



## Original Research Article

# Comparison of the hypnotic potency of sevoflurane and desflurane using bispectral index at equivalent minimum alveolar concentration: A prospective randomised controlled trial

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## Abstract

**Background and Objectives:** The bispectral index (BIS), derived from EEG signals, is widely used to assess the depth of anaesthesia, ensuring optimal dosing and preventing intra-operative awareness. Sevoflurane and desflurane, commonly used volatile anaesthetics, share an equivalent minimum alveolar concentration (MAC) but may differ in hypnotic potency. This study compares their hypnotic effects at equi-MAC using BIS and evaluates associated haemodynamic parameters, including heart rate (HR) and mean arterial pressure (MAP).

**Materials and Methods:** A prospective, randomised trial included 80 adult patients (ASA I-II, aged 18–55 years) undergoing elective surgery under general anaesthesia. Patients were allocated into two groups: Group S (sevoflurane) and Group D (desflurane), receiving the respective agent at 1 MAC. Anaesthesia induction was standardized, and BIS, HR, and MAP were recorded at baseline and every 5 minutes for 30 minutes post-equilibration. Data were analyzed using independent t-tests, with  $p < 0.05$  considered significant.

**Results:** Desflurane resulted in lower BIS values (mean  $44 \pm 3$ ) compared to sevoflurane (mean  $49 \pm 4$ ), reflecting a notable decrease of approximately 10.2% in BIS with desflurane. Desflurane increased HR and MAP, likely due to sympathetic stimulation which may be significant in patients with cardiovascular conditions like hypertension, coronary artery disease or arrhythmias, as it could elevate myocardial oxygen demand and perioperative risk. Recovery times were faster with desflurane, with shorter durations for eye-opening ( $6.8 \pm 1.9$  minutes) and verbal response ( $8.5 \pm 2.0$  minutes) compared to sevoflurane ( $10.2 \pm 2.1$  and  $12.3 \pm 2.4$  minutes, respectively).

**Conclusion:** Desflurane offers greater hypnotic potency and more rapid recovery than sevoflurane at equivalent minimum alveolar concentrations (MAC). However, its pronounced haemodynamic effects necessitate caution in hemodynamically unstable patients, highlighting the importance of tailoring anaesthetic management to individual clinical conditions.

**Keywords:** Anaesthesia, Bispectral Index, Sevoflurane, Desflurane, Haemodynamic.

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## 1. Introduction

The depth of anaesthesia is a fundamental component of perioperative management, influencing anaesthetic drug usage, patient outcomes, and the prevention of adverse events, including intraoperative awareness.<sup>1</sup> The bispectral index (BIS), derived from electroencephalographic signals, has become one of the most widely used and reliable methods for monitoring anaesthetic depth. BIS provides a numerical value ranging from 0 (complete cortical suppression) to 100

(fully awake), allowing for individualized titration of anaesthetic agents and reducing the risk of under- or overdosing. Its use has been validated across a range of clinical settings, with studies demonstrating reductions in anaesthetic consumption and improvements in postoperative recovery profiles.<sup>1</sup>

Volatile anaesthetics such as sevoflurane and desflurane remain essential agents in modern anaesthetic practice. Both are low-solubility inhalational agents offering rapid onset and

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offset, which are advantageous in fast-paced surgical environments. Sevoflurane is commonly preferred for inhalational induction, particularly in paediatric patients, due to its non-pungent odour and minimal airway irritation.<sup>2</sup> Desflurane, by contrast, has the lowest blood-gas partition coefficient among commonly used agents, resulting in faster equilibration and more rapid recovery, making it especially suitable for short-duration and ambulatory procedures.<sup>3</sup> Although sevoflurane and desflurane share similar minimum alveolar concentration (MAC) values in comparable patient populations,<sup>4</sup> emerging evidence suggests they differ in their hypnotic potency when administered at equivalent MAC.

MAC is defined as the alveolar concentration of an inhaled anaesthetic that prevents movement in response to a surgical stimulus in 50% of patients and is widely accepted as a measure of anaesthetic potency. Despite comparable MAC values, studies have indicated that desflurane produces significantly lower BIS values than sevoflurane at equi-MAC, suggesting a greater depth of hypnosis.<sup>5</sup> Hypnotic potency, which reflects the depth of anaesthesia independent of immobility, can be more precisely evaluated using BIS monitoring.

These differences in hypnotic effect are likely attributable to pharmacokinetic and pharmacodynamic variations between the agents. Desflurane's lower solubility facilitates rapid alveolar wash-in and wash-out, promoting quicker equilibration between alveolar and brain concentrations and enhancing hypnotic depth.<sup>6</sup> In contrast, sevoflurane's relatively higher solubility may delay equilibration and blunt its hypnotic effect.<sup>7</sup> These characteristics are particularly relevant in clinical scenarios requiring tight control of anaesthetic depth alongside cardiovascular stability.

Both sevoflurane and desflurane can cause dose-dependent decreases in systemic vascular resistance and myocardial contractility, contributing to hypotension. However, desflurane has been associated with transient sympathetic stimulation, resulting in increased heart rate (HR) and mean arterial pressure (MAP), particularly during rapid increases in inspired concentration.<sup>8</sup> This response is believed to result from airway irritation and subsequent catecholamine release. In patients with underlying cardiovascular disease or those at risk of haemodynamic instability, these effects necessitate careful consideration.<sup>9</sup>

The application of BIS monitoring in comparative anaesthetic studies has enhanced understanding of agent-specific profiles. BIS-guided anaesthesia has been associated with reduced intraoperative awareness, lower anaesthetic requirements, and improved emergence times.<sup>10</sup> However, variability in BIS values among different agents at equivalent MAC highlights the importance of context-specific interpretation. While both sevoflurane and desflurane are effective at achieving surgical anaesthesia, desflurane may

produce deeper hypnosis as reflected by lower BIS values, alongside greater cardiovascular stimulation.

This study aims to compare the hypnotic potency and haemodynamic effects of sevoflurane and desflurane using BIS monitoring at equi-MAC. Several factors may influence these outcomes, including patient characteristics such as age, baseline BIS variability, and preoperative medication use.<sup>11</sup> Pharmacokinetic properties also play a critical role; desflurane's lower blood-gas partition coefficient allows for faster equilibration and potentially deeper hypnosis, while its stimulatory effects on the sympathetic nervous system may elevate HR and MAP.<sup>12</sup> Additionally, desflurane's airway irritant properties can impact anaesthetic stability. Methodological considerations, such as inter-individual variability in MAC requirements and the known limitations of BIS monitoring—such as its sensitivity to electromyographic activity—must also be acknowledged<sup>14</sup>. Standardization of these variables is essential to ensure the reliability and generalizability of findings.

## 2. Materials and Methods

Following ethical committee approval (IEC No. IEC/2022/2/08), this prospective, randomized controlled trial was conducted in the Department of Anaesthesiology over six months to compare the hypnotic potency of sevoflurane and desflurane at equivalent minimum alveolar concentration (equi-MAC), with the bispectral index (BIS) as the primary outcome measure. The trial was registered under the Clinical Trials Registry of India (CTRI/2022/09/045869). Secondary objectives included evaluating the haemodynamic effects of the two agents, specifically their impact on heart rate (HR) and mean arterial pressure (MAP). Written informed consent was obtained from all participants prior to enrolment.

Eligible participants included adult patients aged 18 to 55 years, classified as American Society of Anaesthesiologists (ASA) physical status I or II, and scheduled for elective surgical procedures under general anaesthesia. Exclusion criteria comprised patients with known cardiac, pulmonary, or neurological disorders, allergy to volatile anaesthetics, those undergoing emergency procedures, pregnant or lactating women, individuals with a body mass index (BMI) greater than 35 kg/m<sup>2</sup>, and those who declined to provide informed consent.

Participants were randomly assigned to one of two groups using a computer-generated random number sequence. Allocation concealment was maintained using sealed, opaque envelopes opened by a staff member not involved in the study. Group S received sevoflurane, while Group D received desflurane as the primary volatile agent. To minimize observer bias, the anaesthesiologists involved in intraoperative data collection were blinded to group allocation. Randomization and anaesthetic preparation were handled by a separate investigator, and those assessing

intraoperative parameters were not involved in anaesthesia administration.

Sample size estimation was based on data from a previous study comparing the effects of sevoflurane and desflurane on BIS values.<sup>13</sup> To achieve 80% statistical power at a 5% significance level, a minimum of 34 patients per group was required. To account for potential dropouts, 40 patients were recruited for each group, resulting in a total of 80 participants.

All patients were fasted for a minimum of eight hours prior to surgery. Upon arrival in the operating room, standard monitors—including non-invasive blood pressure, electrocardiography, and pulse oximetry—were applied. BIS electrodes were positioned according to the manufacturer’s guidelines, and baseline BIS values were recorded. Anaesthesia induction was standardized across both groups using intravenous fentanyl (2 µg/kg), propofol (2 mg/kg), and vecuronium (0.1 mg/kg) to facilitate tracheal intubation. Ventilation was set at a tidal volume of 6–8 mL/kg with the respiratory rate adjusted to maintain end-tidal CO<sub>2</sub> between 35 and 40 mmHg.

Anaesthesia was maintained with sevoflurane in Group S and desflurane in Group D. Both agents were administered at 1 MAC, adjusted for age using the Mapleson formula:<sup>14</sup>

$$MAC_{age} = MAC_{40} \times 10^{-0.00269 \times (Age - 40)}$$

A fresh gas flow of 2 L/min consisting of 50% oxygen and 50% nitrous oxide was used for both groups. Once equilibrium was achieved, defined as a stable end-tidal concentration maintained for at least 10 minutes, BIS values were recorded at five-minute intervals over a 30-minute

period. Concurrently, haemodynamic parameters (HR and MAP) were measured at the same intervals. Recovery times were recorded as secondary outcomes and included the time from discontinuation of the volatile agent to spontaneous eye opening and the ability to respond verbally. Spontaneous eye opening was defined as unassisted eyelid movement, while verbal response was marked by the patient's ability to articulate a coherent word or phrase following a command. These endpoints were recorded using a stopwatch to ensure objectivity.

Data analysis was performed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation and analyzed using the independent t-test. Categorical variables were presented as frequencies and percentages and compared using the chi-square test. A p-value of < 0.05 was considered statistically significant. Differences in primary (BIS) and secondary outcomes (HR, MAP, and recovery times) between the two groups were assessed accordingly.

3. Results

A total of 80 patients were enrolled in the study, with 40 patients allocated to each group, as illustrated in **Figure 1**. The demographic characteristics, including age, gender distribution, and ASA physical status, were comparable between Group S (sevoflurane) and Group D (desflurane), with no statistically significant differences observed (**Figure 2**). The mean age in Group S was 34.2 ± 8.1 years, compared to 35.1 ± 7.9 years in Group D (p = 0.42). Gender distribution (male/female) was 22/18 in Group S and 21/19 in Group D (p = 0.89). ASA physical status (I/II) was recorded as 24/16 in Group S and 25/15 in Group D (p = 0.78), as shown in **Table 1**.

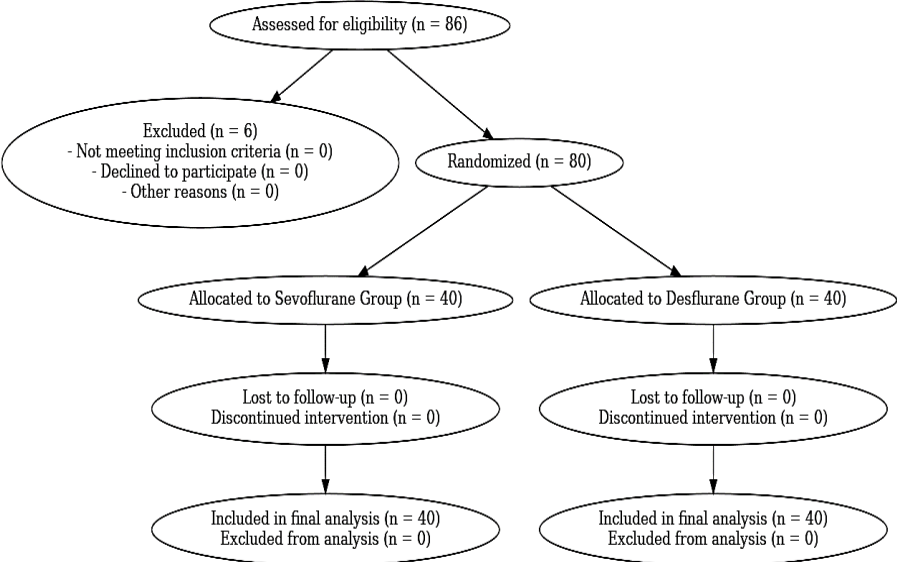
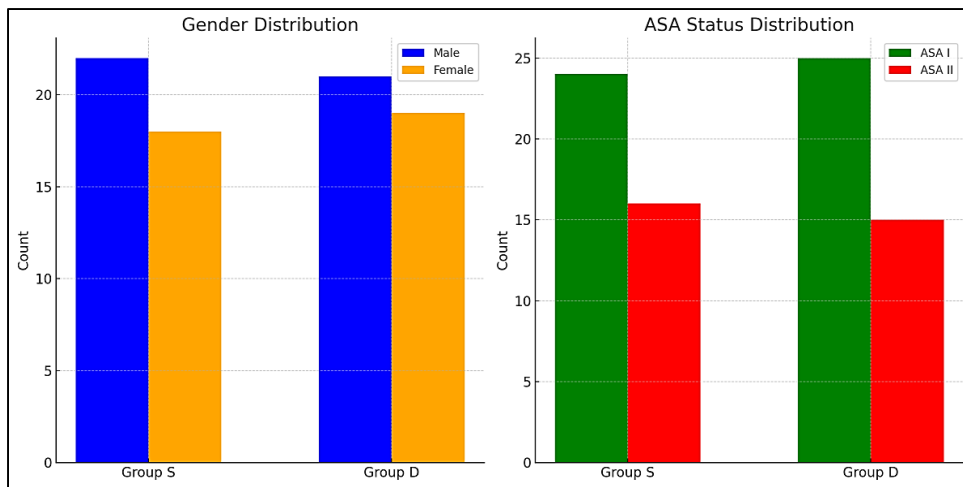
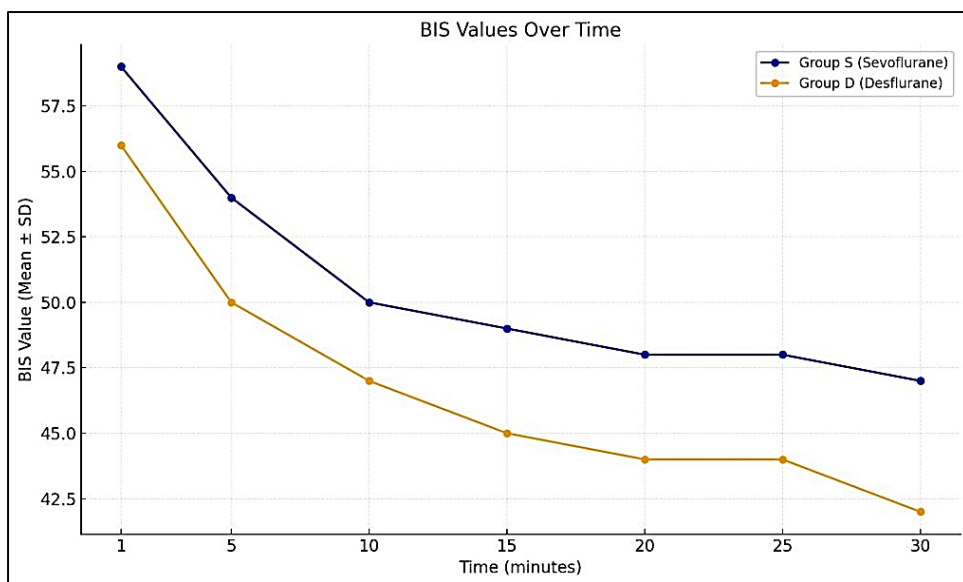


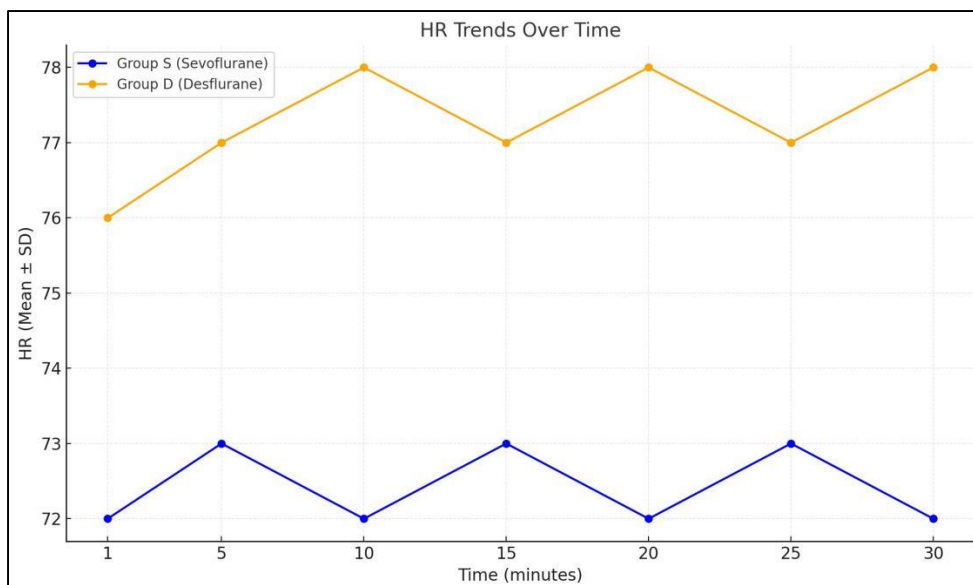
Figure 1: CONSORT flowchart



**Figure 2:** Bar graphs comparing categorical variables (e.g., Gender, ASA Status) and age distribution



**Figure 3:** Line graph showing trends over time for both groups.



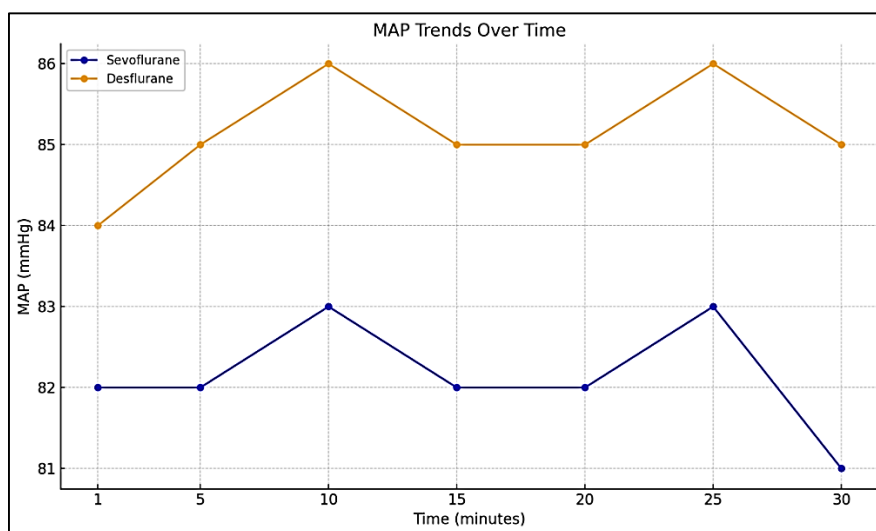
**Figure 4:** Line graph illustrating HR trends over time for both groups.

BIS values were significantly lower in Group D at all recorded time points compared to Group S (**Figure 3**). At 1-minute post-equilibration, the BIS value was  $59 \pm 5$  in Group S and  $56 \pm 4$  in Group D ( $p = 0.04$ ). This trend persisted throughout the 30-minute observation period, with BIS values at 30 minutes being  $47 \pm 4$  in Group S and  $42 \pm 3$  in Group D ( $p < 0.001$ ). These findings indicate that desflurane was associated with a deeper hypnotic effect than sevoflurane at equivalent-MAC concentrations.

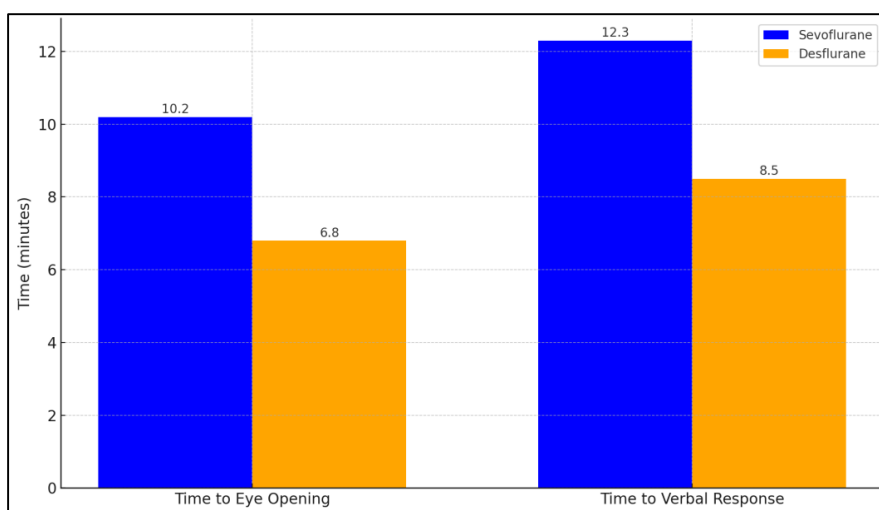
Heart rate (HR) measurements were consistently higher in Group D compared to Group S throughout the observation period, as summarized in **Figure 4**. At 1 minute, the mean HR in Group S was  $72 \pm 6$  beats per minute (bpm), while it was  $76 \pm 5$  bpm in Group D ( $p = 0.03$ ). At 30 minutes, the HR remained elevated in Group D ( $78 \pm 5$  bpm) compared to Group S ( $72 \pm 5$  bpm) ( $p = 0.02$ ). These results suggest a greater sympathomimetic response associated with desflurane.

Mean arterial pressure (MAP) was also significantly higher in Group D at all measured time points (**Figure 5**). At 1 minute, the MAP was  $82 \pm 5$  mmHg in Group S and  $84 \pm 4$  mmHg in Group D ( $p = 0.03$ ). This difference continued through the study, with MAP at 30 minutes recorded as  $81 \pm 5$  mmHg in Group S and  $85 \pm 5$  mmHg in Group D ( $p = 0.02$ ). These findings indicate that desflurane maintained relatively higher arterial pressures compared to sevoflurane.

Recovery parameters also differed significantly between the two groups (**Figure 6**). The mean time to spontaneous eye opening was  $10.2 \pm 2.1$  minutes in Group S versus  $6.8 \pm 1.9$  minutes in Group D ( $p < 0.001$ ). Time to verbal response was  $12.3 \pm 2.4$  minutes in Group S and  $8.5 \pm 2.0$  minutes in Group D ( $p < 0.001$ ). These results demonstrate that desflurane facilitated a more rapid emergence from anaesthesia than sevoflurane.



**Figure 5:** Line graph depicting MAP trends over time



**Figure 6:** Comparison of recovery times between the groups. Time to eye opening and time to verbal response were significantly shorter in the Desflurane group compared to the Sevoflurane group ( $p < 0.001$  for both)

**Table 1:** Comparison of demographic, BIS, hemodynamic, and recovery parameters between sevoflurane and desflurane groups

| Parameter                                               | Group S (Sevoflurane) | Group D (Desflurane) | p-value |
|---------------------------------------------------------|-----------------------|----------------------|---------|
| <b>Demographics</b>                                     |                       |                      |         |
| Age (years)                                             | 34.2 ± 8.1            | 35.1 ± 7.9           | 0.42    |
| Gender (M/F)                                            | 22/18                 | 21/19                | 0.89    |
| ASA Status (I/II)                                       | 24/16                 | 25/15                | 0.78    |
| <b>BIS Values Over Time (minutes)</b>                   |                       |                      |         |
| 1                                                       | 59 ± 5                | 56 ± 4               | 0.04    |
| 5                                                       | 54 ± 4                | 50 ± 3               | 0.01    |
| 10                                                      | 50 ± 3                | 47 ± 3               | 0.02    |
| 15                                                      | 49 ± 4                | 45 ± 3               | 0.01    |
| 20                                                      | 48 ± 4                | 44 ± 3               | <0.001  |
| 25                                                      | 48 ± 4                | 44 ± 3               | <0.001  |
| 30                                                      | 47 ± 4                | 42 ± 3               | <0.001  |
| <b>Heart Rate (HR) Over Time (minutes)</b>              |                       |                      |         |
| 1                                                       | 72 ± 6                | 76 ± 5               | 0.03    |
| 5                                                       | 73 ± 5                | 77 ± 5               | 0.02    |
| 10                                                      | 72 ± 5                | 78 ± 4               | 0.01    |
| 15                                                      | 73 ± 5                | 77 ± 4               | 0.02    |
| 20                                                      | 72 ± 6                | 78 ± 5               | 0.01    |
| 25                                                      | 73 ± 5                | 77 ± 5               | 0.02    |
| 30                                                      | 72 ± 5                | 78 ± 5               | 0.02    |
| <b>Mean Arterial Pressure (MAP) Over Time (minutes)</b> |                       |                      |         |
| 1                                                       | 82 ± 5                | 84 ± 4               | 0.03    |
| 5                                                       | 82 ± 4                | 85 ± 5               | 0.02    |
| 10                                                      | 83 ± 5                | 86 ± 4               | 0.01    |
| 15                                                      | 82 ± 5                | 85 ± 4               | 0.02    |
| 20                                                      | 82 ± 5                | 85 ± 4               | 0.03    |
| 25                                                      | 83 ± 5                | 86 ± 4               | 0.01    |
| 30                                                      | 81 ± 5                | 85 ± 5               | 0.02    |
| <b>Recovery Parameters</b>                              |                       |                      |         |
| Time to eye opening (min)                               | 10.2 ± 2.1            | 6.8 ± 1.9            | <0.001  |
| Time to verbal response (min)                           | 12.3 ± 2.4            | 8.5 ± 2.0            | <0.001  |

#### 4. Discussion

This study aimed to compare the hypnotic potencies of sevoflurane and desflurane at equi-MAC using the bispectral index (BIS), which is derived from electroencephalographic (EEG) data. BIS values have been shown to correlate with the minimum alveolar concentration (MAC) of inhalational agents, including sevoflurane and desflurane.<sup>15</sup> Studies indicate that BIS values decrease linearly with increasing end-tidal concentrations of desflurane, similar to the trends observed with sevoflurane.<sup>16</sup> Secondary objectives included evaluating the haemodynamic effects of the agents. The findings indicate that desflurane exhibits greater hypnotic potency than sevoflurane, as evidenced by lower BIS values across all time points. Additionally, desflurane was associated with faster recovery times but demonstrated a

greater tendency to increase heart rate (HR) and mean arterial pressure (MAP) compared to sevoflurane.

The lower BIS values observed with desflurane, despite both agents being administered at 1 MAC, suggest that desflurane induces a deeper hypnotic state than sevoflurane. This observation is consistent with previous studies that demonstrated lower BIS values with desflurane compared to sevoflurane under comparable conditions.<sup>17</sup> The differences in hypnotic potency can be attributed to variations in the pharmacokinetics of the agents. Several studies have shown that desflurane's lower blood-gas partition coefficient allows for more rapid equilibration between alveolar and brain concentrations, thereby facilitating greater hypnotic potency at equi-MAC.<sup>18,19</sup> In contrast, sevoflurane's higher solubility may delay this equilibration, resulting in comparatively higher BIS values.<sup>20</sup>

The haemodynamic profiles of sevoflurane and desflurane revealed notable differences. Both agents are known to cause dose-dependent reductions in MAP, primarily due to decreased systemic vascular resistance<sup>23</sup>. However, desflurane has been associated with transient sympathetic activation, resulting in tachycardia and hypertension, particularly when its concentration is rapidly increased.<sup>21</sup> This response is attributed to catecholamine release and may pose challenges in patients with cardiovascular comorbidities.<sup>22</sup> Studies assessing vasodilatory effects using the perfusion index (PI) have shown that desflurane produces a higher PI than sevoflurane at equi-MAC, indicating more pronounced vasodilation and a corresponding reduction in MAP.<sup>23,24</sup> Moreover, sevoflurane has demonstrated myocardial protective effects through mechanisms such as ischaemic preconditioning, which may reduce the risk of perioperative myocardial infarction.<sup>25</sup> However, this cardioprotective potential may also necessitate careful consideration in patients requiring tight haemodynamic control.<sup>26,27</sup>

Given these characteristics, sevoflurane may be preferred in patients with cardiovascular instability due to its more stable haemodynamic profile. Its lower propensity to cause tachycardia or hypertension makes it a safer option for high-risk populations, including those with coronary artery disease or compromised cardiac function. Nevertheless, the clinical significance of these haemodynamic differences must be balanced against other considerations such as speed of recovery and the demands of specific surgical procedures.

In terms of respiratory effects, both agents exhibit dose-dependent respiratory depression; however, desflurane is more likely to cause airway irritation, including coughing, breath-holding, and laryngospasm, particularly at higher concentrations.<sup>28</sup> This can make inhalational induction with desflurane challenging in un-premedicated patients. In contrast, sevoflurane is characterized by lower pungency and minimal airway irritation, making it more suitable for inhalational induction.<sup>29</sup> These properties contribute to sevoflurane's widespread use in paediatric anaesthesia, where a smooth and atraumatic induction is essential.<sup>30</sup>

Desflurane demonstrated significantly faster recovery times compared to sevoflurane, as reflected by shorter durations to spontaneous eye opening and verbal response. This finding is consistent with existing literature attributing desflurane's rapid emergence to its low blood and tissue solubility, which enables quick elimination upon discontinuation.<sup>31</sup> Such pharmacokinetic properties make desflurane a suitable agent for ambulatory and short-duration surgical procedures, where early cognitive recovery and discharge readiness are important. Conversely, sevoflurane, although slower in emergence, may be advantageous in cases requiring sustained anaesthetic depth or gradual recovery. The clinical relevance of these differences is particularly important in populations such as children and the elderly,

where rapid recovery may help reduce the incidence of postoperative agitation or cognitive dysfunction. Moreover, recent studies suggest that sevoflurane may offer neuroprotective benefits through modulation of inflammatory pathways and reduction of neuronal apoptosis, which may have implications in neuroanaesthesia.

The observed differences in hypnotic potency, haemodynamic profiles, respiratory effects, and recovery characteristics between sevoflurane and desflurane emphasize the importance of individualized anaesthetic planning. Desflurane's superior hypnotic potency and rapid recovery profile make it a preferred choice for outpatient and short-duration surgeries. However, its haemodynamic stimulation and airway irritant properties necessitate caution in patients with cardiovascular instability or reactive airway disease. In contrast, sevoflurane's smoother haemodynamic response and lower airway irritancy may make it a safer choice for high-risk populations, including those with chronic obstructive pulmonary disease or those undergoing prolonged and complex procedures.<sup>32</sup>

This study had some limitations despite the use of robust methodology such as randomization, blinding, and BIS-guided monitoring. BIS accuracy may be compromised in obese individuals due to challenges with sensor placement and in paediatric populations where adult-derived algorithms may not accurately reflect cerebral activity.<sup>33</sup> Additionally, the controlled clinical environment may not capture the variability encountered in routine practice. The inclusion of only ASA physical status I–II patients further limit generalizability to higher-risk populations. It is also important to note that the study evaluated only short-term outcomes, without assessment of long-term cognitive or functional recovery. Further research involving broader patient populations and extended follow-up is warranted to address these gaps.

## 5. Conclusion

The study demonstrates key pharmacodynamic differences between sevoflurane and desflurane, reinforcing the need for individualized anaesthetic management. Variations in hypnotic potency, haemodynamic effects, and recovery profiles support the use of desflurane in short-duration procedures requiring rapid emergence, while sevoflurane may be more suitable for patients requiring haemodynamic stability. Recognizing these variations serves as a guide for selecting appropriate anaesthetic agents to improve patient safety and enhance recovery outcomes.

## 6. Source of Funding

None.

## 7. Conflicts of Interest

There are no conflicts of interest.

## 8. Acknowledgement

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