Original Article

A prospective randomized double-blind study to compare the early recovery profiles of desflurane and sevoflurane in patients undergoing laparoscopic cholecystectomy

Gauri R. Gangakhedkar[1,2], Joseph N. Monteiro[2]

[1]Department of Anaesthesiology, Seth G.S. Medical College and K. E. M. Hospitals, [2]Department of Anaesthesiology, P.D. Hinduja National Hospital and MRC, Veer Savarkar Marg, Mahim, Mumbai, Maharashtra, India

Abstract

Background and Aims: General anesthesia using agents like Desflurane or Sevoflurane are beneficial for early recovery especially for ambulatory procedures. The aim of this randomised controlled double-blind study was to compare the early recovery profiles of sevoflurane and desflurane in patients undergoing laparoscopic cholecystectomy.
Material and Methods: ASA I, II patients, undergoing laparoscopic cholecystectomy were randomly assigned to receive desflurane (n = 30) or sevoflurane (n = 30), using Bispectral Index System (BIS) to determine the depth of anaesthesia. An independent adjudicator, who was blinded to the agent used, recorded the events during the recovery phase. The time required for extubation, eye opening, verbal response and achievement of a modified Aldrete score of 9 were recorded.
Results: The time required for extubation and for eye opening was significantly shorter in the Desflurane group as compared to the Sevoflurane group [9.1 min ± 5.0 versus 12.5 min ± 7.1, P = 0.049 and 10.1 min ± 5.2 versus 6.3 min ± 4.0, P = 0.008]. Verbal Response also occurred significantly faster in the Desflurane group [12.7 min ± 5.4 versus 8.7 min ± 4.7, P = 0.002]. A significantly higher mean modified Aldrete score was seen at extubation [7.1 ± 0.6 vs 6.0 ± 0.8, $P < 0.001$] in the Desflurane group, which also achieved a modified Aldrete score of ≥9 significantly sooner [11.1 min ± 4.6 versus 17.8 min ± 6.9, $P < 0.001$] than the Sevoflurane group. The frequency of adverse effects was not significantly different in either of the groups.
Conclusion: The time required for early recovery from anaesthesia, was significantly shorter in the Desflurane group compared to the Sevoflurane group.

Keywords: Ambulatory, anesthesia, desflurane, recovery, sevoflurane

Introduction

Ambulatory surgeries enable patients to resume oral intake within a few hours after surgery, to be ambulatory at discharge, to resume their daily activities, and even go back home on the same day as the surgery. This provides great benefits to not only the patients but also healthcare providers and hospitals. With an increasing use of minimal invasive procedures, a large variety of procedures are now being carried out as ambulatory surgeries; laparoscopic cholecystectomy is one such procedure. Mortality and major morbidity associated directly with ambulatory surgery have a very low incidence,[1] and there are several important advantages of ambulatory surgery when compared with inpatient surgeries, such as a lower rate of cancellations, and reductions in waiting times, hospital costs, and the risk of nosocomial infection.[2]

Address for correspondence: Dr. Gauri R. Gangakhedkar, 13/14, Chandangad Apartments, Next to Rahul Nagar, Near Karve Putala, Kothrud, Pune, Maharashtra, India.
E-mail: gauri2903@gmail.com

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Although local and regional anesthesia techniques are increasingly used in the ambulatory setting because they allow a more rapid recovery, general anesthesia is still the most common anesthetic technique. Rapid and shorter-acting anesthetic drugs, analgesics, and muscle relaxants have now been developed, whose pharmacological profiles make them ideally suited for use in the ambulatory setting.

Sevoflurane and desflurane are inhaled anesthetic agents with low blood/gas solubility (0.69 and 0.42, respectively) and low fat/blood solubility (48 and 27, respectively), making them suitable for ambulatory anesthesia.[3] Out of the two, desflurane has the lower blood/gas and fat/blood solubility. This allows anesthetic alveolar concentration to remain near inspired concentration permitting a rapid and large change, with precise control in the anesthetic depth, and early awakening.

Although there are many studies to prove the efficacy of desflurane with respect to recovery from anesthesia, very few of them are double-blinded trials. We, therefore, compared the early recovery profiles between patients who received desflurane and those who received sevoflurane while undergoing laparoscopic cholecystectomy.

Material and Methods

The trial was registered with CTRI (CTRI/2017/12/010853). After approval from the Institutional Ethics Committee, 60 ASA I and II patients between the ages of 20 and 60 years, who were scheduled to undergo laparoscopic cholecystectomy were enrolled for this prospective, randomized, double-blind comparative study. Using a computer generated table, patients were randomized into two groups receiving either sevoflurane [1-2%](Group S) or Desflurane [3-6%](Group D) as the anesthetic agent for maintainance.

Our exclusion criteria consisted of patients who had a history of drug allergy or abuse, morbid obesity, hiatal hernia, those with moderate to severe cardiopulmonary, hepatic, renal dysfunction, endocrine or neurological dysfunction, and patient refusal. Patients in whom intraoperative conversion of procedure from laparoscopic to open was required were to be excluded during analysis. Written informed consent was administered to the patients by either the principle investigator or coinvestigator.

Inside the operating room, electrocardiogram monitor, pulse-oximeter, and noninvasive blood pressure monitor were attached. Bispectral index strip (BIS) (Aspect Medical Systems Inc., Newton, MA) was attached to the forehead. A peripheral nerve stimulator was attached to the nondominant hand to record train of four responses. Baseline hemodynamic details, BIS, and Train of Four readings were recorded before induction of anesthesia. Intravenous cannulation was done using a 20 G/18 G cannula on the nondominant hand and balanced salt solution was started. All the patients received intravenous fentanyl citrate 2 μg/kg and glycopyrrolate 0.2 mg after preoxygenation. Anesthesia was induced with intravenous propofol 2 mg/kg, neuromuscular blockade was achieved with intravenous atracurium besylate 0.5 mg/kg. The airway was secured with an appropriately sized endotracheal tube, and the patient was ventilated using a closed circuit and a mechanical ventilator (Datex Ohmeda Avance S/5). Temperature monitoring, end tidal capnometry, and anesthetic gas monitoring were instituted via a Phillips Intellivue MP40 mutli-para monitor. The patients were ventilated to maintain an $EtCO_2$ of 32–36 mm Hg using pressure-controlled ventilation. The BIS values seen at induction were recorded. The patients subsequently received either sevoflurane 1–2% or desflurane 3–6% with 50% air in oxygen with fresh gas flows at 1 Liter/minute. The maintenance dose of the anesthetic agents was titrated to maintain a Bispectral index [BIS] value of 40–60. Additional bolus doses of fentanyl citrate 0.5–0.75 μg/kg were administered to control acute hemodynamic changes not responding to a 50% increase in inspired concentration of the volatile drug, so as to maintain MAP within 20% of the baseline values. Muscle relaxation was maintained using intermittent doses of atracurium besylate at appropriate intervals with TOF monitoring. Intra-abdominal pressures were maintained between 10 and 14 mm of Hg. Analgesia in the form of intravenous paracetamol 15 mg/kg body weight, 0.1 mg/kg body weight of ondansetron, and 40 mg of inj. pantoprazole to prevent gastric acid secretion were given to all patients. The primary anesthetic was discontinued after the last skin suture was placed. Port site infiltration was given with 0.25% bupivacaine. An independent adjudicator (principal investigator or coinvestigator), who was not a part of the team that administered anesthesia, was called in after the agent was switched off and the gas monitoring was turned off, so that he/she was blinded to the agent that was being used for maintenance of anesthesia.

The neuromuscular block was reversed with intravenous glycopyrrolate 0.008 mg/kg and neostigmine 0.05 mg/kg on achieving a TOF of ≥3. The blinded independent adjudicator then recorded the hemodynamic variables, at BIS readings at skin closure, dressing, reversal, extubation and then at 1, 3, 5, 10, 15 minutes, and further on until the patient achieved an Aldrete score of 9. The adjudicator also recorded the modified Aldrete score at extubation and then on till the patient achieved a modified Aldrete score of 9. The time of the first incidence of eye opening, that of first verbal response and any untoward events if any did occur, in the form of excessive secretions, coughing, or bronchospasm were also recorded.

Only on achieving an Aldrete score of ≥9, patients were shifted to the post-anesthesia care unit (PACU), where they were nursed in propped up position. Oxygen was administered via Hudson mask at 4–6 L/minute.

Statistical analysis

Data analysis was done using SPSS Software version 15. Qualitative data are presented with the help of frequency and percentage tables and association among study group was assessed with the help of Chi-square test and independent *t*-test. *P* value <0.05 was taken as significant.

Results

The baseline characteristics of patients, including age, sex, body mass index, and ASA (American Society of Anesthesia) classification, were comparable in both the groups. The total duration of surgery also did not differ significantly between the two groups [Table 1].

None of the patients required an intraoperative conversion of the procedure from laparoscopic to open cholecystectomy. Since there was insignificant difference between mean and median values in baseline characteristics except for gender, rest of the parameters recorded in the above table, are given in mean values.

The BIS monitoring revealed comparable preoperative values but significantly lower values at induction in the desflurane group as compared with the sevoflurane group [44.8 ± 11.8 vs 51.6 ± 13.3, P = 0.018]. Though comparable values were again seen at reversal and extubation, significantly higher values of BIS were seen in the desflurane group at 1, 3, and 5 minutes postextubation [91.5 ± 4.0 vs 87.6 ± 4.8, P = 0.002; 95.1 ± 2.3 vs 90.2 ± 4.6, P < 0.005; 98.0 ± 0.9 vs 93.8 ± 3.2, P = 0.001].

The mean modified Aldrete score was significantly higher at extubation in the desflurane group [7.07 ± 0.6 versus 6.0 ± 0.8, P < 0.001]. The modified Aldrete scores remained significantly higher in this group at 1, 3, and 5 minutes postextubation [8.2 ± 0.7 vs 6.5 ± 0.6, P < 0.001; 8.8 ± 0.5 vs 7.4 ± 0.7, P < 0.001; 9.0 ± 0.0 vs 8.2 ± 0.9, P = 0.036].

Various times recorded as recovery variables are given in Table 2.

Though complications such as secretions, coughing, and bronchospasm occurred more frequently in the desflurane group, it was not statistically significant [Table 3].

Discussion

One of the most common procedures to be carried out laparoscopically is laparoscopic cholecystectomy.[4] Since the procedure is associated with very little postoperative morbidity, these patients can potentially recover much earlier and be discharged from hospital care. The pharmacokinetics of desflurane and sevoflurane favor better intraoperative control of anesthesia and a rapid postoperative recovery. They have significantly lower blood/gas partition coefficients than isoflurane (1.4) or halothane (2.4). The lower fat/blood partition coefficient of desflurane, should favor its early elimination from the body resulting in early recovery.[3]

There are a few double-blind trials reported in the literature comparing desflurane and sevoflurane. Our randomized double-blinded study showed both statistically and clinically that the early recovery profile of desflurane was indeed better

Table 1: Patient Demographics and Duration of Surgery

Parameter	Group D (n=30)	Group S (n=30)	P
Gender (M/F)	9/21	13/17	<0.05
ASA (I/II)	13/17	13/17	<0.05
Age (years)	46.9±11.4	50.9±13.8	<0.05
Weight (kg)	67.0±12.1	69.6±11.6	<0.05
Height (m)	1.6±0.1	1.6±0.1	<0.05
BMI (kg/m^2)	25.9±3.7	26.6±3.6	<0.05
Duration of surgery (min)	77.0±19.0	79.7±25.9	<0.05

**Age, Weight, Height, BMI and Duration of Surgery are have values in the form - mean ± standard deviation*

Table 2: Recovery variables

Recovery variables	Group D	Group S	CI	P
Time from skin closure to extubation (min)	9.1±5.0	12.5±7.1	>95%	0.049
Time for eye opening (min)	6.7±4.0	10.1±5.2	>95%	0.008
Time for Verbal response (min)	8.9±4.7	12.7±5.4	>95%	0.001
Time for Modified Aldrete score >9 (min)	11.1±4.6	17.8±7.0	>95%	<0.001

**Values in mean ± standard deviation*

Table 3: Complications

	Group D	Group S
Yes	4 (13.3%)	1 (3.3%)
No	26 (86.7%)	29 (96.7%)

**Using the Fisher's Exact test, P=0.353, hence the difference between the complications occurring in both groups is not statistically significant* than that of sevoflurane. The data are consistent with the faster kinetic profile of desflurane and its faster washout from the body.

We used BIS to ensure adequate depth anesthesia. BIS values between 40 and 60 correlate well with clinical endpoints of sedation and loss of consciousness and is relatively agent independent.[5] Though the BIS values in both groups were comparable in the preoperative period, the BIS value at induction was significantly lower in the desflurane group suggestive of a faster wash in for desflurane. On continuing to monitor BIS values in the early recovery period, we found that the BIS values remained consistently and significantly higher in the desflurane group after the agent was turned off. These patients achieved preoperative BIS values sooner than their counterparts who received sevoflurane.

Unlike Suzuki *et al*.[6] we noted that the patients receiving desflurane got extubated sooner than those receiving sevoflurane. It is possible that this difference arose because the anesthetists in that study were allowed to titrate the inhalational agent based on their clinical judgment. Neither MAC (Minimum Alveolar Concentration) nor BIS were used as markers of depth of anesthesia. Interoperator bias is also likely since they did not have a single anesthetist administering anesthesia to all the patients.

In contrast to the results found by Pavlin *et al*.,[7] we found that the patients who received desflurane appeared to recover faster by achieving a modified Aldrete score of 9 sooner. This could be attributed to the fact that their patients received nonuniform anesthesia in the form of induction agents, opioids, and local anesthetic blocks.

Karlsen *et al.*[8] found no difference in the early recovery profiles between patients receiving desflurane, sevoflurane, and isoflurane; however, their trial was open in the preoperative period, so it is possible that there was a bias in selecting patients to a particular group.

Though Tarazi *et al.*[9] in a double-blinded study reported contradictory findings, their study used neither BIS monitoring nor TOF to guide the maintenance of anesthesia.

Vallejo *et al*. did not conclude the same at the end of their double-blinded trial comparing the two agents.[10] While their study was double-blinded like ours, they used MAC equivalents to decide depth of anesthesia. The use of BIS reduces anesthetic requirement[11] and reduces early recovery time;[12,13] which probably resulted in the difference of result.

Our results are supported by a number of previous studies;[14-24] out of which only a few are double blinded. They include studies by Kim *et al*., White *et al*., and La Colla *et al*. that differ from our study design. Kim *et al*. used MAC equivalents to titrate depth of anesthesia instead of BIS, whereas White *et al.* used BIS monitoring and their target was to achieve an MAC of 0.72 for sevoflurane and 0.8 for desflurane. La Colla *et al*. had a study design that was similar to ours; in fact, they used remifentanil and cis-atracurium to shorten the period required for recovery; however, unlike our study, their patient population included patients undergoing an open procedure, which lasted for 180 min on an average.

While the number of patients who had respiratory complications (excessive secretions, coughing, and bronchospasm) in the periextubation period was higher in patients in whom desflurane was used, the number is not statistically significant. This finding was supported by a number of studies.[14,15,20]

However, our study has certain limitations. Our patient population did not include geriatric patients or obese patients, who are more likely to benefit from a faster recovery from anesthesia. Our study design did not include a follow-up to see if the benefits of early recovery from anesthesia extended in to the intermediate and late recovery period.

Conclusion

We conclude that the early recovery profile of desflurane is better than that of sevoflurane in patients undergoing laparoscopic cholecystectomy. This enhanced early recovery may translate into a faster discharge readiness from the PACU.

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Conflicts of interest
There are no conflicts of interest.

References

1. Shnaider I, Chung F. Outcomes in day surgery. Curr Opin Anaesthesiol 2006;19:622-9.
2. Smith I, Cooke T, Jackson I, Fitzpatrick R. Rising to the challenges of achieving day surgery targets. Anaesthesia 2006;61:1191-9.
3. Eger E. I, II New inhaled anesthetics. Anesthesiology 1994;80:906-22.
4. Wilmore DW, Sawyer F, Kehlet H, Management of patients in fast track surgery. BMJ 2001;322:473-6.
5. Sandler NA. The use of bispectral analysis to monitor outpatient sedation. Anesthesia Progress 2000;47:72-83.
6. Suzuki T, Kurazami T, Ueda T, Nagata H, Yamada T, Kosugi S,

et al. Desflurane anesthesia worsens emergence agitation in adult patients undergoing thyroid surgery compared to Sevoflurane anesthesia. JA Clin Rep 2017;3:36.
7. Pavlin JD, Souter KJ, Hong JY, Freund PR, Bowdle TA, Bower JO. Effects of bispectral index monitoring on recovery from surgical anesthesia in 1,580 inpatients from an academic medical center. Anesthesiology 2005;102:566-73.
8. Karlsen KL, Persson E, Wennberg E, Stenqvist O. Anaesthesia, recovery and postoperative nausea and vomiting after breast surgery. A comparison between desflurane, sevoflurane and isoflurane anaesthesia. Acta Anaesthesiol Scand 2000;44:489-93.
9. Tarazi ME, Philip BK. A comparison of recovery after sevoflurane or desflurane in ambulatory anesthesia. J Clin Anesth 1998;10:272-7.
10. Vallejo MC, Sah N, Phelps AL, O'Donnell J, Romeo RC. Desflurane versus sevoflurane for laparoscopic gastroplasty in morbidly obese patients. J Clin Anesth. 2007;19:3-8.
11. Muralidhar K, Banakal S, Murthy K, Garg R, Rani GR, Dinesh R. Bispectral index-guided anaesthesia for off-pump coronary artery bypass grafting. Ann Card Anaesth 2008;11:105-10.
12. Punjasawadwong Y, Boonjeungmonkol N, Phongchiewboon A. Bispectral index for improving anaesthetic delivery and postoperative recovery. Cochrane Database Syst Rev 2007;CD003843. Review. Update in: Cochrane Database Syst Rev 2014;6:CD003843. PubMed PMID: 17943802.
13. Punjasawadwong Y, Phongchiewboon A, Bunchungmongkol N. Bispectral index for improving anaesthetic delivery and postoperative recovery. Cochrane Database Syst Rev 2014;CD003843. doi: 10.1002/14651858.CD003843.pub3.
14. Dalal KS, Choudhary MV, Palsania AJ, Toal PV. Desflurane for ambulatory anaesthesia: A comparison with sevoflurane for recovery profile and airway responses. Indian J Anaesth 2017;61:315-20.
15. Kim E-H, Song I-K, Lee J-H, Kim HS, Kim HC, Yoon SH, *et al*. Desflurane versus sevoflurane in pediatric anesthesia with a laryngeal mask airway: A randomized controlled trial. Medicine (Baltimore) 2017;96:e7977.
16. Gupta P, Rath GP, Prabhakar H, Bithal PK. Comparison between sevoflurane and desflurane on emergence and recovery characteristics of children undergoing surgery for spinal dysraphism. Indian J Anaesth 2015;59:482-487.
17. Kaur A, Jain AK, Sehgal R, Sood J. Hemodynamics and early recovery characteristics of desflurane versus sevoflurane in bariatric surgery. J Anaesthesiol Clin Pharmacol 2013;29:36-40.
18. Jindal R, Kumra VP, Narani KK, Sood J. Comparison of maintenance and emergence characteristics after desflurane or sevoflurane in outpatient anaesthesia. Indian J Anaesth 2011;55:36-42.
19. Magni G, Rosa IL, Melillo G, Savio A, Rosa G. A comparison between Sevoflurane and desflurane anesthesia in patients undergoing craniotomy for supratentorial intracranial surgery. Anesth Analg 2009;109:567-71.
20. White PF, Tang J, Wender RH, Yumul R, Stokes OJ, Sloninsky A, *et al*. Desflurane versus sevoflurane for maintenance of outpatient anesthesia: The effect on early versus late recovery and perioperative coughing. Anesth Analg 2009;109:387-93.
21. La Colla L, Albertin A, La Colla G, Mangano A. Faster wash-out and recovery for Desflurane versus Sevoflurane in morbidly obese patients when no premedication is used. Br J Anaesth 2007;99:353-8.
22. Mahmoud NA, Rose DJ, Laurence AS. Desflurane or sevoflurane for gynaecological day-case anaesthesia with spontaneous respiration? Anaesthesia. 2001;56:171-4.
23. Naidu-Sjösvärd K, Sjöberg F, Gupta A. Anaesthesia for videoarthroscopy of the knee. A comparison between Desflurane and sevoflurane. Acta Anaesthesiol Scand 1998;42:464-71.
24. Nathanson MH, Fredman B, Smith I, White PF. Sevoflurane versus desflurane for outpatient anesthesia: A comparison of maintenance and recovery profiles. Anesth Analg 1995;81:1186-90.