Original Article

Comparative study of recovery of airway reflexes and cognitive function following sevoflurane versus desflurane anaesthesia

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ABSTRACT

Background and Aims: Sevoflurane and desflurane have almost similar blood-gas solubility but recent studies suggest that desflurane compared to sevoflurane leads to faster recovery of airway reflexes, but the recovery of cognitive function varies significantly. We conducted this study to compare the times of recovery from anaesthesia following desflurane versus sevoflurane anaesthesia. **Methods:** This randomised double-blinded study was conducted on 60 patients of American Society of Anesthesiologists (ASA) classification I–II, age between 18 and 60 years with body mass index (BMI) $\leq$30 kg/m^2 who underwent elective cholecystectomy. A standard general anaesthesia protocol was followed with either sevoflurane (group A = 30 patients) or desflurane (group B = 30 patients) along with bispectral index and neuromuscular monitoring. Following extubation, tests for recovery of airway reflexes and cognitive function were conducted and various time intervals were noted. Statistical analysis was carried out using Statistical Package for Social Sciences (SPSS) standard software version 17. **Results:** The mean time from first verbal response to first passing the swallowing test was comparable in both the groups (5.50 ± 3.45 vs. 4.10 ± 3.42 min, *P* value = 0.120). Patients receiving desflurane showed faster response to verbal commands (5.93 ± 4.13 vs. 8.20 ± 3.39 min, *P* value = 0.024), passed the swallowing test earlier (10.03 ± 4.97 vs. 13.70 ± 3.48 min, *P* value = 0.009) and Short orientation memory concentration test (SOMCT) earlier (9.83 ± 4.51 vs. 14.10 ± 4.31 min, *P* value $\leq$0.001) compared to sevoflurane. **Conclusion:** In patients undergoing laparoscopic cholecystectomy under controlled conditions, earlier recovery is seen with desflurane compared to sevoflurane.

Key words: Airway reflexes, cognitive function, desflurane, sevoflurane

INTRODUCTION

Early recovery from anaesthesia is desirable for day care surgeries.[1] Quick regaining of consciousness in terms of responding to verbal commands and eye opening are not enough to avoid the risk of aspiration-related pulmonary complications.[2,3] Inhalational anaesthetics that provide smooth and rapid induction, optimal operating conditions, and rapid recovery with minimal side effects like nausea, vomiting, bleeding, postoperative pain and cognitive dysfunction, are appropriate for this purpose.[4] The faster recovery after desflurane and sevoflurane anaesthesia compared with other inhaled anaesthetics is attributable to their low solubility (blood-gas partition coefficient are 0.69 and 0.42, respectively).[5] Though the difference between the blood-gas coefficient seems minimal, it has been observed that there is a significant difference in the recovery profile of these two inhaled anaesthetics. Recent studies suggest that desflurane compared to sevoflurane leads to earlier recovery of airway reflexes.[2,3] However, comparative results of recovery

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of cognitive function vary significantly.[5,6] After standardising all the factors that can affect recovery from anaesthesia, this study was conducted with the aim of evaluating and comparing the times of recovery of airway reflexes and cognitive function following sevoflurane and desflurane anaesthesia.

METHODS

After obtaining institutional ethics committee approval and written informed consent from the patients, this prospective, randomised, double-blinded study was conducted on 60 patients of American Society of Anesthesiologists (ASA) classification I–II, age between 18 and 60 years with body mass index (BMI) ≤30 kg/m^2 who underwent elective laparoscopic cholecystectomy under general anaesthesia with intubation, over a year. Patients with cardiovascular diseases, asthma or reactive airway diseases, obstructive sleep apnoea, neurological and neuropsychiatric disorders, liver and kidney diseases, with conditions interfering with gastric emptying, patients on opioids, with drug or alcohol abuse and with contraindication or previous adverse response to any of the study drugs were excluded from the study.

A total of 75 patients were assessed for eligibility and finally, 60 patients were enrolled who were randomly divided into two groups by computer-generated random numbers – group A: received sevoflurane (n = 30) and group B: received desflurane (n = 30) [Figure 1].

All the patients were assessed for baseline cognitive function by Short orientation memory concentration test (SOMCT)[7] [Table 1] by an anaesthesiologist blinded to the conduct of anaesthesia and were premedicated with oral alprazolam 0.5 mg at night before surgery.

Table 1: Short Orientation Memory Concentration Test (SOMCT)*

Question	Score
What is the current year?	Correct answer score: 4
	Incorrect answer score: 0
What is the current month?	Correct answer score: 3
	Incorrect answer score: 0
What time is it?	Correct answer score: 3
	Incorrect answer score: 0
Count backwards from 20 to 1	Maximum score: 4
Say the months of the year backwards	Maximum score: 4
Repeat the information given in the preceding sentence	Maximum score: 10

*These six variables yield scoring varying from 0 to 28, with higher scores indicating better cognitive function

On the morning of surgery, patients were asked to take 20 ml of water from a paper cup to swallow in one effort for preoperative swallowing test. Passing the swallowing test is defined as swallowing the entire volume of water in one effort without drooling from lips, pooling in the hypopharynx, gagging and coughing.[2,8] Then the patients were taken inside the operation theatre (OT) and placed in supine position on operation table. All the ASA standard monitoring devices were attached, such as electrocardiogram (ECG), pulse oximetry, non-invasive blood pressure (NIBP) and skin temperature probe. In addition to these, bispectral index (BIS)[9] and train of four (TOF-Watch) monitoring devices were also attached to monitor the depth of anaesthesia and neuromuscular blockade,[10] respectively. After securing an intravenous (i.v.) line and starting the i.v. fluid through that, a standard general anaesthesia protocol was followed. After preoxygenation with 100% oxygen for 3 min, induction was done with administration of injection (inj.) fentanyl 1.5 μg/kg lean body mass (LBM)[11] and 1–2 mg/kg propofol (titrated to loss of verbal response) i.v. Along with that either sevoflurane or desflurane was started as per group allocation at 1 MAC minimum alveolar concentration), that is, 6% for desflurane and 1.85% for sevoflurane. Then the TOF-Watch electrodes, placed over the left ulnar nerve were calibrated to the baseline for 2 s delivering a single twitch once every minute. Additional propofol was permitted as necessary during calibration of the TOF-Watch. Inj. rocuronium 0.6 mg/kg LBM i.v. was administered to facilitate endotracheal intubation under direct laryngoscopy with appropriate-sized endotracheal tube, that is, 7–7.5 mm ID (internal diameter) for female and 8–8.5 mm ID for male patients. After successful intubation, controlled ventilation was established with a target end-tidal carbon dioxide ($EtCO_2$) value between 32 and 36 mmHg, and anaesthesia was maintained with either sevoflurane or desflurane in O_2:N_2O (oxygen: nitrous oxide) in 1:2 ratio with a fresh gas flow of 3 L/min in circle system targeting the BIS value between 40 and 60. Adequate analgesia and muscle relaxation were achieved by infusion fentanyl at 1 μg/kg LBM/h and infusion rocuronium at 0.5 mg/kg LBM/h. Fentanyl infusion was continued at the fixed rate throughout the surgery and inhalational agent was titrated to keep the BIS value between 40 and 60 intraoperatively. Moreover, 20–30 min before the anticipated conclusion of the surgery, fentanyl and rocuronium infusion were stopped while inhaled anaesthetics were reduced to

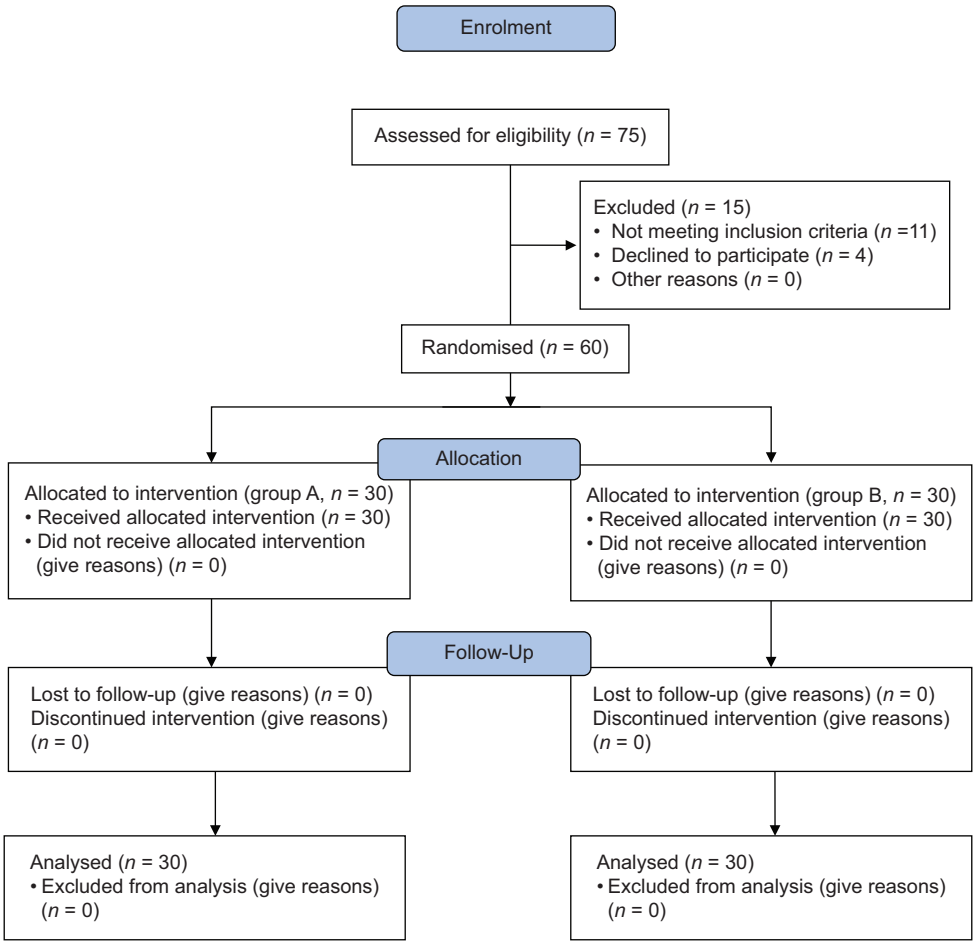

Figure 1: CONSORT flow diagram – group A: sevoflurane, group B: desflurane

end-tidal value of 0.5 MAC. Inj. paracetamol 1 g i.v. over 10–15 min and inj. ondansetron 4 mg i.v. were given at the same time. During the closure, wound infiltration was done with 0. 25% inj. bupivacaine.

TOF monitoring was started after discontinuation of rocuronium infusion every 2 min. When at least one response was palpable at the adductor pollicis in response to the ulnar TOF stimulation, reversal was done with inj. neostigmine 60 μg/kg LBM with inj. glycopyrrolate 10 μg/kg LBM i.v. When TOF reached ≥0.7, the inhaled anaesthetic was turned off and the time was noted. At the same time, fresh gas flow was changed to 100% oxygen at 10 L/min and controlled ± assisted ventilation was continued with a target $EtCO_2$ of 36–44 mmHg. Time was noted on switching off the inhaled anaesthetics.

Thereafter, at 30 s intervals, the verbal commands 'open your eyes' and 'squeeze my hand' were given and the time was noted at the first appropriate response. The duration from turning off inhaled anaesthetics till the first response was taken as T1. The patient's trachea was extubated at the peak of spontaneous inspiration when deemed appropriate by the anaesthesiologist. After extubation, each patient was assessed for excessive sedation, breathing discomfort, hypotension (mean arterial pressure <30% of baseline value) and any other instability. The patient was made propped up to 60° if stable. Then at 2 min after the first appropriate response to command, the recovery of airway reflexes (swallowing test) and cognitive function (SOMCT) were assessed by the same anaesthesiologist who assessed them preoperatively and was blinded to conduct of anaesthesia. Passing the SOMCT was considered when patients achieved their baseline score evaluated the night before surgery.

The time of first passing the swallowing test and SOMCT was noted and after that, the patient's participation in the study ended. If either test was unsuccessful, it was repeated at 5 min interval until the tests were passed. A series of time intervals were recorded and compared between the two groups [Table 2]. None of the patients showed any instability

or excessive sedation after extubation to be excluded from the study.

The sample size was calculated for 90% of significance with an airway reflex recovery probability of 0.6 in sevoflurane group and 0.95 in the desflurane group, which was based on a recent study by McKay *et al*.[2] We used another appropriate formula based on our study design and calculated sample size for our study was 50 with 25 patients in each group though we finally included total 60 patients with 30 in each group.

Patients per group (N) = $[\{P1\ (1 - P1) + P2\ (1 - P2)\}/(P2 - P1)\ 2] \times f\ (\alpha, \beta)$

$= [\{0.6\ (1 - 0.6) + 0.95\ (1 - 0.95)\}]/(0.95 - 0.6)\ 2] \times 10.5$

$= 25$

Where $P1$ = Airway reflex recovery probability in Sevoflurane group (0.6),

$P2$ = Airway reflex recovery probability in Desflurane group (0.95) and

$f\ (\alpha, \beta)$ = 10.5 for 90% power and 5% significance ($\beta = 0.90$ and two-sided $\alpha = 0.05$)

Statistical analysis was carried out using Statistical Package for Social Sciences (SPSS) standard software version 17.0. The qualitative variables (e.g., demographic characteristics) were presented in terms of frequency percentage (%) and statistical significance between the two groups was compared using Chi-square test/Fisher's exact test. The quantitative variables were presented in terms of range (minimum, maximum), mean and standard deviation and statistical significance was determined by using Student's *t*-test. The non-normally distributed continuous variables such as (T1, T2, T3 and T4) were presented in terms of median (IQR) and statistical significance was determined by using nonparametric Wilcoxon rank sum test. The level of statistical significance was taken as ≤0.05.

RESULTS

A total of 60 patients were enroled for the study and randomly allocated into two groups by the computer-generated random numbers, with 30 in each group (group A: received sevoflurane and group B: received desflurane).

The demographic characteristics were comparable in both the groups [Table 3]. Mean age of the patients was 34.93 ± 9.28 and 33.43 ± 8.80 years ($P = 0.523$) and the mean BMI was 23.47 ± 3.66 and 23.37 ± 3.59 ($P = 0.919$) in group A and B respectively. Among 60 patients, 51 were of ASA grade I and 9 were of ASA grade II. No participants experienced any complications, adverse events or observable harm during the whole study period.

The mean time from first verbal response to first passing the swallowing test was comparable in both the groups (T2: one of the secondary outcomes) (groups A vs. B: 5.50 ± 3.45 vs. 4.10 ± 3.42 min, $P = 0.120$) [Table 4].

Total 16 out of 30 passed the swallowing test first time after the first verbal response in desflurane group and total 24 out of 60 patients passed the swallowing test first time after the first verbal response in both the groups with a relative risk (RR) of 1.7.

Table 2: Evaluating parameters (Time intervals)

Time Intervals†	Descriptions
T1	Time elapsed from the discontinuation of the anaesthetic until first response to command
T2	Time from the first response to command until first ability to swallow
T3 (T1 + T2)	Time from the anaesthetic discontinuation until first ability to swallow
T4	Time from anaesthetic discontinuation to first passing the SOMCT

†Series of time gaps between two perioperative events for each patient were evaluated and presented as mean±SD. SOMCT - Short Orientation Memory Concentration Test

Table 3: Demographic characteristics of the patients in two groups

Demographic characteristics‡	Total (60)	Group A (30)	Group B (30)	*P*
Age (years)	18-60	34.93±9.28	33.43±8.80	0.523
Gender (M/F)	52/8	24/6	28/2	0.254
ASA (I/II)	51/9	27/3	24/6	0.278
BMI	-	23.47±3.66	23.37±3.59	0.919
LBW	-	43.79±7.34	42.88±5.54	0.590

‡Data presented as mean±SD or actual numbers; ASA - American Society of Anesthesiologists; BMI - Body mass index; LBW - Lean body weight

Table 4: Comparison of mean T1, T2, T3 and T4 in two groups

Time intervals†	Group A (Sevoflurane)	Group B (Desflurane)	*P*
T1 (min) (mean±SD)	8.20±3.39	5.93±4.13	0.024
T2 (min) (mean±SD)	5.50±3.45	4.10±3.42	0.120
T3 (min) (mean±SD)	13.70±3.48	10.03±4.97	0.009
T4 (min) Mean±SD	14.10±4.31	9.83±4.51	<0.001

†Series of time gaps between two perioperative events for each patient were evaluated and presented as mean±SD

Though the mean duration of surgery was significantly more in desflurane group compared to sevoflurane group (102.50 ± 29.76 vs. 85.77 ± 17.04 min, $P = 0.010$), patients receiving desflurane showed a faster response to verbal commands after discontinuation of inhaled anaesthetics compared to sevoflurane (T1: secondary outcome) (5.93 ± 4.13 vs. 8.20 ± 3.39 min, $P = 0.024$). Patients receiving desflurane also passed the swallowing test and SOMCT at shorter time intervals after discontinuation of inhaled anaesthetics compared to sevoflurane (T3 as primary and T4 as secondary outcomes, respectively) (10.03 ± 4.97 vs. 13.70 ± 3.48 min, $P = 0.009$ and (9.83 ± 4.51 vs. 14.10 ± 4.31 min, $P < 0.001$, respectively) [Table 4 and Figure 2].

DISCUSSION

With the advent of minimally invasive surgeries, patients are being discharged from the hospital as early as possible, sometimes on the same day following surgery for which early recovery from anaesthesia is of utmost importance.[1] Factors influencing the recovery are patient characteristics like age, BMI and ASA class, duration of anaesthesia, choice of inhaled anaesthetics, intraoperative use of analgesia, neuromuscular blocking agents and technique of reversal.[2,3]

We chose and compared the recovery profile of the two less soluble inhaled anaesthetics, that is, sevoflurane and desflurane for laparoscopic cholecystectomy. Though they have almost similar blood-gas coefficients (0.69 vs. 0.42), a significant difference in the recovery profile of the two inhalational anaesthetics has been observed in previous studies.[2,3]

Previous studies compared both these inhaled anaesthetics for recovery profile in terms of clinical signs such as response to verbal commands, eyes opening etc., but these are not proven signs to prevent postoperative aspiration.[3,12-14] McKay *et al*. in 2005, for the first time, used more authentic 20 ml water swallowing test while comparing these two inhaled anaesthetics for recovery of airway reflexes and concluded that desflurane resulted in significantly faster recovery than sevoflurane. In this study, LMA was used without the use of muscle relaxants.[2,8] Thereafter in 2016, in another study in intubated patients, McKay *et al*. found the same results without any complication, using the same water swallowing test.[2]

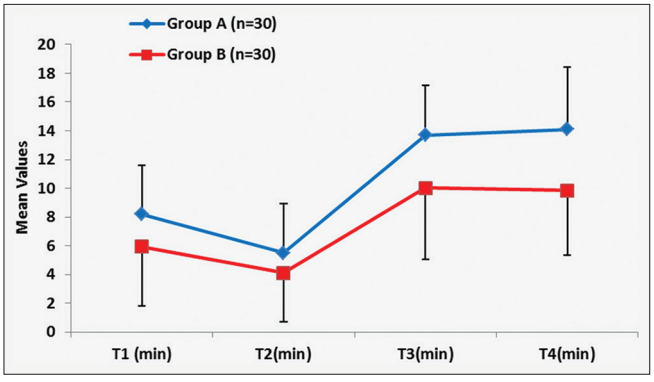

Figure 2: Comparison of mean T1, T2, T3 and T4 in the two groups (group A: sevoflurane, group B: desflurane)

Our study also used the 20-ml water swallowing test for comparing recovery of airway reflexes along with other clinical signs like response to verbal commands, such as 'open your eyes' and 'squeeze my hand' and we found that patients receiving desflurane passed the swallowing test at shorter time intervals compared to sevoflurane (T3: primary outcome) ($P = 0.009$). We also observed a statistically significant ($P = 0.024$) faster response to verbal commands after discontinuation of inhaled anaesthetics compared to sevoflurane (T1: secondary outcome) even though the duration of surgery was significantly more in desflurane group ($P = 0.010$) [Table 4 and Figure 2]. Among 30 patients in desflurane group, 16 patients passed swallowing test in 2 min with a relative risk of 1.7, which was 1.8 in a study by McKay *et al*. in 2016.[2]

Along with recovery of airway reflexes, we also studied recovery of cognitive function using a single standardised tool, that is, SOMCT[7] and observed that patients receiving desflurane also passed SOMCT at shorter time intervals compared to sevoflurane (T4: secondary outcome) ($P < 0.001$) [Table 4 and Figure 2].

Though several studies compared the same, they reported confusing results. Some reported early recovery of cognitive function with desflurane compared to sevoflurane[1,6] while others found no difference.[15,16] In contrast, Jadhav *et al*. found early recovery of cognitive function with sevoflurane when compared with desflurane.[5] They also used different tools to assess the recovery of cognitive function, which was not standardised.[1,6,15,16]

Not only that, all the previous studies also suffered from a lack of standardisation regarding surgical

procedure, duration of surgeries, neuromuscular monitoring, depth of anaesthesia monitoring and intraoperative use of opioid analgesia. Being the key determining factors of the recovery, these could influence their results.

Considering the above fact, for the first time, we conducted this study in a unique way where all the patients underwent same surgery (laparoscopic cholecystectomy) following a standard anaesthetic technique under BIS and neuromuscular monitoring for standardising the depth of anaesthesia (BIS between 40 and 60) and adequate neuromuscular blockade and reversal. Along with that, the fixed-rate infusions of fentanyl and rocuronium based on LBW were used to standardise intraoperative analgesia and neuromuscular blockade and thereby avoiding overdosing and eliminating the cause of infusion-related excessive sedation and inadequate reversal. All the infusions were stopped at a specific time before the completion of surgery. Neuromuscular monitoring was used to assess recovery from neuromuscular blockade. A standard 20-ml water swallowing test was conducted to assess recovery of protective airway reflexes and a standard test, that is, SOMCT was conducted in each patient to assess the recovery of cognitive function, which was compared with the preoperative results of the same. After standardising all these factors that might influence postoperative recovery, we found that in addition to response to verbal commands, recovery of airway reflexes and cognitive function were significantly faster with desflurane compared to sevoflurane.

The above findings have some practical implication. Wherever we need an early recovery of airway reflexes and cognitive function like in day care surgeries or patients prone to delayed emergence like those with hypothyroidism, elderly and obese patients, desflurane is the preferred choice over sevoflurane.

Though our study was done on demographically homogenous population, it has some limitations in not considering the various effects of genetic variations on pharmacokinetics and pharmacodynamics of the inhalational agents and not considering the effects of nitrous oxide on BIS and inhaled anaesthetics because of nonavailability of air in our hospital. Future studies should consider including these above two facts also for more accurate standardisation.[17-20]

CONCLUSION

We concluded that in patients undergoing laparoscopic cholecystectomy with endotracheal intubation under controlled conditions, earlier recovery is seen with desflurane compared to sevoflurane in terms of response to verbal commands, recovery of airway reflexes and recovery of cognitive function.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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