



Anaesthesiology

A COMPARATIVE STUDY BETWEEN SEVOFLURANE AND PROPOFOL USING BISPECTRAL INDEX MONITORING TO ASCERTAIN WHICH IS A BETTER AGENT FOR SHORT DURATION SURGERIES

Pradyumna Kulkarni	Assistant Professor, Department of Anaesthesia and Critical Care, Command Hospital (Western Command) Chandimandir, Panchkula, Haryana - 134107
Parmeet Bhatia*	Assistant Professor, Department of Anaesthesia and Critical Care, Command Hospital (Southern Command) Pune. 411040. Maharashtra. *Corresponding Author
Saurabh Sud	Assistant Professor, Department of Anaesthesia and Critical Care, Command Hospital (Southern Command) Pune. 411040. Maharashtra.
Jagdeep Singh Bhatia	Associate Professor, Department of Anaesthesia and Critical Care. Command Hospital (Southern Command) Pune. 411040.
Deepak Dwivedi	Associate Professor, Department of Anaesthesia and Critical Care. Command Hospital (Southern Command) Pune. 411040.

ABSTRACT In this era of day care surgery there is continuous endeavor in ensuring early and clear-headed recovery of patient's post-surgery, enabling their discharge to home same day. Sevoflurane and propofol are considered to be the agents of choice in surgeries of short duration due to their better recovery profile and fewer post-operative complications. Bispectral monitoring helps in titrating the doses of anesthetics so as to prevent under dosage or over dosage, leading to maintenance of adequate depth of anaesthesia, prevention of recall and early and complete recovery. This prospective randomized study was planned using a bispectral index monitoring to compare sevoflurane and propofol during induction, tracheal intubation, maintenance and postoperative awakening to find out which is better agent for short surgeries. A total of 60 eligible patients were divided randomly into two groups, Group P (Propofol n=30) and Group S (Sevoflurane n=30). Our study shows that sevoflurane is haemodynamically more stable than propofol during induction and maintenance of anaesthesia. Sevoflurane produces slower induction but deeper plane of anaesthesia as compared to propofol. Therefore, these both drugs are good for short duration surgeries and have their own advantages & side effects. But since sevoflurane causes more side effects, propofol is the better choice as an agent for induction of anaesthesia for short procedures.

KEYWORDS : Propofol, Sevoflurane, General anesthesia, Induction, Hemodynamic response.

INTRODUCTION

In this era of day care surgery, we need patients to be completely awake with faster recovery and minimal postoperative morbidity after general anaesthesia (GA). By virtue of its kinetic properties propofol, has become the preferred intravenous (IV) anesthetic agent for short duration surgeries as it produces rapid induction, faster emergence with clear headed recovery and low incidence of post-operative nausea & vomiting (PONV). Moreover, airway reflexes are blunted allowing insertion of endotracheal tube (ETT) or supraglottic airway (SGA) devices without muscle relaxation. Sevoflurane, a halogenated volatile anesthetic agent has a pleasant, non-pungent odour with minimal airway irritability. Its low blood gas partition coefficient facilitates rapid induction, allowing more precise control over the depth of anaesthesia and rapid emergence from anaesthesia. It has a favorable safety profile characterized by relative cardiovascular stability, good airway relaxation, a wide safety margin, and minimal end organ defects.

Bispectral analysis (BIS) takes the data generated by electroencephalography through various steps to calculate a single number which correlates with the depth of anaesthesia/hypnosis. BIS values of 60 to 85 indicate sedation and values of 40 to 60 indicates adequate depth for general anaesthesia. Bispectral monitoring helps in titrating the doses of anesthetics so as to prevent over dosage. We propose to compare sevoflurane with propofol using BIS during induction, tracheal intubation, maintenance and postop awakening to find out which is a better agent for short surgeries

MATERIALS AND METHODS

This randomized clinical study was conducted at our tertiary care center over a period of six months after obtaining approval from the institutional ethical review committee (IERC). Written informed consent was obtained from each patient after explaining about the technique of anaesthesia and surgery. The inclusion criteria included, patients belonging to American Society of Anesthesiologists (ASA) physical status I and II, females aged 20 to 35 years, undergoing routine diagnostic hystero-laparoscopy for primary or secondary infertility. Exclusion criteria included patients with clinical or laboratory evidence of hepatic or renal disease, pregnant patients,

patients having psychiatric illness and patients allergic to propofol and sevoflurane.

The patients were randomly allocated using computer generated random number tables into two groups, Propofol group (P) and Sevoflurane group (S). Sixty patients were included in the study and were randomized equally into respective groups on the day of surgery. All patients were kept fasting for 6 hours prior to surgery and no premedication was administered. On arrival in operation theatre (OT) after confirming the nil per oral (NPO) status and patency of intravenous line (I.V), standard monitors were attached which included noninvasive blood pressure (NIBP), pulse-oximeter (SpO₂), electrocardiography (ECG), end tidal carbon dioxide (ETCO₂) and baseline readings were noted. Analgesia in both the groups was provided with injection fentanyl 2µg/kg before induction.

Group S patients were induced with 8% sevoflurane at FGF of 8L/min with normal tidal volume breathing. Induction end point was taken when there was loss of eyelash reflex and BIS at < 60. The patients were then given Inj atracurium at 0.5 mg/kg to carry out tracheal intubation. Maintenance was achieved with sevoflurane 1-3% at FGF rate of 2L/min (or as deemed necessary by investigator) in a mixture of 60% N₂O in O₂. End tidal sevoflurane was adjusted and maintained at the discretion of investigator and to keep the BIS values between 40 and 60. Residual neuromuscular blockade was reversed with neostigmine at the dose of 50 µg/kg and glycopyrolate at the dose of 10 µg/kg.

Group P were induced with bolus of propofol of 2.5 mg/kg administered at the rate of 40mg every 10 sec. The end point for induction was considered same as group S. The muscle relaxant doses were same as Group S. The patients were maintained with propofol administered at an infusion rate of 2-12 mg/kg/hr in combination of 60% N₂O with O₂. The infusion rate for maintenance was titrated to keep the BIS values between 40-60. Residual neuromuscular blockade was reversed with neostigmine at the dose of 50 µg/kg and glycopyrolate at the dose of 10 µg/kg. The use of BIS monitor enabled us to mark a standard end point for induction that is the point at which the BIS value ≤ 60 is achieved. This nullified the observer error to find

this end point. The more important use of the BIS monitor was during the maintenance of anaesthesia where the BIS values are kept in between 40-60 by titrating the anaesthetics agents. This prevented under dosing or overdosing of drugs and the recovery times calculated by us was accurate, as the BIS index is more accurate indicator of hypnosis than hemodynamics. The time from the administration of the anaesthetics to the time of induction and the time of intubation were noted. All the parameters were recorded at the time interval of 2 minutes and 6 minutes from the time of administration of the anaesthetics. Recovery time (R1) was taken from the time of discontinuation of anaesthetic to eye-opening on command. Recovery time (R2) was time from discontinuation of anaesthetics to the time the patient could tell her name on request. The BIS value of all the events were recorded at 2 minutes and 6 minutes from the time of administration of anaesthetics. ECG, heart rate and blood pressure were recorded throughout at all end points to get the hemodynamic assessment of both the groups. Occurrence of cough and uneasiness during induction, pain on I.V injection, PONV and recall during surgery were noted. Overall assessment was made of the quality of anaesthesia and the ease of control of the depth of anaesthesia.

Primary outcome was to compare the time for induction and recovery from anaesthesia with sevoflurane and propofol. Secondary outcomes were the changes in hemodynamics during induction, intubation, maintenance and recovery of anaesthesia. Other secondary outcomes included the comparison of the side effects in both the groups.

Statistical analysis: All parametric data were analyzed using unpaired t test, data is expressed as mean (SD) and a SPSS version 17 (SPSS Inc, Chicago, IL, USA) applied for the statistical analysis.

RESULTS

The study included 60 patients who completed the study and were divided equally into the two groups. [Figure1]

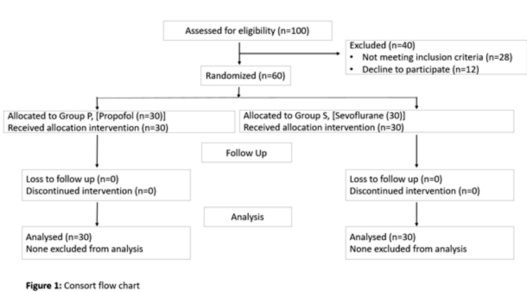


Figure 1: Consort flow chart

Demographic characteristics were comparable between the two groups as being expressed in [Table1]. The induction time was significantly less in propofol group (<0.05). Recovery time (R1) and (R2) was significantly lower in sevoflurane gp (<0.05).

Table 1: Demographic characteristics

Parameter	Group P n=30 (Propofol) (Mean±SD)	Group S n=30 (Sevoflurane) (Mean±SD)	P value
Age(year)	27.7 ± 2.79	28.4 ± 2.80	0.34
Weight (Kg)	55.5 ± 6.66	57.03 ± 6.04	0.36
Sex M/F	30	30	-
ASA I/II	23/07	22/08	-
Duration of surgery (min)	24.2 ± 5.0	26.3 ± 5.6	0.03
Duration of anaesthesia (min)	32.1 ± 5.1	34.1 ± 4.2	0.103
Induction time	0.95 ± .48	1.6 ± .43	0.0001
R 1	3.39 ± .81	2.24 ± .45	0.0001
R 2	6.51 ± 1.1	5.04 ± .75	0.0001

P value< 0.05 is considered significant. ± Values expressed as proportion.

Starting from induction to 6 min post induction the propofol group showed significant fall in HR compared to the sevoflurane group (<0.05). The fall in HR in propofol gp could be due to the dose dependent cardiovascular depression and impairment of the baroreceptor reflexes by propofol.

Table 2: Mean heart rate in both the Groups

TIME	GROUP P (Mean±SD)	GROUP S (Mean±SD)	'P' VALUE
HR Premedication	83.8 ± 9.1	83.0 ± 13.2	0.785
HR Induction	72.8 ± 6.3	85.6 ± 11.09	0.0001
HR 2 Min	71.4 ± 6.9	86.2 ± 10.3	0.0001
HR Intubation	76.3 ± 10.7	89.4 ± 12.2	0.0001
HR 6 Min	78.2 ± 9.1	88.4 ± 10.1	0.0001
HR R1	87.5 ± 11.8	89.5 ± 11.09	0.50
HR R2	85.5 ± 10.8	89.8 ± 10.25	0.12

P value< 0.05 is considered significant. ± Values expressed as proportion.

There was significant fall in SBP & DBP in propofol gp as compared to sevoflurane gp at induction, 2 mins post induction, intubation, and 6 mins post induction [Table 3,4].The cause of decrease in SBP & DBP in propofol gp could be due to the greater fall in peripheral vascular resistance caused by negative inotropic effect and peripheral pooling of blood leading to reduction in preload.

Table 3: Systolic Blood Pressure in both the Groups

TIME	GROUP P (Mean±SD)	GROUP S (Mean±SD)	'P' VALUE
SBP Premedication	126 ± 8.6	129 ± 10.1	0.20
SBP Induction	110.7 ± 11.8	119.6 ± 11.3	0.004
SBP 2 Min	106.7 ± 10.8	118.9 ± 10.3	0.0001
SBP Intubation	102.6 ± 10.8	124.4 ± 8.9	0.0001
SBP 6 Min	104.8 ± 9.2	119.2 ± 8.1	0.0001
SBP R1	124.9 ± 10.9	123.4 ± 8.1	0.547
SBP R2	128.5 ± 8.2	128.2 ± 8.9	0.892

P value< 0.05 is considered significant. ± Values expressed as proportion.

Table 4: Diastolic blood pressure in both the groups

TIME	GROUP P (Mean±SD)	GROUP S (Mean±SD)	'P' VALUE
DBP Premedication	83.3 ± 5.7	84.0 ± 7.3	0.680
DBP Induction	73.3 ± 5.09	80.1 ± 4.6	0.0001
DBP 2 Mins	71.5 ± 5.6	80.8 ± 6.5	0.0001
DBP Intubation	78.8 ± 5.5	78.5 ± 6.6	0.849
DBP 6 Mins	84.9 ± 5.9	79.9 ± 5.7	0.0015
DBP R1	85.8 ± 6.07	79.7 ± 7.51	0.0010
DBP R2	84.6 ± 5.7	81.3 ± 6.09	0.0344

P value< 0.05 is considered significant. ± Values expressed as proportion.

BIS values fell faster in the propofol group compared to the sevoflurane group during induction. The BIS decreased to a lower value in the sevoflurane group at 2 min and during tracheal intubation compared to that in the propofol group. The difference was significant [Table 5]. The BIS values in sevoflurane group increased significantly after tracheal intubation but remained stable in the propofol group.

Table 5: Mean changes of BIS in both the groups

TIME	GROUP P (Mean±SD)	GROUP S (Mean±SD)	'P' VALUE
BIS Premedication	91.7 ± 4.1	90.6 ± 4.6	0.332
BIS 2 Min	54.6 ± 3.7	55.0 ± 6.2	0.762
BIS Intubation	49.8 ± 4.5	39.6 ± 6.8	0.0001
BIS 6 Mins	48.9 ± 5.2	55.2 ± 4.9	0.0001
BIS R1	79.1 ± 5.6	83.2 ± 8.3	0.0287
BIS R2	90.3 ± 3.6	90.9 ± 4.0	0.543

P value< 0.05 is considered significant. ± Values expressed as proportion.

Table 6: Side Effects

Effects	GROUP P	GROUP S
Cough	3/30	7/30
Pain	4/30	NIL
PONV	2/30	9/21
Apnoea	15/30	4/30

DISCUSSION

Propofol^[1-5] and sevoflurane^[6-9] have gained popularity for induction

and maintenance of general anaesthesia because of their smooth and rapid onset of action. Faster, shorter and clear-headed recovery makes these both drugs ideal for day care surgery. BIS helps in titrating the drugs to maintain adequate level of sedation and hypnosis. The finite clinical points can be found and not merely being dependent on the hemodynamic response which is affected by certain drugs and so not an accurate indicator of hypnosis.^[10,11]

In our study there was no significant difference in the age, weight, sex, ASA classification, duration of surgery and duration of anaesthesia. Jellish WS et al had found decreased induction time in propofol gp as compared to sevoflurane gp which was similar in our study and was statistically significant^[12] [Table 1]. Following induction, the propofol group showed a significant fall in HR compared to the sevoflurane group. Propofol causes a dose dependent cardiovascular depression and also impairs the baroreceptor reflexes.^[5] There was an increase in heart rate following intubation in both the groups as shown in [Table 2]. There was significant fall in both SBP & DBP during induction, 2 mins post induction, intubation, and 6 mins compared to the values during premedication in both the groups. The fall in SBP and DBP is more in the propofol group as compared to the sevoflurane group and the difference was statistically significant [Table 3,4]. The cause of greater fall in SBP & DBP in propofol gp is due to the greater fall in peripheral vascular resistance caused by negative inotropic effect and peripheral pooling of blood leading to reduction in preload.^[13] The reductions of BP are in BIS dependent manner. Sevoflurane is cardio stable and cardio-protective with minimal or no effect on heart rate and cardiac parasympathetic tone.^[14,15] BIS values fell faster in the propofol group compared to the sevoflurane group during induction. The BIS decreased to a lower value in the sevoflurane group at 2 min and during tracheal intubation compared to that in the propofol group. The difference was significant [Table 5]. The BIS values in sevoflurane group increased significantly after tracheal intubation but remained stable in the propofol group. This shows that patients could obtain a deep hypnotic level during induction with sevoflurane. BIS fell at a faster rate in the propofol group, commensurate with a faster induction in this group compared to sevoflurane group. During recovery the BIS rose faster in the sevoflurane group, showing that the recovery is faster in the sevoflurane group compared to the propofol group.^[16-20] The BIS values finding of ours were similar to the ones which are given in literature. R1 and R2 were lesser in sevoflurane gp as compared to propofol gp resulting in faster recovery in sevoflurane gp [Table 1]. The cause of rapid recovery in sevoflurane gp could be its low blood gas solubility which permits rapid elimination from the CNS and faster recovery.^[21] In our study PONV were statistically significant between the two groups [Table 6]. 13.3 % of patients with propofol had pain on I.V injection compared to none with sevoflurane as was seen by brooker et al.^[22] The incidence of apnea was 50% with propofol compared to 13.3% with sevoflurane which could be due to the respiratory depression caused by propofol. PONV incidence was 6.6% in propofol gp as compared to 42.8% in sevoflurane gp. Our finding of reduction in PONV in propofol gp as compared to sevoflurane gp are supported by many studies.^[23-26] Borgeat A et al had shown 81% reduction in PONV in patients who received GA with propofol and it was attributed to the 'intrinsic' antiemetic properties of propofol.^[27] The incidence of cough on induction was 10% with propofol compared to 23.3% with sevoflurane and was not statistically significant.

CONCLUSION

Our study shows that sevoflurane is haemodynamically more stable than propofol during induction and maintenance of anaesthesia. Sevoflurane produces slower induction but deeper plane of anaesthesia as compared to propofol. Post-operative recovery is faster with sevoflurane. Thus, we conclude that both these drugs are good for short duration surgeries and have their own advantages and side effects. Therefore, the use of these drugs depends upon the individual choice of anesthesiologist.

REFERENCES:

1. Doze VA, Westphal LM, White PF. Comparison of propofol with methohexital for outpatient anesthesia. *Anesth Analg* 1986; 65:1189-95.
2. Randel GI, Levy L, Kothary SP, Pandit SK. Propofol versus thiamylal-enflurane anesthesia for outpatient laparoscopy. *J Clin Anesth* 1992;4:185-92
3. Ding Y, Fredman B, White PF. Recovery following outpatient anesthesia: Use of enflurane versus propofol. *J Clin Anesth* 1993; 5:447-50.
4. Fredman B, Nathanson MH, Smith I, Wang J, Klein K, White PF. Sevoflurane for outpatient anesthesia: A comparison with propofol. *Anesth Analg* 1995; 81:823-8.
5. Smith I, White PF, Nathanson M, Gouldson R. Propofol. An update on its clinical use. *Anesthesiology* 1994; 81:1005-43.
6. Strum DP, Eger EI 2nd. Partition coefficients for sevoflurane in human blood, saline, and olive oil. *Anesth Analg* 1987; 66:654-6.

7. Song D, Joshi GP, White PF. Fast-track eligibility after ambulatory anesthesia: A comparison of desflurane, sevoflurane and propofol. *Anesth Analg* 1998;86:267-73
8. Smith I, Nathanson M, White PF. Sevoflurane - A long-awaited volatile anaesthetic. *Br J Anaesth* 1996; 76:435-45.
9. Thwaites A, Edmonds S, Smith I. Inhalation induction with sevoflurane: A double-blind comparison with propofol. *Br J Anaesth* 1997; 78:356-61.
10. Song D, van Vlymen J, White PF. Is the bispectral index useful in predicting fast-track eligibility after ambulatory anesthesia with propofol and desflurane? *Anesth Analg* 1998; 87:1245-8.
11. Schmidt GN, Bischoff P, Standl T, Jensen K, Voigt M, Schulte Am Esch J. Narcotrend and Bispectral index monitor are superior to classic electroencephalographic parameters for the assessment of anesthetic states during propofol-remifentanyl anaesthesia. *Anesthesiology* 2003; 99:1072-7.
12. Jellish WS, Lien CA, Fontenot HJ, Hall R. To study the comparative effects of Sevoflurane versus Propofol. *Anaesthesia analgesia*, 1996; 82:40 - 85.
13. Claeys MA, Gepts E, Camu F. Haemodynamic changes during anaesthesia induced and maintained with Propofol. *British Journal of Anaesthesia* 1988; 60: 3 - 9.
14. Kanaya N, Hirata N, Kurosawa S, Nakayama M, Namiki A. Differential effects of Sevoflurane and sevoflurane on heart rate variability. *Anesthesiology* 2003; 98:34-40
15. Hert SD, Linden PV, Cromheecke S, Meeus R, Nelis A, Reeth VV, Roecke PWB, Bllier IGD. Cardio protective properties of sevoflurane in patients undergoing coronary surgery with cardiopulmonary bypass are related to the modalities of its administration. *Anesthesiology*, 2004; 101: 299 - 310
16. Orhon ZN, Devrim S, Celik M, Dogan Y, Yildirim A, Basok EK. Comparison of recovery profiles of propofol and sevoflurane anaesthesia with bispectral index monitoring in percutaneous nephrolithotomy. *Korean J Anesthesiol* 2013;64:223-8.
17. Coloma N, Zhou T, White PF, Markowitz SD, Forestner JE. Fast-tracking after outpatient laparoscopy. Reasons for failure after propofol, sevoflurane and desflurane anesthesia. *Anesth Analg* 2001; 93:112-5.
18. Peduto VA, Peli S, Amicucci G, Giardina B, Pelaia P, Pasetto A, et al. Maintenance of and recovery from anaesthesia in elderly patients. A clinical comparison between sevoflurane and isoflurane. *Minerva Anesthesiol* 1998; 64:18-25.
19. Jellish WS, Lien CA, Fontenot HJ, Hall R. The comparative effects of sevoflurane versus propofol in the induction and maintenance of anaesthesia in adult patients. *Anesth Analg* 1996; 82:479-85.
20. Wandel C, Neff S, Böhner H, Browne A, Motsch J, Martin E. Recovery characteristics following anaesthesia with sevoflurane or propofol in adults undergoing out-patient surgery. *Eur J Clin Pharmacol* 1995; 48:185-8.
21. Smith I, White PF, Nathanson M. The role of Sevoflurane in outpatient anaesthesia. *British Journal of Anaesthesia*, 1995; 81:565 - 72.
22. Brooker CD, Sutherland J, Cousins MJ. Propofol maintenance to reduce post-operative emesis in thyroidectomy patients: a group sequential comparison with isoflurane / Nitrous oxide. *Anaesthesia Intensive care*. 1998; 26 (6): 625 - 29.
23. Chen HP, Hsu YH, Hua KC, Lin CC, Lo YF, Yu HP. Comparison of sevoflurane versus propofol under auditory evoked potential monitoring in female patients undergoing breast surgery. *Biomed J* 2013; 36:125-31.
24. Pollard BJ, Elliott RA, Moore EW. Anaesthetic agents in adult day care surgery. *Eur J Anaesthesiol* 2003; 20:1-9.
25. Vari A, Gazzanelli S, Cavallaro G, De Toma G, Tarquini S, Guerra C, et al. Post-operative nausea and vomiting (PONV) after thyroid surgery: A prospective, randomized study comparing totally intravenous versus inhalational anesthetics. *Am Surg* 2010; 76:325-28.
26. Won YJ, Yoo JY, Chae YJ, Kim DH, Park SK, Cho HB, et al. The incidence of postoperative nausea and vomiting after thyroidectomy using three anaesthetic techniques. *J Int Med Res* 2011; 39:1834-42.
27. Borgeat A, Wilder-Smith OH, Saiah M, Rifat K. Subhypnotic doses of propofol possess direct antiemetic properties. *Anesth Analg* 1992; 74:539-41.