

EFFECT OF NITROUS OXIDE ON BISPECTRAL INDEX VALUES AT EQUI-MINIMUM ALVEOLAR CONCENTRATIONS OF SEVOFLURANE AND DESFLURANE

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ABSTRACT

Background: Monitoring the depth of anaesthesia is crucial for patient safety during spine surgeries. The bispectral index (BIS) is widely used to assess hypnotic depth, and volatile anaesthetics such as Sevoflurane and Desflurane may produce different BIS responses at equi-MAC, especially with adjunct nitrous oxide (N₂O). **Objective:** To compare the effect of Sevoflurane and Desflurane on BIS values when used with air-oxygen and N₂O-oxygen, and to assess changes in heart rate (HR) and mean arterial pressure (MAP) during spine surgeries. **Materials and Methods:** A prospective, randomised study was conducted on 64 patients undergoing spine surgeries, divided equally into Sevoflurane (n=32) and Desflurane (n=32) groups. BIS, HR, and MAP were measured at 1 MAC with air-oxygen and after switching to N₂O-oxygen. **Result:** Baseline demographics, ASA status, HR, MAP, and BIS values were comparable between groups (mean age 43.66 ± 11.79 vs. 42.63 ± 12.38 years; p>0.05). HR and MAP remained stable with both carrier gases in the Sevoflurane and Desflurane groups. BIS values with air-oxygen were 35.78 ± 2.27 (Sevoflurane) and 36.5 ± 2.65 (Desflurane), while with N₂O-oxygen, BIS increased to 45.62 ± 2.58 and 40.75 ± 2.94, respectively. Inspired and end-tidal concentrations decreased with N₂O: Sevoflurane inspired 2.52 ± 0.30 vs. 1.21 ± 0.15, end-tidal 2.26 ± 0.22 vs. 1.67 ± 3.16; Desflurane inspired 7.45 ± 0.34 vs. 3.54 ± 0.27, end-tidal 7.24 ± 0.37 vs. 3.38 ± 0.25. **Conclusion:** Sevoflurane and Desflurane provide comparable hemodynamic stability at equi-MAC. BIS values are elevated with N₂O, particularly with Sevoflurane, indicating the need for careful monitoring of anaesthetic depth when N₂O is used.

INTRODUCTION

Monitoring the depth of consciousness during general anaesthesia is crucial for ensuring patient safety and optimal surgical conditions.^[1] The bispectral index (BIS), introduced in 1994, is a processed electroencephalographic parameter developed to assess the hypnotic component of anaesthesia.^[2] BIS is derived from multiple electroencephalographic analyses, including the spectrogram, bispectrum, and burst suppression patterns. The resulting index is expressed on a scale from 0 to 100, where lower values correspond to deeper anaesthesia. Ideally, a particular BIS value should represent a similar depth of hypnosis, regardless of the anaesthetic agent used.^[3] Inhalational anaesthetics vary in their hypnotic and immobilising properties. As a result, even at

equivalent minimum alveolar concentration (MAC) levels, different agents may yield distinct BIS readings.^[4] Among the commonly used volatile anaesthetics, sevoflurane and desflurane are preferred in many clinical settings due to their rapid onset and faster recovery profiles. At 1 MAC, their effects on the electroencephalogram are broadly comparable when administered with oxygen and air. However, subtle differences have been reported: desflurane tends to produce greater electroencephalographic suppression at higher concentrations, whereas sevoflurane can occasionally induce spike activity.^[5] These variations highlight the importance of a more thorough evaluation of BIS responses when comparing agents at equi-MAC levels.

Nitrous oxide (N₂O) is often administered as an adjunct to volatile anaesthetics. Its use reduces the

requirement for other agents to maintain the desired anaesthetic depth, a phenomenon known as the MAC-sparing effect.^[6] While this effect is well established, the influence of N₂O on BIS values remains less clearly defined. Some reports suggest that N₂O has little or no effect on BIS, whereas others indicate possible interactions with volatile anaesthetics that may alter electroencephalographic patterns.^[7,8] Since BIS monitoring is widely employed to titrate anaesthetic depth in daily practice, clarifying its behaviour in the presence of N₂O alongside different volatile agents holds clinical importance.^[8]

In addition to depth of hypnosis, both volatile anaesthetics and N₂O influence hemodynamic stability.^[9] Heart rate (HR) and mean arterial pressure (MAP) may vary depending on the anaesthetic combination used. These changes are of particular concern in spine surgeries, where maintaining stable anaesthesia and hemodynamics contributes significantly to favourable surgical outcomes.^[10] Given these considerations, it becomes important to compare the effects of sevoflurane and desflurane on BIS values at equi-MAC levels, both with and without N₂O. Simultaneous assessment of changes in HR and MAP will provide a more comprehensive understanding of their clinical impact. The present study is designed to address these aspects and to provide evidence on the interaction of N₂O with two widely used volatile anaesthetics.

Aim

To compare the effects of sevoflurane and desflurane on BIS values at equi-MAC with air-oxygen and N₂O-oxygen, and to assess associated changes in HR and MAP during spine surgery.

MATERIALS AND METHODS

This prospective, randomised clinical trial included 64 patients undergoing spine surgery at Tamil Nadu Government Multi-Super Speciality Hospital, Omandurar Estate, Chennai, conducted over one year in the neurosurgery operating theatre. The approval was obtained from the Chengalpattu Medical College Institute's Ethics Committee, and written informed consent was taken from all patients before enrollment.

Sample size calculation

Based on the study by Mishra et al., the standard deviation of N₂O was taken as 9.2. With a power of 80% ($\beta = 0.20$) and a significance level of 5% ($\alpha = 0.05$), the required sample size was calculated to detect a difference of 7 points, which came to 28 patients per group. Allowing for a 15% dropout rate, the final sample size was increased to 32 patients in each group, making a total of 64 patients. The calculation was done using the formula: $n = 2\sigma^2 (Z\alpha + Z\beta)^2 / d^2$.¹¹

Inclusion Criteria

Patients of either gender aged 18 to 65 years, belonging to ASA physical status I or II, scheduled

for spine surgeries under general anaesthesia, and who provided valid informed consent.

Exclusion Criteria

Patients with > 20% deviation from ideal body weight, history of alcohol addiction, use of hypnotics or antidepressants, neurologic or cardiac disorders, those receiving β -blockers, ejection fraction below 35%, severe renal or hepatic impairment, known drug allergy, bradycardia with HR < 45/min.

Methods

The patient was randomly divided into two groups: Group S (Sevoflurane, n = 32) and Group D (Desflurane, n = 32). The parameters studied included BIS values, HR, MAP, SpO₂, and temperature. BIS was measured at 5-minute intervals using a Covidien BIS loc2 Channel transducer with a Philips Intellivue G5 processor. In the operating room, standard monitoring was applied, and the patient's age was entered to calculate age-adjusted MAC values. After applying the BIS sensor on the forehead, anaesthesia was induced with fentanyl, propofol, and atracurium to facilitate intubation. Temperature was monitored with a nasopharyngeal probe, and ventilation was adjusted to maintain normocapnia. Patients received either sevoflurane or desflurane for maintenance with oxygen and air or oxygen and N₂O (FiO₂ 0.4). Data on BIS, HR, and MAP were collected at 1.0 MAC, every minute for 5 minutes, and averaged after a 15-minute steady state. In stage one, readings were noted with air-oxygen, and in stage two, the carrier gas was switched to N₂O-oxygen while maintaining 1.0 MAC. Blood pressure changes greater than 20% were corrected with ephedrine.

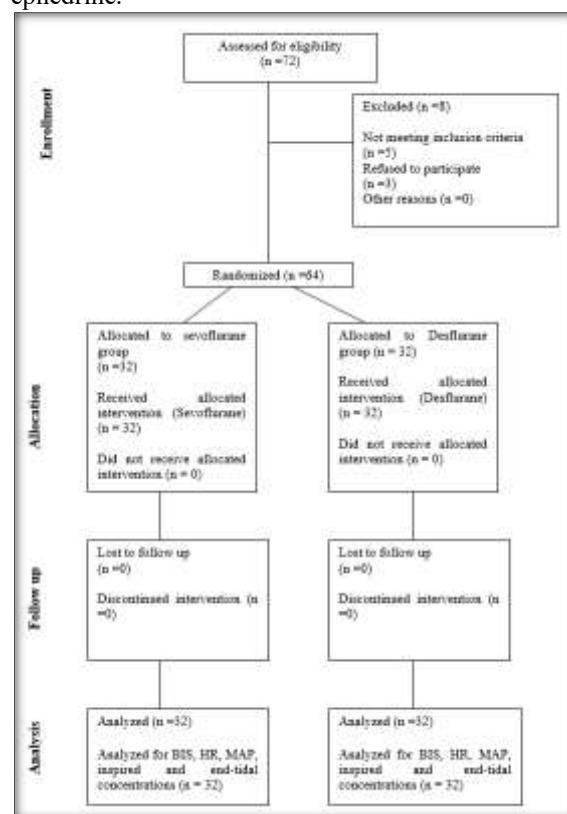


Figure 1: Consort flow diagram

Statistical Analysis

Data were analysed using IBM SPSS Statistics v27. Continuous variables, such as age, HR, MAP, inspired concentration, end-tidal concentration, and BIS values, were presented as mean $\pm$ SD. Categorical variables, including gender and ASA status, were expressed as frequencies and percentages. Comparative analysis between the Sevoflurane and Desflurane groups, as well as across different carrier gases, was performed using the independent Student's t-test for continuous data and Chi-square test for categorical data. A p-value ≤ 0.05 was considered statistically significant.

RESULTS

The mean age was 43.66 ± 11.79 years in the Sevoflurane group and 42.63 ± 12.38 years in the Desflurane group ($p = 0.73$). Gender distribution was similar, with males 18 (56.25%) versus 19 (59.38%) and females 14 (43.75%) versus 13 (40.6%) ($p = 0.30$). ASA status was equally distributed with 16 (50%) in ASA I and 16 (50%) in ASA II in both groups ($p = 0.30$). Preoperative HR, systolic and diastolic blood pressure, and baseline BIS were comparable between groups (HR 76.41 ± 6.95 vs 75.75 ± 6.17 , $p = 0.69$; SBP 114.63 ± 7.14 vs 115.37 ± 5.73 , $p = 0.64$; DBP 73.44 ± 5.73 vs 75.19 ± 5.15 , $p = 0.20$; BIS 99.94 ± 0.35 vs 100 ± 0.0 , $p = 0.32$). [Table 1]

Table 1: Demographic, ASA status, and preoperative baseline hemodynamic parameters of groups

Variable	Sevoflurane	Desflurane	p-value
Age (years)	<30	4 (12.5%)	0.98
	31–40	10 (31.25%)	
	41–50	9 (28.1%)	
	>50	9 (28.1%)	
Gender (N,%)	Male	18 (56.25%)	0.30
	Female	14 (43.75%)	
ASA status	ASA I	16 (50%)	0.30
	ASA II	16 (50%)	
Preoperative baseline hemodynamic	HR	76.41 ± 6.95	0.69
	SBP	114.63 ± 7.14	0.64
	DBP	73.44 ± 5.73	0.20
	BIS	99.94 ± 0.35	0.32

The HR was higher in the Desflurane group compared to the Sevoflurane group when using air as the carrier gas (85.93 ± 4.96 vs 79.63 ± 7.46 , $p = 0.01$), while with N₂O the values were similar (74.65

± 2.73 vs 74.56 ± 7.89 , $p = 0.95$). MAP was comparable between groups with both air (77.84 ± 4.89 vs 75.87 ± 5.27 , $p = 0.12$) and N₂O (78.19 ± 3.52 vs 75.94 ± 5.94 , $p = 0.07$). [Table 2]

Table 2: HR and MAP with two carrier gases between groups

Parameter	Carrier gas	Sevoflurane	Desflurane	p-value
HR	Air	79.63 ± 7.46	85.93 ± 4.96	0.01
	N ₂ O	74.56 ± 7.89	74.65 ± 2.73	0.95
MAP	Air	75.87 ± 5.27	77.84 ± 4.89	0.12
	N ₂ O	75.94 ± 5.94	78.19 ± 3.52	0.07

The inspired concentration was higher in the Desflurane group compared to the Sevoflurane group with air (7.45 ± 0.34 vs 2.52 ± 0.30 , $p = 0.001$) and N₂O (3.54 ± 0.27 vs 1.21 ± 0.15 , $p = 0.001$). End-tidal concentration was also higher in the Desflurane group with air (7.24 ± 0.37 vs 2.26 ± 0.22 , $p = 0.001$)

and N₂O (3.38 ± 0.25 vs 1.67 ± 3.16 , $p = 0.01$). BIS values with air were 36.5 ± 2.65 versus 35.78 ± 2.27 ($p = 0.24$) and with N₂O 40.75 ± 2.94 versus 45.62 ± 2.58 ($p = 0.001$) for Desflurane and Sevoflurane, respectively. [Table 3]

Table 3: Inspired and end-tidal concentrations and BIS values between groups with two carrier gases between groups

Parameter	Carrier Gas	Sevoflurane	Desflurane	p-value
Inspired concentration	Air	2.52 ± 0.30	7.45 ± 0.34	0.001
	N ₂ O	1.21 ± 0.15	3.54 ± 0.27	0.001
End-tidal concentration	Air	2.26 ± 0.22	7.24 ± 0.37	0.001
	N ₂ O	1.67 ± 3.16	3.38 ± 0.25	0.01
BIS	Air	35.78 ± 2.27	36.5 ± 2.65	0.24
	N ₂ O	45.62 ± 2.58	40.75 ± 2.94	0.001

DISCUSSION

This study compares sevoflurane and desflurane on BIS values with air-oxygen and N₂O-oxygen during spine surgeries. Sevoflurane and Desflurane showed

similar hemodynamic stability, while BIS increased with N₂O, especially with Sevoflurane. Carrier gas influences anaesthesia depth monitoring. The Sevoflurane and Desflurane groups were comparable in age, gender, and ASA status, with similar

preoperative HR, blood pressure, and BIS values across both groups. Similarly, Nelson et al. found in a study that included Sevoflurane and Desflurane groups with a mean age below 40 years, showing no significant difference between them ($P = 0.512$). Both groups had patients in ASA I and II categories equally distributed ($P = 0.267$), and male subjects predominated, with no significant difference in gender distribution ($p = 0.243$).^[12]

Taschner et al. found in a study that included adults over 65 years undergoing low- to moderate-risk noncardiac surgery, with males predominating in both groups and no significant difference in gender distribution ($p = 0.243$). ASA I and II patients were evenly represented ($p = 0.267$), and preoperative HR, blood pressure, and BIS were similar between groups.^[13] Özdoğan et al. reported that in a study of both Sevoflurane and Desflurane maintained stable hemodynamics during surgery, with no significant differences in systolic blood pressure, diastolic blood pressure, HR, or SpO₂ at any measured time point ($p > 0.05$).^[14] Therefore, comparable baseline demographics and hemodynamics strengthen the reliability of group comparisons. Further research could stratify patients by higher ASA status or comorbidities to test external validity.

In our study in the Sevoflurane group, HR and MAP remained stable with both Air and N₂O. Similarly, the Desflurane group also demonstrated stable values under both carrier gases, indicating comparable hemodynamic stability across groups. Similarly, Mishra et al. found that with air-oxygen as the carrier gas, BIS values were comparable between Sevoflurane and Desflurane (37.8 ± 9.9 vs. 36 ± 7.3 ; $P = 0.44$), while the addition of 60% N₂O significantly increased BIS for both agents, with higher values in the Sevoflurane group (47.6 ± 9.6 vs. 41.4 ± 8.8 ; $P = 0.01$).^[7] Hendrix and Kramer reported that N₂O does not alter MAP and can counteract the MAP-lowering effects of halogenated anaesthetics like Sevoflurane. There were no significant differences in any parameter between the isoflurane group ($n = 27$) and any other group.^[15] In this case, HR and MAP stability indicate clinical safety. BIS elevation with N₂O suggests altered anaesthetic depth monitoring, recommending cautious BIS interpretation when N₂O is used.

Our study shows that in the Sevoflurane group, both inspired and end-tidal concentrations showed expected variations with Air and N₂O. A similar pattern was observed in the Desflurane group, reflecting consistent agent behaviour under different carrier gases. BIS values increased with the addition of N₂O in both groups, indicating its influence on the depth of anaesthesia. Similarly, Kumar et al. found that adding N₂O significantly lowered end-tidal Desflurane at anaesthetic off ($4.17 \pm 0.86\%$ vs. $2.76 \pm 1.39\%$, $P < 0.001$) and spontaneous respiration ($1.91 \pm 0.59\%$ vs. $1.45 \pm 0.72\%$, $P < 0.001$), with higher age-adjusted MAC at anaesthetic off (0.85 ± 0.16 vs. 0.72 ± 0.11 , $P < 0.001$).^[16]

Fassoulaki et al. in a study found that in a pre-treatment with 50% N₂O accelerated Sevoflurane uptake, reflected by lower BIS values during induction ($P = 0.001$ at 60–150 s and 270 s) and a faster rise in inspired and end-tidal Sevoflurane, alongside lower EtCO₂ ($P = 0.001$), reduced tidal volume ($P = 0.041$), and higher respiratory rate ($P = 0.007$).^[17] Jinks et al. found that halothane caused a MAC-dependent suppression of dorsal horn responses, with a 30–41% reduction between 0.9 and 1.1 MAC, whereas isoflurane paradoxically enhanced responses at 1.1 MAC despite an 89% reduction in withdrawal force, highlighting agent-specific differences in anaesthetic depth and neuronal modulation.^[18] So that N₂O modifies inspired/end-tidal concentrations and increases BIS, especially with Sevoflurane. Clinical monitoring should integrate multiple parameters beyond BIS to ensure accurate depth assessment under combined anaesthesia.

Our study highlights that Sevoflurane and Desflurane provided similar hemodynamic stability at equi-MAC. However, BIS values were influenced by N₂O more with Sevoflurane. This shows the importance of considering carrier gases in anaesthetic monitoring.

Limitations

Long-term outcomes such as recovery and cognitive effects were not evaluated. The potential interindividual variability in anaesthetic response was not fully addressed.

CONCLUSION

Both Sevoflurane and Desflurane provided comparable hemodynamic stability in patients undergoing spine surgeries at equi-MAC levels. HR and MAP remained stable with either Air or N₂O as carrier gases, indicating clinical safety. BIS values were similar between the two agents when using air-oxygen; however, the addition of N₂O increased BIS values, particularly with Sevoflurane, suggesting altered depth of anaesthesia monitoring. These findings highlight the importance of considering carrier gases when interpreting BIS. Overall, both agents are effective for maintaining anaesthetic depth, but BIS should be carefully evaluated during combined N₂O administration.

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