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Original Article

# Comparison of recovery and side effects after optimal isoflurane/sevoflurane/desflurane anaesthesia with BIS monitoring in patients undergoing laparoscopic abdominal surgery

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## ABSTRACT

**Aims**: Rapid recovery of the patient after the surgery is important for the patient to gain consciousness quickly and full wakefulness is important for both anesthesiologist and for the patient. This becomes more important especially in daily surgeries such as laparoscopic surgery procedures. Rapid recovery of consciousness after extubating, spontaneous respiratory sufficiency, adequacy of protective airway reflexes minimizes respiratory side effects during recovery period. In patients under general anaesthesia, EEG activity reverts from low-voltage fast waveform to high-voltage slow waveform. Bispectral index (BIS) anaesthesia, as an EEG variant, is a simple and easy-to-use monitor that measures the depth of anaesthesia. With this monitor, it is easier to measure the depth of anaesthesia and evaluate the recovery. In our study, we aimed to evaluate the difference between recovery times and side effect rates after isoflurane/sevoflurane/desflurane anaesthesia.

**Methods**: 105 patients in ASA I-II risk group between 18-60 years of age whose elective laparoscopic cholecystectomy was planned in our hospital were included in our research. All patients were induced with 2 μg/kg of fentanyl, 2.5 mg/kg of propofol, 0.6 mg/kg of rocuronium for general anaesthesia. After intubation, 0.5-1.5% Isoflurane was given to group I, 1-4% sevoflurane to group II, and 2-6% desflurane to group III patients as inhaler agents.

**Results**: In patient groups for which demographic data do not have any statistically significant difference, monitoring with BIS reduces the amount of anaesthetic used in three groups and prevents intraoperative awareness. When compared between groups desflurane was the fastest recovered group with fastest rising BIS score due to the low blood/gas partition levels. However, contrary to our expectations, sevoflurane was not very different from Isoflurane. In addition, contrary to expected, the incidence of nausea after extubating was higher in this group. But at the end of the 1$^{st}$ hour, emetic symptoms were significantly higher in the sevoflurane group.

**Conclusion**: This study demonstrates that BIS monitoring allows for optimized anaesthetic depth control, resulting in faster recovery and fewer postoperative side effects. Among the agents compared, desflurane led to the fastest recovery, likely due to its low blood/gas partition coefficient. The findings support the use of BIS in laparoscopic procedures for improved recovery quality. Future research should explore cost-effectiveness and patient satisfaction metrics associated with BIS-guided anaesthesia.

**Keywords**: General anaesthesia, BIS monitoring, recovery

## INTRODUCTION

Laparoscopic surgery was first performed by Philipe Mouret Farnat in 1988. Intraoperative and postoperative complication rate is less than open surgery. It also reduces the length of hospital stay and cost. Due to the benefits it provides, it has been used at increasingly widespread rates in the world in approximately fifteen years. In laparoscopic surgical procedures, it is expected that the anaesthesia method to be chosen should provide the optimal depth of anaesthesia, few postoperative side effects and be cost effective. Anaesthetic agents with rapid onset of action, rapid recovery and short duration of action are preferred by anaesthetists in this type of surgery.

It is known that the depth of anaesthesia can be measured with EEG waves as a result of developing technologies.[1-3] In recent publications, it has been shown that the depth of anaesthesia can be measured by bispectral index (BIS) to titrate anaesthetic agents and reduce the amount of drugs used. By decreasing the amount of anaesthetic agents used, patients wake up faster and postoperative hospital stay is shortened. Side effects that may be caused by anaesthetic drugs can be observed less frequently since there is no need to use unnecessarily high doses of anaesthetic agents. The use of BIS is also one of the most important preoperative concerns of patients today.

Intraoperative wakefulness, which is one of the sources of anxiety, can be prevented. For this reason, BIS increases its preferability as it is an easy-to-use monitor that offers numerical evaluation.

Our aim in planning this study was to monitor laparoscopic cholecystectomy patients with BIS and to compare isoflurane, a medium-acting inhalation agent, with sevoflurane and desflurane, known to have a short duration of action, in terms of haemodynamic data, extubation, recovery, nausea-vomiting and side effects in the perioperative period and to compare which inhalation agent or agents provide more comfortable anaesthesia and anaesthetic costs.

## METHODS

### Ethics

The study was taken from the 2003 Faculty of Medicine Ankara University Specialization Thesis. Institutional approval was obtained. All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

### Patient Selection

105 patients in the ASA I-II risk group aged 18-60 years who were to undergo laparoscopic cholecystectomy in our hospital were included in our study. Exclusion criteria were as follows: -operation shorter than 20 min and longer than 150 min, -liver, kidney, endocrine dysfunction, -uncontrolled hypertension, -psychiatric disorder, -opioid hypersensitivity, -history of chronic opioid, benzodiazepine, clonidine use, and use up to 12 hours before surgery, -chronic alcohol and drug dependence, -pregnancy or breastfeeding at the time of operation. All patients were informed about the anaesthesia method to be applied before surgery and consent was obtained.

### Method of Anaesthesia

Pethidine 25 mg+atropine 0.5 mg was administered intramuscularly to all patients half an hour before surgery for premedication. When the patients were taken to the operating room, a venous line was routinely opened with a 20G intravenous bag from the back of the hand 0.9% NaCl infusion was started. Standard monitoring included 3-channel ECG, noninvasive blood pressure measurement with systolic/diastolic/average pressures, peripheral blood oxygen saturation and BIS monitoring (Aspect A-2000 monitor and disposable BIS sensor). Patients were then randomly divided into 3 groups.

After the baseline monitor values of the patients were recorded, all patients were preoxygenated with 100% oxygen for 3 min. For induction of anaesthesia, fentanyl 2µg/kg and propofol 2.5 mg/kg were administered to all patients as standard, and neuromuscular block was achieved with rocuronium 0.6 mg/kg after verbal stimulus response and loss of eyelash reflex. After adequate depth of anaesthesia and neuromuscular block were achieved, tracheal intubation was performed and anaesthesia maintenance was started. Nitrogenprotoxide+oxygen mixture was routinely administered with a fresh gas flow of 4 L/min. Afterwards, maintenance anaesthesia was performed with isoflurane 0.5-1.5% in group I (group F), sevoflurane 1-4% in group II (group S), and desflurane 2-6% in group III (group D).

The precense of eyelash and corneal reflexes, the precense of pupillary light reflex, eyeball movement, at least a 25% increase in blood pressure and heart rate compared to the initial value in response to the initialing surgery, sweating, tear formation physical findings such as movement, swallowing, eye opening , grimacing in the patient and/or a BIS score of 60 or higher were considered as alertness in the patient.

In the presence of anaesthesia (value of 60 and above), anaesthetic gas concentration was increased, If these findings persisted despite the adjustment, a controlled bolus of remifentanil (1 µg/kg) was administered as a controlled bolus if there was no improvement in the findings despite the increase.

Inhaled anaesthetic agents were discontinued at the end of the operation and the patient was ventilated with 100% oxygen. Neostigmine 40 µg/kg and atropine 10 µg/kg were administered intravenously for neuromuscular block antagonisation. After spontaneous respiration was achieved (10/min and above), extubation was performed. Extubation time and spontaneous eye opening time were recorded. Diclofenac 75 mg intramuscularly for postoperative pain and metoclopramide 10 mg intravenously for nausea were administered before extubation. Postoperative nausea/vomiting times were recorded and ondansetron 4 mg intravenously was administered in the presence of persistent vomiting.

Data collection times were recorded at 5 min intervals preoperatively, at the end of induction, after intubation, after surgical incision, intraoperatively, after extubation, and at 5 min intervals in the first hour of the postoperative recovery period.

Recovery was evaluated with modified aldrete recovery score, steward recovery score, Abramowitz emesis score and BIS value.

Postoperative side effects; hypo/hypertension, bradycardia, nausea/vomiting, tremor, pruritus, urinary retention, muscle rigidity were recorded during recovery.

### Statistical Analysis

The data were analysed using SPSS (SPSS for Windows 10.0 IL) for statistical analysis. One-way analysis of variance was used in the evaluation between groups and p<0.05 was considered statistically significant. The results obtained in this study are given as mean±standard deviation.

## RESULTS

No difference was found between demographic data, anaesthesia and surgical times in the three groups of patients included in the study (Table 1).

When the blood pressures of the patients were compared, we observed that group D patients had higher blood pressures both intraoperatively and postoperatively compared to the other groups. Systolic blood pressures were statistically significantly higher than the other groups, especially at intraoperative 5th minute, 15th minute and extubation (Table 2, Figure 1). however, blood pressure elevation was at a level that did not require medical intervention.

When the heart rates of the patients were compared, was found that the heart rates were significantly higher in group F patients at 25 min intraoperatively (group F; 93.9±15.9, group S; 84.4±12.9, group D; 83.7±13.8) and lower in group D patients at 10 min postoperatively (group F; 99.9±19.9, group S; 101±10.7, group D; 81.4±10.9).

When we compared peripheral oxygen saturation in group F patients after extubation, postoperative 5. min, At 10 min, we observed that it was lower than the other two groups (Table 3, Figure 2).

When the BIS scores were compared between the groups, we observed that the BIS score was least affected by the surgical incision in group F (group F; 46.2±9.8, group S; 51.4±6.4, group D; 49.5±7.9), and the BIS value increased the most in group S patients at 0 min after incision (group F; 47.9±6.5, group S; 53.8±5.6, group D; 47.4±9.6). At 0. min, we found that the BIS value increased the most in group S patients (group F; 47.9±6.5, group S; 53.8±5.6, group D; 47.4±9.3). We found that the BIS score measured after extubation and at 5 and 10 minutes postoperatively was significantly higher in group D (Table 4).

When the three groups were compared in terms of spontaneous respiration onset time, we found that group D had a significantly shorter time than the other groups in terms of spontaneous respiration onset (group F; 7.3±3.9, group S; 4.4±1.6, group D; 2.05±1.6). When extubation times were compared, extubation time of group D was shorter than the other groups (group F; 13.1±3.2, group S; 6.2±2.5, group D; 4.3±2.7). When the response time to postoperative verbal stimuli was compared, we found that the duration was

**Table 2.** Systolic blood pressure changes

| | Intraop 5th min | Extubation | Extubation 5th min | Extubation 15th min |
|---|---|---|---|---|
| Isoflurane | 122 | 125 | 134 | 127 |
| Sevoflurane | 125 | 126 | 127 | 129 |
| Desflurane | 134 | 142 | 142 | 131 |

Min: Minute, Inraop: Intraoperative

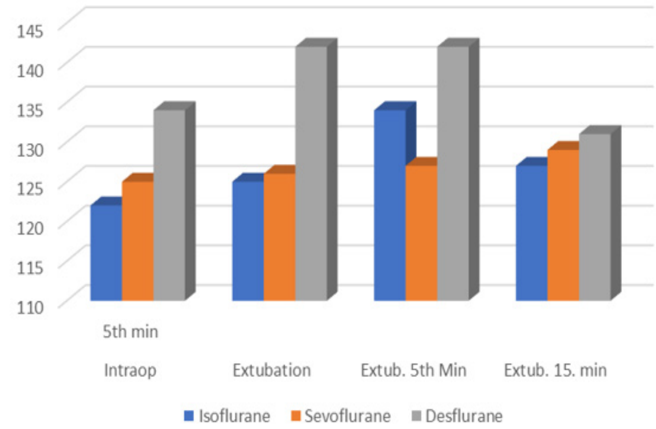


**Figure 1**. Systolic blood pressure changes between the three groups
(Pressure : mmHg/, time), Min: Minute, Inraop: Intraoperative, Extub: Extubation

**Table 3.** Evaluation of peripheral oxygen saturations in the first 15 min after extubation

| | After extubation | Postop 5th min | Postop 15th min |
|---|---|---|---|
| Isoflurane | 99.3 | 98.7 | 98.9 |
| Sevoflurane | 99.5 | 99.4 | 99.4 |
| Desflurane | 99.9 | 99.7 | 99.5 |

Min: Minute, Postop: Postoperative

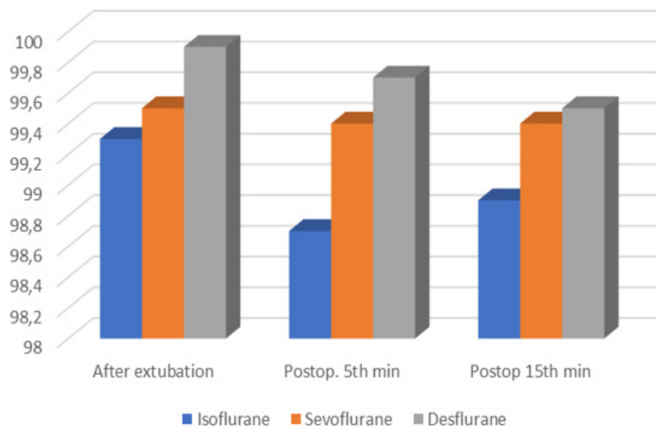


**Figure 2**. graComparison of peripheral oxygen saturations in the first 15 min after extubation
(Saturation %/, time), Min: Minute, Postop: Postoperative

**Table 1.** Demographic data

| Inhaler agent used | Age (years) | Height (cm) | Weight (kg) | Surgical time | Duration of anaesthesia |
|---|---|---|---|---|---|
| Isoflurane | 40.9±10.6 | 162.2±10.07 | 66.5±7.4 | 88±32.6 | 93.9±31.5 |
| Sevoflurane | 42.9±11.3 | 164.5±6.9 | 69.2±12.3 | 69.5±30.1 | 77.2±30.9 |
| Desflurane | 44.5±8.5 | 163.05±7.7 | 66.7±8.7 | 72.5±21.9 | 80.2±23.4 |

**Table 4.** Evaluation of significant differences in BIS value between groups

| | Surgical incision | 0 min incision | After extubation | Postop 5th min | Postop 15th min |
|---|---|---|---|---|---|
| Isoflurane | 46.2±9.8 | 47.9±6.5 | 54.4±11.4 | 70±13.7 | 79.2±12.8 |
| Sevoflurane | 51.4±6.4 | 53.8±5.6 | 56.4±8.2 | 67.3±13.7 | 81±7.4 |
| Desflurane | 49.5±7.9 | 47.4±9.3 | 67.9±13.04 | 89.4±8.9 | 94.8±11.2 |

BIS: Bispectral index, Min: Minute, Postop: Postoperative

significantly shorter in group D (group F; 25.2±8.5, group S; 13.7±4.6, group D; 9.8±6.2) (Table 5).

**Table 5.** Comparison of waking times of the three groups

| | Spontaneos breathing | Extub time | Verbal stimulus response | Continuous compilation |
|---|---|---|---|---|
| Isoflurane | 7.3±3.9 | 13.1±3.2 | 21.1±7.6 | 25.2±8.5 |
| Sevoflurane | 4.4±1.6 | 6.2±2.5 | 10.4±3.62 | 13.7±4.6 |
| Desflurane | 2.05±1.6 | 4.3±2.7 | 7.05±5.1 | 9.8±6.2 |

When the recovery scores between the groups were evaluated, Steward and Modified Aldrete scores were significantly faster in group D, whereas no significant difference was observed between groups F and S. In the comparison of Abramowitz emesis scores, we found that this rate was higher in group D, and it was higher in the same group at the 12th hour (group F; 0±0, group S; 0.3±0.4, group D; 0.5±0.3). Postop 24 hours, we found that 6 patients in group F, 14 patients in group S and 9 patients in group D needed antiemetic.

Sympathetic response to intubation occurred only in two patients in group F and remifentanil requirement occurred in two patients in the same group. In the comparison of the side effects, the rate was significantly higher in group D after extubation and higher in group S at 60 min postoperatively (Table 6).

**Table 6.** Comparison of side effects

| | After extub | Postop 5th min | Postop 15th min | Postop 30th min | Postop 60th min | Postop hour 2nd |
|---|---|---|---|---|---|---|
| Isoflurane | 0 | 2 | 2 | 4 | 0 | 2 |
| Sevoflurane | 0 | 4 | 6 | 4 | 6 | 2 |
| Desflurane | 4 | 4 | 6 | 2 | 2 | 0 |

Min: Minute, Postop: Postoperative

## DISCUSSION

Rapid recovery of patients from anaesthesia after surgical operations, rapid recovery of consciousness and full alertness are of great importance for the patient and anaesthetist as well as for the surgeon.[4] In order to evaluate these criteria and to optimise the depth of anaesthesia, BIS is an easy-to-use and understandable monitoring method.[5] The use of inhaler agents is reduced with balanced anaesthesia given by keeping the BIS score between 40-60.[6,7] In forms of anaesthesia using TIVA (total intravenous anaesthesia), it reduces propofol consumption and decreases the cost.[7,8] In our study, we found that adjusting the depth of anaesthesia with BIS monitoring was easy and comfortable.

No complete correlation has been observed between the BIS value measured during anaesthesia and the haemodynamic data of the patient.[9] While the BIS value indicates deep anaesthesia, blood pressure increase or heart rate increase may be observed. In a study by Hug et al,[9] a barbiturate-based anaesthesia induction was applied in patients, and while the BIS value indicated deep anaesthesia, elevated blood pressure was found in patients. The sympathetic response that occurs during the surgical procedure is related with the autonomic nervous system and is not reflected in the BIS score because the stimulus cannot reach the cortex during general anaesthesia.[11] During our study, intraoperative at 25 min, we found that the BIS score of the patients in group F was 47 and the heart rate was 93±9.8. We found that the patients in group D were more hypertensive in the intraoperative period compared to the other groups, although there was no awakening.

In our study, contrary to other studies, the incidence of nausea/vomiting was higher in group D than in group S after extubation. While these rates were equalised between the two groups at the 5th postoperative minute, we found that the incidence of nausea/vomiting was higher in group S in the following period in proportion to other studies.

Since group D patients had the lowest blood/gas partition coefficient in the recovery process, we found it to be faster. In group S, unlike other studies, we found it close to group F. However, peripheral oxygen saturation was lower in group F patients than in other groups. Burrow et al.[12] randomly divided a patient group of 345 patients into two groups, one group was monitored with BIS and given general anaesthesia and the other group was given standard anaesthesia. They found that patients monitored with BIS were more active and awake in the recovery process than the non-monitored group. In a similar study, Cooper and Epstain[13] again found that extubation was faster in patients monitored with BIS, but when they looked at recovery times, they did not find any difference from non-monitored patients. In our experience, considering our previous anaesthesia experiences, we observed that monitoring with BIS provided faster recovery. In a similar study, Bannister et al.[14] performed a BIS monitoring study in 202 paediatric patients. In pediatric patients, similar to adult patients, they observed faster recovery in children monitored with BIS. They also found that sevoflurane use decreased up to 25% in these patients.

In a study by Olofsen[15] in which isoflurane and sevoflurane were compared in terms of induction and extubation, no significant difference was found between these two inhaler agents and recovery times were similar. In our groups, although we observed shorter recovery times in the sevoflurane group, no significant difference was found in statistical analysis.

Again, the time for eye opening and verbal response after sevoflurane use was found to be 5±2 min in Tang's study, 8.4 min in Elbert's study, 7.5±0.5 min in Frink's study and 8 min in Cartillon's study.[16] In Palvin's[17] study, which was also performed for this purpose, this time was found to be 8.7±4 min. Galvin and Pavlin also found that the amount of agent used decreased with the use of BIS.[18] In our study, we found that the recovery time of patients in whom sevoflurane was used was 10.4±3.6 min, which was longer than in other studies. We think that the longer recovery time in our patients was related with the use of neuromuscular blockers in our study.

Xioguag conducted a study with sevoflurane and desflurane and found no difference between postoperative nausea/vomiting levels, and in the same study, the researchers also found no difference between postoperative side effects.[20] In the same study, the response time to verbal stimuli was significantly shorter in the desflurane group (8±2.7 min) than in the sevoflurane group (12.5±7.4). In contrast to Xioguag's findings, we found a higher rate of nausea/vomiting in our patients. Again, we found a higher rate in the desflurane group after extubation and in the sevoflurane group at 30 minutes postoperatively in our patient groups.

Röbke[20] tried to provide balanced anaesthesia in patients with BIS monitoring in the use of desflurane and found that desflurane use could be reduced in this way. In the same study, they found that none of the patients were awake in the postoperative investigation. Again in this study, they could not titrate a dose that provided complete EEG suppression with surgical stimulus.[21] Johansen[21] investigated the use of desflurane for the same purpose and found the same rate of decrease in the use of desflurane in Johansen in correlation with the other study. In the same study, the mean recovery time was found to be 10 minutes. In Song's study, the recovery time was found to be 13.4±4 min.[22] In our study, although we provided a deeper anaesthesia than Song's study, we found the recovery time to be 9.8 min.

In his study on intraoperative wakefulness, O'Connor[22] found 50% wakefulness rate in their study with BIS monitoring and based on this, they argued that it is not clear whether the BIS value is sufficient to measure the depth of anaesthesia. Again in this study, they argued that monitoring of each patient with BIS increased the cost. In the same direction, Mychaskiw[23] presented a 28-year-old coronary by-pass patient who was intraoperatively awake while BIS showed adequate depth of anaesthesia, and we did not find intraoperative awakening in any patient in our study. We were able to achieve optimal depth of anaesthesia in all patients, we also ensured rapid recovery and length of stay in the hospital, and we observed that postoperative anaesthesia-related side effects were less. We think that BIS monitoring plays an important role in increasing the comfort of anaesthesia in anaesthesiologist and patient, but we also think that it may bring extra burden in terms of cost due to the price of disposable sensors of the monitor.

## CONCLUSION

In our patient groups in which demographic data did not show statistically significant differences, the use of BIS decreased the amount of inhaler agents used and prevented intraoperative awareness. In our opinion, BIS is a very suitable method for measuring the depth of anaesthesia. This study demonstrates that BIS monitoring allows for optimized anaesthetic depth control, resulting in faster recovery and fewer postoperative side effects. Among the agents compared, desflurane led to the fastest recovery, likely due to its low blood/gas partition coefficient. The findings support the use of BIS in laparoscopic procedures for improved recovery quality. Future research should explore cost-effectiveness and patient satisfaction metrics associated with BIS-guided anaesthesia.

## ETHICAL DECLARATIONS

### Ethics Committee Approval

The study was taken from the 2003 Faculty of Medicine Ankara University Specialization Thesis. Institutional approval was obtained.

### Informed Consent

All patients signed and free and informed consent form.

### Referee Evaluation Process

Externally peer-reviewed.

### Conflict of Interest Statement

The authors have no conflicts of interest to declare.

### Financial Disclosure

The authors declared that this study has received no financial support.

### 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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