27) software and statistical methods including Chi-square, independent t-test, and paired t-test. A significance level of **P < 0.05** was considered.
Findings: The results showed that at 40 minutes after the intervention, the mean agitation level in patients receiving dexmedetomidine **[0.22 (0.72)]** was lower than that of the propofol group **[0.63 (0.81)],** indicating better sedation. This difference was statistically significant (**p = 0.028).**
Conclusion: Dexmedetomidine may be recommended as a preferable option for anesthesia management in patients undergoing laparoscopic cholecystectomy.

Keywords: Propofol, Dexmedetomidine, Anesthesia, Laparoscopic Cholecystectomy, Agitation

Introduction

Surgery can be painful and stressful for patients due to complications. In the late 20th century, with the introduction of laparoscopic surgery, significant progress was made in reducing these complications (1). The use of laparoscopic surgery has reduced pain in patients and shortened the recovery period (2). Several factors influence the complications, pain, and level of restlessness of patients after surgery. One of these factors is the type of anesthetic used. The drugs used to induce anesthesia can induce endocrine, immunological, and metabolic responses in patients (3). Therefore, one of the key issues in modern anesthesia is the correct selection of anesthetic and its management for postoperative sedation to prevent possible complications in patients (4).

One of the most common drugs used for general anesthesia is propofol. This intravascular anesthetic is highly lipid-soluble. Its half-life is 2–8 minutes. After two and a half hours of anesthesia with this drug, patients are still excreting the drug and its metabolites for up to sixty hours. Less than one percent of the drug is excreted unchanged in the urine and only two percent is excreted in the stool (5). Propofol inhibits the release of acetylcholine in the hippocampus and prefrontal cortex. Its hypnotic activity is mediated by increasing the flow of chloral GABA by binding to the beta subunit of the GABA receptor. Propofol also has a depressant effect on spinal neurons. The feeling of well-being in patients after propofol is related to an increase in dopamine concentration in the nucleus accumbens (6, 7). In addition, propofol can be used to induce moderate to deep sedation during surgeries performed under spinal and epidural anesthesia, but in some patients, spinal or epidural anesthesia can cause anxiety, increased heart rate, or feelings of restlessness (6). One of the side effects of propofol is respiratory depression, and the most important effect of propofol is a decrease in arterial blood pressure during anesthesia induction, resulting in hemodynamic changes in the patient (8)

Another drug used to anesthetize patients is dexmedetomidine, an alpha-2 agonist that is mainly used in anesthesia and pain relief. Alpha-2 agonists have several advantages, including hypnotic, sedative, sympatholytic, analgesic, anti-anxiety, and norepinephrine-lowering properties without causing significant respiratory depression. Therefore, in recent years, alpha-2 agonists have been used in anesthesia practice due to the aforementioned properties. Its half-life is about 2 hours, which makes it a relatively short-acting drug. The drug is mainly excreted in the urine. (9,10) The positive effects of low-dose dexmedetomidine infusion have been reported in pain relief after laparoscopic cholecystectomy (11-13). Dexmedetomidine is commonly used as a sedative for patients in the intensive care unit and during surgery. It provides rapid sedative effects while maintaining respiratory function, which distinguishes it from other sedatives (14). It should be administered before induction of anesthesia to reduce patient anxiety and stress and can have a sedative effect similar to midazolam (15). In addition, dexmedetomidine facilitates analgesia and anesthesia in the

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patient and reduces the severity of postoperative pain and nausea (16,17) and has a more potent analgesic effect compared to propofol (18). However, this drug can lead to a decrease in arterial pressure and heart rate at lower doses and can cause hypertension at higher doses (19).
Studies by Yang & Gao (2021) (20), Verma et al (2024) (21) showed that dexmedetomidine alone has longer and greater sedative effects than propofol. However, in the study by Srivastava et al. (2015), propofol at a higher dose showed a sedative effect similar to dexmedetomidine (22). Given the significant progress in medical science, the use of drugs with minimal side effects in anesthesia is important. On the other hand, given the large number of anesthetic drugs in use, choosing a drug that has more sedation during anesthesia is important. Therefore, given the contradictory results of studies comparing the effects of these two research interventions, the present study was conducted to determine and compare the effects of propofol and dexmedetomidine infusion on sedation in the Recovery Room in Patients Undergoing Cholecystectomy.

Materials and Methods Design

The present study was a single-blind clinical trial conducted on patients undergoing cholecystectomy surgery at Shahid Jalil Hospital, Yasuj in 1402-1403, and was registered in the Iranian Clinical Trial Registration System with the number IRCT20111009007745N12.

Participants and sampling

The study samples were eligible patients undergoing cholecystectomy surgery that was performed laparoscopically. This study was conducted at Shahid Jalil Hospital, Yasuj in 1403-1402. Inclusion criteria included age over 18 years, patients who were candidates for elective laparoscopic cholecystectomy under general anesthesia, ASA class 1 and 2. Exclusion criteria were history of addiction, emergency surgery, pregnancy or breastfeeding, hypertension, chronic liver disease, diabetes, renal failure, endocrine problems, rheumatic diseases or malignancy, need for concomitant surgery, and recovery time was more than forty-five minutes.
Based on the results of similar studies (Dongare et al. (2021) (23), assuming the values of the parameters $s12$ = 38.44 and S22 = 51.928, and for α and β = 0.05 and 0.20, respectively, and for the mean difference d = 5, the sample size was 29. Considering a 10% dropout rate, the final sample size in each group was determined to be 32 patients.

$$n = \frac{\left(z_{1-\alpha/2} + z_{1-\beta}\right)^2 (s_1^2 + s_2^2)}{(d\ )^2}$$

Patients were randomly divided into two groups receiving propofol and dexmedetomidine using a random number table in Excel.

Instrument and Data gathering

In this study, a form was used to collect and record patient information. The first part of the form included demographic information such as age, gender, and clinical information of the patients such as history of underlying disease and medications. The second part is related to the outcomes of the intervention, namely the level of sedation of the patient in the recovery room.
The level of agitation and sedation of patients is measured based on the RASS (Richmond Agitation-Sedation Scale). The English version of this scale was developed by Ely et al (2003) at Virginia Commonwealth University in Richmond and is used to measure the level of consciousness and agitation or sedation of patients. This scale consists of 10 levels, which are graded from -5 (unawakenable) to 4 (aggressive). It can be assessed using three specific and simple steps and has precise criteria for determining the level of sedation and arousal. It considers the duration of eye contact after verbal stimulation as the main criterion for adjusting the level of sedation. Positive scores (4 to 1): indicate agitation and restlessness in various degrees from 4 aggressive aggressive to 1 restless. A score of zero indicates alertness and calmness. Negative scores (-1 to -5) indicate different degrees of sedation. -1 indicates "drowsiness and confusion" and -5 indicates "no response to any stimulus". Based on studies, this tool has the necessary validity and reliability to measure the level of restlessness of patients (24). In Iran, it was also translated into Persian by Taddihi et al. and its validity and reliability were confirmed (25).

Intervention

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In this study, the intervention was the administration of propofol and dexmedetomidine. The proposal was approved by the Research Ethics Committee of Yasuj University of Medical Sciences. Written informed consent was obtained from patients or their legal guardians to participate in the study. Confidentiality and confidentiality of patient information were observed. Patients were allowed to withdraw from the study at any time during the study. No cost was imposed on patients for the purpose of the study.
After the patients entered the operating room, standard monitoring including electrocardiography, pulse oximetry and non-invasive sphygmomanometer, capnometry of respiratory CO2 changes, and bispectral index (BIS) electroencephalography for monitoring brain status was started. For all patients, oxygenation with 100% O2 was performed by oxygen mask at a rate of 5 L/min for 3 minutes. Midazolam (0.05 mg/kg; Iran Shimi Daru Co.), fentanyl (2 µg/kg; Iran Abu Raihan Co.), sodium thiopental (4 mg/kg; Trita, Germany), and atracurium (0.5 mg/kg; Caspian Tamin) were also used for anesthesia induction. After anesthesia induction, morphine (0.1 mg/kg; Iran Darupakhsh Co.) was administered for analgesia. Endotracheal intubation was performed with a Macintosh laryngoscope with an appropriately sized endotracheal tube. Ventilation was adjusted to maintain ETCO2 (End-tidal carbon dioxide) between 35 and 40 mmHg. Intra-abdominal pressure was maintained at 14 mmHg during laparoscopic surgery. Depth of anesthesia was maintained within the target range of 45 to 50 based on the BIS index. Both groups received intravenous remifentanil (0.7 µg/kg/min) after intubation until the end of surgery. The drug infusion was stopped when the pneumoperitoneum was released. Residual neuromuscular block was managed with neostigmine (40 µg/kg) and glycopyrrolate (10 µg/kg). The surgical procedure used in both groups was the same, and patients were carefully monitored during the intraoperative and postoperative periods.
After the surgery, at the beginning of the recovery period, for sedation and sedation, one group of patients received propofol at a dose of 25-75 µg/kg/min (name of the pharmaceutical company) and the other group received dexmedetomidine at a bolus dose of 0.5-1 µg/kg and then a maintenance dose of 0.1-1 µg/kg/hour (Exir Pharmaceutical Company, Iran).

In this study, the outcome was sedation, which was assessed by the researcher at times zero, and forty minutes using the RASS index.

Blinding

The study was conducted in a triple-blind manner, and the patient, the data collector, and the results analyst were unaware of the type of medication received and the grouping. Blinding was performed in such a way that the person who performed the randomization and allocation of individuals to the groups did not know the patients and had no information about the patients' condition. The patients were also unaware of the medication they received. The preparation of the medications was performed by an anesthesiologist who had no role in the study. The questionnaire was completed by an anesthesiologist who was unaware of the drug group and the statistical analyst was unaware.

Analysis

Data analysis was performed using IBM SPSS version 27 statistical software. Normality of data was checked by Kolmogorov-Smirnov test. In quantitative variables, mean and/or median were used to describe the center of the data and standard deviation and/or interquartile range were used to describe the dispersion of the data. In qualitative variables, frequency and percentage were used to describe the data. Independent t-tests and chi-square test were used to compare quantitative and qualitative variables between two groups, respectively, and paired t-tests were used to compare within each group between different times. The significance level in the tests was set less than 0.05.

Findings

In this study, 71 patients, including 35 in group A (propofol) and 36 in group B (dexmedetomidine), participated and remained until the end of the study. Also, 44 patients were female (62%) and 27 patients were male (38%). There was no significant difference between the two groups in terms of gender and age (Table 1).
The level of agitation and sedation of the patients in the propofol group and the dexmedetomidine group was measured at (0) and (40) minutes after transfer to the recovery room.
The results showed that the mean and standard deviation of RASS at time zero in the propofol group was -0.03(0.75), which indicated that the level of sedation or anesthesia at this time was neither fully conscious nor fully calm. Also, at time 40, the mean increased to 0.63, which indicates a relative increase in the level of consciousness. This change presented that the sedative effect of the drug

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decreased over time. A paired t-test showed that this difference was significant between time points 0 and 40 (P=0.002). (Table2).

However, in the dexmedetomidine group, at time zero, the mean and standard deviation of RASS was -0.33 (0.76). This value presented a greater sedative effect of dexmedetomidine than propofol at time zero, because a more negative value showed a lower level of consciousness. At 40 minutes after surgery, the mean and standard deviation of RASS in the dexmedetomidine group increased from -0.33 (0.76) to 0.22 (0.72), indicated a relative increase in patients' consciousness during this time period, and this difference in score between times 0 and 40 was significant in this group (P=0.003) (Table 2).

Comparison of the mean RASS scores between the two groups of propofol and dexmedetomidine showed that the mean RASS score at time 0 was not significant between the two groups (P=0.09), but this score at time 40 minutes in the dexmedetomidine group was 0.22 (0.72) lower than that of the propofol group 0.63 (0.81)), and this difference was significant (P=0.028). (Table 3)

To determine whether these significant effects were the effect of time or group or the interaction effect of time and group, repeated measures analysis of variance test was used. The interaction effect of time by group was not significant (P=0.67). The effect of group was significant (P=0.009), with the most significant effect related to dexmedetomidine compared to propofol. However, the effect size was low (0.09). Also, the effect of time was significant, such that each of the two interventions had a higher level of sedation at 40 minutes after surgery compared to time zero (P=0.001) (table 4).

Discussion

Appropriate management of sedation during the postoperative recovery period remains one of the major challenges in anesthetic care. Selecting an optimal sedative agent plays a crucial role in enhancing patient outcomes, minimizing adverse effects, and improving satisfaction among both patients and healthcare providers. Accordingly, the present study compared **dexmedetomidine** and **propofol** in terms of their sedative duration during recovery in patient after cholecystectomy.

The findings of this study indicate that the mean RASS score in the dexmedetomidine group at time zero (arrival to recovery) and at 40 minutes postoperatively demonstrated a deeper sedative effect compared with the propofol group. At 40 minutes post-surgery, the mean RASS score was 0.22 in the dexmedetomidine group versus **0.63** in the propofol group, reflecting a faster return to consciousness in patients receiving propofol and a more sustained sedative effect in those given dexmedetomidine.

This observation can be explained by the pharmacological differences between the two agents. Dexmedetomidine is a selective α2-adrenergic agonist that exerts sedative effects primarily by reducing norepinephrine release in the locus coeruleus, resulting in sedation without significant respiratory depression—an important advantage over many other sedative agents (26). Conversely, propofol acts as a GABA-A receptor agonist, enhancing chloride influx and inhibiting neuronal activity. Its rapid onset and short half-life contribute to a faster recovery of consciousness (27).

Several studies have supported these findings. For instance, Bhutia and Rai (2017) reported that patients receiving dexmedetomidine experienced deeper and more prolonged sedation compared with those administered propofol**,** which is consistent with the results of the present study (28). Likewise, in the study by Yang and Gao (2021)**,** the combination of dexmedetomidine and propofol increased the overall duration of sedation; however, dexmedetomidine alone produced longer-lasting sedative effects than propofol, further aligning with the observations of the current study (23).

Moreover, Verma et al. (2024) demonstrated that patients who received dexmedetomidine exhibited greater sedation during the recovery phase, with a gradual and more uniform return of consciousness, whereas propofol led to a more rapid awakening. This finding also supports the conclusions of the present study (21).

Additionally, Alinaghimaddah et al. (2023) found that among patients undergoing cataract surgery, when comparing three groups receiving midazolam, propofol, and dexmedetomidine, the latter was the preferable sedative agent in individuals with hypertension and palpitations. This further reinforces dexmedetomidine's effectiveness in specific patient populations (29)

However, some studies have reported different results. In the study of Srivastava et al. (2015), it was found that in some patients, higher doses of propofol can have a similar sedative effect to dexmedetomidine, but more fluctuations in the level of sedation and faster recovery were observed (22). Therefore, this study can be considered inconsistent with the present study. This difference could be related to the difference in the dose and method of administration of the drugs. Also, the

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results of some studies indicate the effect of the time and dose of dexmedetomidine on pain, restlessness and hemodynamic status of patients (26). Also, in the study of Loie, no significant difference was shown between dexmedetomidine and propofol in sedation. Perhaps the reason for the difference is the different type of study, which was conducted as a retrospective cohort (30). In the study of Djaiani et al. (2016), it was also shown that the sedation score 24 hours after surgery was not significantly different between the two groups (31). Additionally, in the study by Shah et al. in the intensive care unit, the depth of sedation and recovery time were similar between the two groups with propofol and dexmedetomidine, but patients with propofol required more analgesics for analgesia (32). The difference in the results of these studies with the present study could be due to the different type of disease, samples size, and dose used.

The results of this study showed that dexmedetomidine produced greater sedation than propofol, although the effect size was not large and further studies are needed. These characteristics could make dexmedetomidine a more suitable option for patients requiring sustained sedation. In contrast, propofol, due to its faster onset of action and earlier return to consciousness, may be more useful in situations where rapid awakening is required.

However, the results of this study should be interpreted with some limitations in mind. These include the relatively small sample size, which may limit the generalizability of the results, the lack of examination of the long-term effects of these drugs after the patient is discharged, and the lack of assessment of the effects of the drugs in patients with specific conditions such as cardiovascular or renal disease. Also, the effect of adverse factors such as the patient's baseline condition, the amount of fluid therapy, and the use of adjuvant medications was not examined in this study, which could affect hemodynamic outcomes

Conclusions

According to the results of the present study, dexmedetomidine has a greater sedative effect compared to propofol and seems to be a more appropriate choice for patients who need longer sedation during the recovery period, although the difference was not large. However, in patients who need a faster return to the level of consciousness, propofol may be a better option. Therefore, if the results are repeated in other similar comparative studies, the results of this study can be suggested to improve the clinical conditions of patients. Therefore, future studies with larger samples by examining different clinical conditions and evaluating the long-term consequences of sedation can help to better understand the differences between these two drugs

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Conflict of Interest

The authors declare that they have no conflicts of interest

Author's Contribution

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Ethical Permissions

This study was registered with the Research Ethics Committee of Yasuj University of Medical Sciences with the ethics code YUMS.REC.1403.045. Participants were informed of the objectives of the study and written informed consent was obtained from them. In addition, they were assured that their personal information would remain confidential and would not be disclosed. Participants were explained that their participation and withdrawal from the study were voluntary. The Declaration of Helsinki was taken into account in all stages of the study.

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