Original Article

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Comparison of Recovery Profile and Cost-effectiveness of Sevoflurane and Desflurane using Low Flow Anaesthesia in Adults: A Randomised Clinical Study

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ABSTRACT

Introduction: Newer inhalational agents, like sevoflurane and desflurane, offer advantages of rapid induction and early recovery due to their low blood gas solubility. However, cost remains a major drawback of these agents, despite the reduction in agent consumption achieved through low flow anaesthesia.

Aim: To evaluate the recovery profile and cost-effectiveness of sevoflurane and desflurane using low flow anaesthesia in adults.

Materials and Methods: A randomised clinical study was conducted at, Department of Anaesthesia, Bharati Vidyapeeth Medical College, Pune, Maharashtra, India, during October 2019 to August 2021, with 60 patients classified as American Society of Anaesthesiologists (ASA) I or II, aged 18-65 years, undergoing elective surgeries lasting 1-4 hours under general anaesthesia with the low flow technique. Group S received sevoflurane, while group D received desflurane. Anaesthesia was maintained using a 50/50 mixture of oxygen/air and either sevoflurane or desflurane, depending on the group. The inhalational agents were titrated intraoperatively to achieve a Minimum Alveolar Concentration (MAC) of approximately one. The amount of inhalational agent consumed was calculated, and recovery profiles were studied. The means of continuous variables were compared using an Independent sample t-test, with p-values <0.05 considered significant.

Results: In Groups S and D, the mean ages were 39.17 years and 41.5 years, and the percentages of males were 30% and 50%, respectively. The mean times to swallowing, spontaneous eye opening, limb movements, establishing spontaneous regular breathing, responding to verbal commands, extubation, stating a name on command, and achieving a modified Aldrete score ≥9 in minutes were 6.13, 4.87, 5.07, 4.57, 7.40, 8.97, 10.40, and 11.50, respectively. These values were significantly lower in group D. The mean cost per hour and average volume consumption were significantly higher in group D.

Conclusion: The study concludes that desflurane provides faster and better recovery from anaesthesia. Although the total cost of desflurane was higher compared to sevoflurane, its use can be beneficial for faster emergence, early transfer from the Post Anaesthesia Care Unit (PACU), and earlier discharge from the hospital.

Keywords: Deglutition, Extubation, General anaesthesia, Patient discharge

INTRODUCTION

Inhalational anaesthetics are essential in modern-day anaesthetic practice. Despite their numerous advantages, they contribute to the cost burden and operative room pollution. The concept of reusing anaesthetic agents has gained importance since the evolution of anaesthetic techniques from the period of Ether using the open drop method to the current closed breathing systems [1]. The choice of anaesthetic technique and drugs used are factors that help determine recovery from anaesthesia. An ideal inhalational agent should have a smooth and rapid induction, optimal operating conditions, early recovery with minimal emergence, and no significant adverse effects [2].

Volatile agents accumulate in adipose tissue, which may delay recovery from anaesthesia. Both sevoflurane and desflurane are characterised by a low blood gas partition coefficient (0.69 and 0.42, respectively), thus aiding in achieving sufficient alveolar concentration and rapid induction [2]. Due to their low solubility, they also facilitate rapid recovery in terms of airway reflexes and responsiveness to commands. The use of low flow anaesthesia has become common practice with the development of modern anaesthetic machines, gas analyser monitors, precision vaporisers, and the introduction of potent volatile agents. Low flow closed breathing systems decreases anaesthetic gas consumption, greenhouse effect, and operating room pollution [1].

Chudasama PA and Mehta MV conducted a study in patients undergoing day care surgeries and compared sevoflurane and desflurane with respect to vital parameters and recovery profile, study showed that the sevoflurane group showed significantly longer time for spontaneous eye opening, recalling names, and recognising surroundings [2]. Gangakhedkar GR and Monteiro JN conducted a double-blinded study in patients undergoing laparoscopic cholecystectomy and found that the desflurane group had faster and better recovery [3]. Most studies focus on recovery profile, with very few discussing cost-effectiveness. Therefore, this study aims to compare both aspects.

Sevoflurane is an ether compound with fluoromethyl and 1,1,1,3,3,3-hexafluoro isopropyl as the two alkyl groups. It is an inhalational anaesthetic agent used to induce and maintain general anaesthesia. It is a volatile, non inflammable compound with low solubility and blood gas partition coefficient (0.60). Unlike other volatile anaesthetics, sevoflurane has a pleasant odour and does not irritate the airway. The haemodynamic and respiratory effects of sevoflurane are well tolerated [4].

Desflurane is an organofluorine compound. It is a volatile anaesthetic that is more rapidly cleared and less metabolised than other inhaled anaesthetics. It is a liquid with a slight, non pungent odour and has low solubility and blood gas coefficient (0.42). It has a short duration of action as it is rapidly cleared [5]. The present study aims to compare sevoflurane and desflurane primarily for recovery characteristics and cost analysis using low flow anaesthesia. The secondary objectives were to monitor for any adverse effects, including haemodynamic parameters.

MATERIALS AND METHODS

A single-blinded randomised clinical study was conducted at Bharati Hospital and Research Centre, a tertiary care hospital located in Pune, Maharashtra, India, between October 2019 and August 2021, after approval from the ethical committee (BVDUMC/IEC/85). Written informed consent was obtained from all participants, and the study was conducted in accordance with the Helsinki Declaration of 1975.

Inclusion criteria: Patients classified as ASA I or II, aged 18-65 years, undergoing elective surgeries lasting 1-4 hours under general anaesthesia were included in the study.

Exclusion criteria: Patients who refused to participate in the study and patients with severe systemic disorders were excluded from the study.

Sample size: The sample size was calculated based on the standard deviation from a previous study using recovery characteristics as a variable, with a power of 80% and a confidence interval of 95% [6]. (According to the sample size calculation, it was estimated as 100 but was reduced to 60 due to the pandemic). Final sample size was 60 patients.

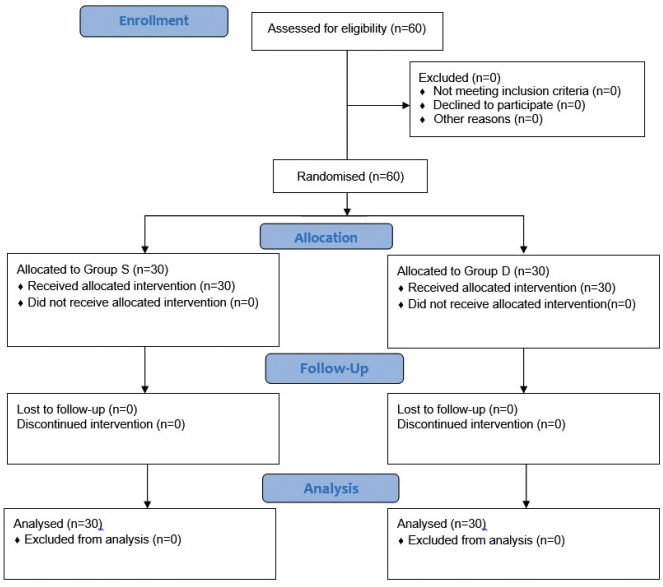
Procedure

The patients included in the study were blinded to the intervention. A total of 60 patients who met the inclusion criteria were randomly divided into two groups of 30 each, using computer-generated randomisation [Table/Fig-1]. Group S received sevoflurane, and group D received desflurane for the maintenance of anaesthesia. Detailed preanaesthetic assessments were conducted for all patients scheduled for surgery, and patients were kept nil by mouth for six hours prior to surgery. The surgeries included Ear Nose and Throat (ENT) procedures like ear exploration, tympanoplasties, Functional Endoscopic Sinus Surgery (FESS), and general surgery procedures such as laparoscopic hernia repairs and fibroadenomas. Written informed consent was obtained after shifting the patient inside the operating theater, and standard multiparameter monitors were attached. Premedication with intravenous glycopyrrolate 0.04 mg/kg and intravenous ondansetron 4 mg was given. Preoxygenation was performed with 100% O_2 for three minutes. Preinduction, intravenous midazolam 0.05 mg/kg, and intravenous fentanyl 1 mcg/kg were given. Anaesthesia was induced with intravenous propofol 2 mg/kg and intravenous succinylcholine 2 mg/kg, followed by endotracheal intubation and controlled ventilation with a closed circuit. During an initial phase of 5-10 minutes, a fresh gas flow of approximately 4 L/min was set, which was later reduced to a total flow of 1 L/min. Anaesthesia was maintained using sevoflurane at a concentration of 0.2 to 2% or desflurane at a concentration of 3 to 6%, depending on the group they belonged to, with a mixture of 50% O_2, 50% air, and top-up doses of intravenous atracurium. The concentration of the vaporiser dial was adjusted to achieve a MAC of approximately one in both groups. Intraoperative heart rate, non invasive blood pressure, oxygen saturation, end-tidal CO_2, and vaporiser dial concentration were continuously monitored and noted at regular intervals until the end of surgery. Intraoperative analgesia was achieved with intravenous fentanyl 1 mcg/kg and intravenous paracetamol 1 g. The inhalational agents were switched off after skin closure. Reversal was performed using intravenous neostigmine 0.05 mg/kg with intravenous glycopyrrolate 0.01 mg/kg. Patients were extubated after fulfilling extubation criteria and shifted to the PACU only after achieving a modified Aldrete score ≥9 [7]. The time of discontinuation of the inhalational agent was considered as zero minutes, and recovery variables were measured from this time.

Variables used to compare recovery profiles were:

Time to:

a Spontaneous movement (swallowing, spontaneous eye opening, limb movements)



[Table/Fig-1]: CONSORT diagram.

b. Establish spontaneous regular breathing pattern

c. Respond to verbal commands

d. Extubation

e. State name on command

f. Achieve modified Aldrete score ≥9

Any side-effects like nausea, vomiting, breath holding, laryngospasm, or agitation, if any, were recorded.

The amount of inhalational agent consumed was calculated using the formula given by Ehrenwerth and Eisenkraft:

3×fresh gas flow×volume %=mL liquid used per hour [8].

Sevoflurane was accounted for as Rs 22 per 1 mL, and desflurane was accounted for as Rs 35 per 1 mL (according to market prices).

STATISTICAL ANALYSIS

The intergroup statistical comparison of the distribution of categorical variables was tested using the Chi-square test or Fisher's exact probability test if more than 20% of cells had an expected frequency less than 5. The intergroup statistical comparison of the means of continuous variables was done using Independent sample t-test. The underlying normality assumption was tested before subjecting the study variables to the t-test. In the entire study, p-values <0.05 were considered statistically significant. The entire data were statistically analysed using Statistical Package for the Social Sciences (SPSS ver 22.0, IBM Corporation, USA) for MS Windows.

RESULTS

After analysis, the demographic data shown in [Table/Fig-2] were found to be comparable between both groups. Similarly, the mean values of heart rate, systolic blood pressure, diastolic blood pressure, oxygen saturation, and end-tidal CO_2 at each corresponding time interval showed no significant difference [Table/Fig-3-7].

Variables		Group S (n=30)	Group D (n=30)	p-value
Mean age (years)		39.17±13.73	41.50±13.15	0.504^{NS}
Male		9 (30%)	15 (50.0%)	0.114^{NS}
Female		21 (70%)	15 (50.0%)	
ASA	Grade-I	13 (43.3%)	14 (46.7%)	0.795^{NS}
	Grade-II	17 (56.7%)	16 (53.3%)	
Mean duration (hours)		2.68±0.75	2.67±0.85	0.936^{NS}

[Table/Fig-2]: Statistical analysis of demographic variables.
p <0.05=Statistically significant; NS: Not significant; The p-values for mean age and mean duration have been calculated using independent sample t-test. The p-values for distribution of gender and ASA grading have been calculated using Chi-square test

Heart rate (Per min)	Group S (n=30) Mean±SD	Group D (n=30) Mean±SD	p-value (Intergroup)
Baseline	89.55±5.18	86.53±6.81	0.055^{NS}
15 min	84.90±10.92	80.63±8.53	0.097^{NS}
30 min	82.33±9.43	78.07±8.06	0.065^{NS}
1 hour	79.37±8.73	76.77±7.75	0.228^{NS}
1.5 hour	79.60±8.70	78.24±7.97	0.535^{NS}
2 hour	79.08±7.62	77.72±8.68	0.559^{NS}
2.5 hour	82.86±9.79	78.65±6.78	0.116^{NS}
3 hour	85.50±7.75	83.36±6.67	0.427^{NS}
3.5 hour	85.00±10.68	83.62±5.34	0.761^{NS}
4 hour	88.33±0.58	87.75±1.26	0.49^{NS}

[Table/Fig-3]: Comparison between mean heart rate (independent t-test used to calculate p-value).
Values are mean and SD, p-value [Intergroup] by independent sample t-test. p-value <0.05 is considered to be statistically significant. *p-value <0.05, NS: Statistically non-significant

Systolic BP (mmHg)	Group S (n=30) Mean±SD	Group D (n=30) Mean±SD	p-value (Intergroup)
Baseline	126.43±18.93	125.77±11.71	0.870^{NS}
15 min	116.17±10.78	119.80±9.87	0.1786^{NS}
30 min	107.37±4.80	110.27±7.13	0.069^{NS}
1 hour	108.93±8.03	112.43±6.68	0.07^{NS}
1.5 hour	109.23±12.38	112.28±7.18	0.255^{NS}
2 hour	108.40±6.58	112.40±8.91	0.077^{NS}
2.5 hour	110.91±11.76	114.05±9.84	0.356^{NS}
3 hour	119.62±13.67	119.86±5.17	0.953^{NS}
3.5 hour	114.80±11.63	120.50±8.67	0.332^{NS}
4 hour	123.00±13.53	132.50±1.00	0.207^{NS}

[Table/Fig-4]: Comparison of systolic BP (independent t-test used to calculate p-value).
Values are mean and SD, p-value (Intergroup) by independent sample t-test. p-value <0.05 is considered to be statistically significant. *p-value <0.05, **p-value <0.01, NS: Statistically non-significant

Diastolic BP (mmHg)	Group S (n=30) Mean±SD	Group D (n=30) Mean±SD	p-value (Intergroup)
Baseline	79.30±10.25	81.57±9.88	0.387^{NS}
15 min	69.57±8.48	71.67±5.36	0.256^{NS}
30 min	66.27±8.16	70.10±8.35	0.077^{NS}
1 hour	68.67±9.11	68.63±3.89	0.985^{NS}
1.5 hour	67.87±9.62	68.97±4.95	0.585^{NS}
2 hour	67.72±8.27	70.20±6.58	0.246^{NS}
2.5 hour	68.91±9.91	71.25±8.36	0.415^{NS}
3 hour	74.19±9.85	74.79±8.63	0.862^{NS}
3.5 hour	74.80±11.28	74.75±5.23	0.991^{NS}
4 hour	75.33±11.72	77.50±5.00	0.748^{NS}

[Table/Fig-5]: Comparison of mean diastolic BP (independent t-test used to calculate p-value).
Values are mean and SD, p-value (Intergroup) by independent sample t-test. p-value <0.05 is considered to be statistically significant. *p-value <0.05, NS: Statistically non-significant

SpO_2 (%)	Group S (n=30) Mean±SD	Group D (n=30) Mean±SD	p-value (Intergroup)
Baseline	99.43±0.68	99.10±1.29	0.217^{NS}
15 min	99.57±0.63	99.20±1.35	0.182^{NS}
30 min	99.47±0.63	99.27±1.17	0.414^{NS}
1 hour	99.57±0.63	99.27±1.17	0.221^{NS}
1.5 hour	99.53±0.57	99.17±1.31	0.173^{NS}
2 hour	99.48±0.51	99.32±1.03	0.490^{NS}
2.5 hour	99.50±0.59	99.15±1.27	0.252^{NS}
3 hour	99.50±0.63	99.64±0.63	0.542^{NS}
3.5 hour	99.60±0.55	99.62±0.52	0.935^{NS}
4 hour	99.67±0.58	99.75±0.50	0.846^{NS}

[Table/Fig-6]: Comparison of mean saturation (p-value calculated by independent t-test).
Values are mean and SD, p-value (Intergroup) by independent sample t test. p-value <0.05 is considered to be statistically significant. NS: Statistically non-significant

$ETCO_2$ (%)	Group S (n=30) Mean±SD	Group D (n=30) Mean±SD	p-value (Intergroup)
Baseline	36.20±2.19	36.17±1.02	0.940^{NS}
15 min	35.70±1.70	36.00±1.91	0.524^{NS}
30 min	35.90±1.97	35.93±1.55	0.942^{NS}
1 hour	35.93±1.80	36.30±1.66	0.416^{NS}
1.5 hour	36.62±1.88	36.41±1.59	0.088^{NS}
2 hour	35.92±2.02	36.12±1.54	0.695^{NS}
2.5 hour	36.00±2.11	36.15±1.53	0.796^{NS}
3 hour	36.37±1.82	36.07±1.59	0.633^{NS}
3.5 hour	37.50±0.89	37.00±0.82	0.4395^{NS}
4 hour	37.00±1.73	36.50±1.00	0.646^{NS}

[Table/Fig-7]: Comparison of mean $EtCO_2$ (p-value calculated using independent t-test).
Values are mean and SD, p-value (Intergroup) by independent sample t-test. p-value <0.05 is considered to be statistically significant. *p-value <0.05, NS: Statistically non-significant

The distribution of mean time to swallowing, time to spontaneous eye opening, time to limb movements, time to establish spontaneous regular breathing pattern, time to respond to verbal commands, time to extubation, time to state name on command, and time to achieve a modified Aldrete score ≥9 was significantly lower in Group D compared to group S (p-value <0.05 for all) [Table/Fig-8]. The mean cost per hour and average volume consumption were significantly higher in group D compared to group S [Table/Fig-9]. No significant side-effects were seen in both groups [Table/Fig-10].

Variable (in minutes)	Group S (n=30) Mean±SD	Group D (n=30) Mean±SD	p-value
Time to swallowing	6.13±1.11	4.17±0.70	0.001
Time to spontaneous eye opening	4.87±1.69	3.93±0.58	0.006
Time to limb movements	5.07±1.86	4.27±0.64	0.029
Time to establish spontaneous regular breathing pattern	4.57±1.16	3.73±0.83	0.002
Time to respond to verbal commands	7.40±2.57	5.30±0.95	0.001
Time to extubation	8.97±2.92	5.77±1.36	0.001
Time to state name on command	10.40±2.82	7.00±1.17	0.001
Time to achieve modified Aldrete score ≥9	11.50±2.75	7.83±1.42	0.001

[Table/Fig-8]: Statistical analysis of recovery variables, p <0.05= significant.
p-value for each recovery variable is calculated using independent sample t-test

Variable	Group S (n=30) Mean±SD	Group D (n=30) Mean±SD	p-value
Average volume consumption per hour (in mL)	5.039±0.54	11.157±1.63	0.0001
Average cost per hour (in rupees)	110.86±12.06	398.08±22.73	0.001

[Table/Fig-9]: Statistical analysis of average volume consumption per hour and average cost per hour. p-value is calculated using independent sample t-test.
p<0.05=significant; Sevoflurane was accounted for as Rs 22 per 1 mL, and desflurane was accounted for as Rs 35 per 1 mL (according to market prices)

Side-effects	Group S (n=30) n (%)	Group D (n=30) n (%)	p-value
Nausea and vomiting	6 (20.0)	3 (10.0)	0.472
Agitation	2 (6.7)	0	0.492

[Table/Fig-10]: Intergroup distribution of incidence of side-effects.
Values are n (% of cases), p-value by Chi-square test. p-value <0.05 is considered to be statistically significant

Inhalational agents were used from the beginning of surgery until skin closure.

DISCUSSION

In present times, there is a high demand for day care surgeries due to the use of minimally invasive techniques. This has led to the need for early recovery from anaesthesia and early discharge from hospitals. Sevoflurane and desflurane, with their low blood gas solubility, aid in rapid induction and early recovery from anaesthesia [4,5]. The use of low flow anaesthesia has advantages such as reducing gas consumption and minimising operation theater pollution [1]. Therefore, the use of newer inhalational agents facilitates faster recovery, and employing low flow anaesthesia promotes cost-effectiveness [9,10].

The primary objective of this study was to compare the recovery characteristics of sevoflurane and desflurane, along with a cost analysis of both agents using low flow anaesthesia. The secondary objectives were to compare haemodynamic parameters and note any potential side-effects.

The study found a statistically significant difference in the recovery profiles between the two groups, with the desflurane group demonstrating better and faster recovery [Table/Fig-8]. Patients receiving sevoflurane were extubated in 8.97±2.92 minutes, while those receiving desflurane were extubated in 5.77±1.36 minutes (p-value-0.001). The desflurane group exhibited shorter times for swallowing, spontaneous eye opening, and limb movements. Patients in the desflurane group responded to verbal commands in 5.30±0.95 minutes and stated their names earlier compared to the sevoflurane group, where patients took 7.40±2.57 minutes for the same.

Patients who received sevoflurane achieved a modified Aldrete score of >9 in 11.50±2.75 minutes, while those who received desflurane achieved it in 7.83±1.42 minutes, which was statistically significant (p-value=0.001).

In a study by Bansal T et al., comparing postoperative recovery characteristics and cognitive function of sevoflurane and desflurane in obese patients undergoing laparoscopic abdominal surgeries, both inhalational agents showed similar recovery profiles when bispectral index was used to monitor the depth of anaesthesia [11]. Wu YM et al., conducted a study comparing sevoflurane vs desflurane with and without M-entropy monitoring for depth of anaesthesia [12]. It demonstrated that patients receiving desflurane combined with M-entropy guidance experienced significantly shorter emergence from anaesthesia compared to sevoflurane. Gangakhedkar GR and Monteiro JN studied sevoflurane and desflurane regarding vital parameters, recovery variables, and emergence [3]. The time required for spontaneous eye opening and response to verbal commands was significantly lower in patients receiving desflurane. Srivastava M et al., studied emergence and recovery characteristics using low flow anaesthesia and found that immediate recovery and wake up were faster with desflurane [9].

The study also compared the cost-effectiveness of both agents and found that the volume consumed and cost of sevoflurane were significantly lower when compared to desflurane. The mean volume consumption per hour for the sevoflurane group was 5.039±0.54 mL, while for the desflurane group, it was 11.157±1.63 mL. The mean cost of sevoflurane per hour was 110.86±12.06 rupees, whereas desflurane costed 398.08±22.73 rupees [Table/Fig-9].

Low flow anaesthesia has both ecological and economic advantages as it reduces gas consumption. Kurhekar P et al., conducted a study on the cost-benefit ratio of inhalational agents using low flow anaesthesia [10]. They compared isoflurane, sevoflurane, and desflurane, and found isoflurane to be the most cost-effective among the three, while the cost of sevoflurane was found to be lower than that of desflurane. A recent study published by Taş BA et al., compared minimal flow (0.5 L/min) desflurane and sevoflurane and found that the amount of sevoflurane consumed is less and more cost-effective when compared with desflurane [13]. This study utilised Bispectral Index (BIS) monitoring, which could have reduced the use of inhalational agents.

No significant differences were observed in demographic characteristics [Table/Fig-2] and haemodynamic parameters in the study [Table/Fig-3-7]. Srivastava M et al., conducted a study in cancer patients using low flow anaesthesia and obtained similar results regarding haemodynamic parameters [9]. Similarly, Gupta P et al., conducted a study in children to compare sevoflurane and desflurane in terms of emergence characteristics and found that haemodynamic variables were comparable in both groups [14]. In this study, side-effects like nausea and vomiting, breath holding, laryngospasm, and agitation were comparable in both groups [Table/Fig-10]. However, a study conducted by Chudasma PA and Mehta MV showed a slightly higher incidence of nausea in the sevoflurane group [2].

Limitation(s)

The study does not include specific patient groups, such as morbidly obese individuals or those undergoing longer duration surgeries, where desflurane could be more beneficial for faster recovery. Additionally, the study monitored the MAC of the two inhalational agents as a guide to titrate anaesthetic depth, which could result in over- or under-dosing. While the objective was to measure cost-effectiveness, this study does not consider other aspects of operating room expenditure apart from inhalational agents. The estimated sample size could not be achieved due to the pandemic.

CONCLUSION(S)

The study compared the recovery profile and cost-effectiveness of sevoflurane and desflurane using low flow anaesthesia. Based on this study, it was concluded that desflurane offers faster and better recovery from anaesthesia, characterised by rapid awakening and early extubation. Although the average cost and volume consumed were higher with desflurane, its use can be beneficial for faster emergence, early transfer from the PACU, and earlier discharge from the hospital.

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