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ORIGINAL ARTICLE

Comparison of Regional Cerebral Oxygen Saturation Variations Between Sevoflurane and Propofol Anaesthesia in Gynecological Laparoscopic Surgery

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Background: Measurement of regional cerebral oxygen saturation (rSO_2) is a safe, noninvasive, and portable optical method that can be used to monitor activity within the cortical areas of the human brain. Making use of specific wavelengths of light, near-infrared spectroscopy (NIRS) provides measurements of oxygenated hemoglobin (Hb) and deoxygenated Hb that is in direct relation with hemodynamic changes in the brain. **Aim:** The aim of this study was to compare the changes in rSO_2 at different time points between propofol and sevoflurane anesthesia during gynecological laparoscopic surgery. After approval by the institutional ethics committee, written informed consent was taken from all eligible patients. **Methods:** This randomized clinical study was conducted in a gynecology operation theater complex. Thirty-four patients aged between 18 and 60 years categorized between the American Society of Anesthesiologists (ASA) class I I and II who are scheduled for gynecological laparoscopic surgery under general anesthesia were randomized into two groups with 17 patients in each group. The Group 1 patients receive sevoflurane anesthesia and Group 2 patients receive total intravenous anesthesia using an infusion of propofol. The rSO_2 values were continuously monitored using NIRS. The bispectral index target range during maintenance was 40–50. **Results:** The sevoflurane group showed significantly higher rSO_2 values than the propofol group in gynecological laparoscopic surgery. **Conclusion:** It can be inferred that the sevoflurane group showed significantly higher rSO_2 values than the propofol group in gynecological laparoscopic surgery not only during pneumoperitoneum in the Trendelenburg position but also after desufflation of the abdomen in the neutral position (supine).

Key words: Sevoflurane, propofol, cerebral regional oxygen saturation, laparoscopic surgery, pneumoperitoneum, Trendelenburg position

INTRODUCTION

Anesthetic agents used during general anesthesia disrupt the activity of neurons in a dose-dependent manner to suppress memory formation and awareness.[1-3] Propofol and sevoflurane act differently on cerebral blood vessels. Consequently, cerebral blood flow (CBF) with propofol and sevoflurane anesthesia may differ. In contrast to other means of monitoring, the depth of anesthesia, near-infrared spectroscopy (NIRS) monitors the change in circulatory oxygenation of the cerebral cortex, which can reflect tissue oxygen usage.[4,5] NIRS provides measurements of oxygenated hemoglobin (Hb) and deoxygenated Hb that is in direct relation with hemodynamic changes in the brain.[4-6]

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In gynecologic surgery, laparoscopic operations usually require a steep Trendelenburg position and pneumoperitoneum with CO_2 insufflation. In the steep Trendelenburg position, intracranial pressure (ICP) increases due to increased venous pressure as a result of an increase in cerebral blood volume (CBV) as well as cerebrospinal fluid volume.[7,8] The pneumoperitoneum with CO_2 also elevates ICP as the increased abdominal pressure obstructs venous return from the lumbar venous plexus,[9] and increased CBF due to an increase in arterial partial pressure of carbon dioxide and

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catecholamine release independent of $PaCO_2$.[10] NIRS cerebral oximetry allows continuous and noninvasive monitoring of regional cerebral oxygen saturation (rSO_2). Cerebral oxygen saturation reflects the balance between cerebral oxygen supply and demand. It is affected by changes in blood oxygenation, CBF, hemoglobin content, and cerebral metabolic rate of oxygen.[11] A number of clinical studies have demonstrated the ability of cerebral oximetry monitoring to detect changes in CBF and ischemia.[12-14] Some studies[15,16] demonstrated that with inhaled anesthetics, rSO_2 was increased during abdominal surgery in the Trendelenburg position and this was explained by increased CBF and CBV. With increasing concentration, the direct vasodilatory effects of inhaled anesthetics turn dominant, leading to high CBF and CBV and to elevated ICP. However, propofol reduces $CMRO_2$, CBF, CBV, and ICP in a dose-dependent manner.[17] Several studies have demonstrated that the reduction in CBF is larger than the reduction in $CMRO_2$, which suggests that propofol may have direct cerebral vasoconstricting activity.[18]

Since laparoscopic surgery in the Trendelenburg position also elevates CBF, CBV, and ICP, it is hypothesized that during sevoflurane anesthesia, rSO_2 is more favorable compared with propofol anesthesia during laparoscopic surgery in the Trendelenburg position, hence, evaluated in the present study.

MATERIALS AND METHODS

After approval from the Institutional Ethics Committee (IRB Memo No: IPGMEandR/IEC/2017/221) dated March 27, 2017, and obtaining written informed consent from all the eligible patients for the study, the randomized clinical trial was conducted in gynecology operation theater complex. Thirty-four patients aged between 18 and 60 years in the American Society of Anesthesiologists I and II (ASA) class who are scheduled for gynecological laparoscopic surgery under general anesthesia were randomized into two groups. Group 1: patients receiving sevoflurane anesthesia, and Group 2: patients receiving total intravenous anesthesia using a controlled infusion of propofol.

The sample size was calculated assuming a 5% difference in rSO_2 value as a clinically significant difference. It was calculated that a minimum of 16 subjects were required per group to detect this quantum of difference with 80% power and 5% probability of type I error. The calculation assumes two-sided testing. The sample size was determined by "nMaster 2.0" (devised by the department of Biostatistics, CMC, Vellore) software. Data were expressed as mean ± standard deviation.

Randomization was done on a computerized basis using 34 opaque sealed envelopes, 17 for each group, indicating patient group assignment and describing the anesthetic protocol. Out of 34 patients enrolled in the study, one patient in the propofol group was excluded as cerebral oxygen desaturation occurred. Baseline values of mean arterial pressure (MAP), heart rate (HR), saturation of oxygen (SpO_2), rSO_2, and core body temperature were recorded. For rSO_2 measurement, sensors for cerebral oximetry were placed bilaterally at least 2 cm above the eyebrow on the right and left side of the forehead before induction of anesthesia, and baseline values were obtained. The rSO_2 values of the left ($LrSO_2$) and right ($RrSO_2$) sides were continuously monitored using NIRS. Bispectral index (BIS) was stable between 40 and 50.

Before monitoring, INVOS™ system recording quality was assessed by inspection of the signal strength index (SSI) for each channel. The 5-unit bar scale is a non-linear scale with 1-bar signal strength will be only 4% of that represented by 5 bars. Adequate signal strength is represented by the continuous display of >1-unit bar. If the SSI is unreliable, hardware issues (cables and optodes) are to be suspected and be checked. The pre-procedure baselines were recorded. The rSO_2 values <50% or >80% will be considered as outside the normal range and the difference between the right and left rSO_2 levels >10% indicates asymmetry. The technical causes for such abnormalities should be ruled out. After confirming the initial baseline values, a value <20% of the baseline is considered as decreased rSO_2.

Anesthesia was maintained by a mixture of oxygen and nitrous oxide with a fixed FiO_2 of 0.5 along with either sevoflurane or propofol, and mechanical ventilation was adjusted to maintain an end-tidal CO_2 tension ($ETCO_2$) of 30–35 mmHg throughout the surgery.

After induction of general anesthesia, radial arterial line was done for invasive blood pressure monitoring and arterial blood sampling. Abdominal cavity was insufflated with CO_2 gas with the pressure set to 12-15 mm of Hg. Patients were then placed in a Trendelenburg position of 20° for surgery MAP, HR, SpO_2, rSO_2, $ETCO_2$, ETsevo, infusion rate of propofol (ml/hour), core body temperature, hemoglobin, PaO_2 and $PaCO_2$ were recorded at the mentioned different time points which are T_N-in the neutral position just before pneumoperitoneum, T_P-5 minutes after the pneumoperitoneum, T_T-5 minutes after the Trendelenburg position and T_D-5 minutes after desufflation in the neutral position.

Cerebral oxygen desaturation was defined as rSO_2 values <75% of the baseline value or an absolute of rSO_2 values <50%.

Data analysis

Intragroup comparisons of hemodynamic variables, rSO_2 and blood gases were done by repeated measures ANOVA (Analysis of variance) measurement. The level of statistical significance was set at $P < 0.005$.

RESULTS

The sevoflurane group showed significantly higher rSO_2 values than the propofol group in gynecological laparoscopic surgery not only during pneumoperitoneum in the Trendelenburg position but also after desufflation of the abdomen in the neutral position.

There is no significant statistical difference in the mean age and mean body weight between the two groups.

There was no statistically significant difference in the mean duration of anesthesia, duration of surgery, and duration of pneumoperitoneum to the Trendelenburg between the two groups [Table 1 and Figure 1].

At the neutral position, rSO2 was comparable between the two groups ($P = 0.058$), but thereafter, a significant difference was noted at different time points between the two groups at T_P, T_T, and T_D [Table 2 and Figure 2].

rSO2 at T_P was 70.97 ± 1.452 for the sevoflurane group and 67.91 ± 1.186 for the propofol group. rSO_2 at T_T was 74.21 ± 1.160 for the sevoflurane group and 65.72 ± 1.251 for the propofol group. rSO_2 at T_D was 70.71 ± 1.261 for the sevoflurane group and 64.06 ± 1.263 for the propofol group.

The rSO_2 at T_P ($P = 0.000$), rSO_2 at T_T ($P = 0.000$), and rSO_2 at T_D ($P = 0.000$) values were significantly higher in the sevoflurane group compared with the propofol group. In both groups, the change in rSO_2 among different stages was statistically significant by ANOVA ($P = 0.001$).

There was no statistically significant difference in MAP between the group at T_N ($P = 0.545$), T_p ($P = 0.151$), and T_T ($P = 0.056$). However, MAP at T_D was significantly higher ($P = 0.000$) in the sevoflurane group at 83.06 ± 5.528 as compared to the propofol group at 76.19 ± 4.004 [Table 3 and Figure 3].

Also, there was no statistically significant difference in mean $PaCO_2$ between the group at T_N ($P = 0.67$), T_T ($P = 0.269$), and T_D ($P = 0.506$). However, the mean $PaCO_2$ was significantly higher at T_p ($P = 0.014$) in the sevoflurane group 33.75 ± 1.708 as compared to the propofol group 32.40 ± 1.232.

Mean PaO_2 in the sevoflurane group was higher starting from the neutral position, at Tp and T_T as compared to propofol. However, mean PaO_2 was similar in both the groups at 5 min after desufflation in the neutral position.

There was no statistically significant difference in the hemoglobin, BIS values, and temperature in between the groups. $ETCO_2$ concentration was maintained between 30 and 35 mmHg throughout the surgery.

No patient complained of nausea, vomiting, headache, and blurring of vision after recovery from anesthesia.

Table 1: Comparison of duration between the groups

Group	*n*	Mean	SD	*P*
Duration of Surgery (in minutes)				
Group 1	17	99.18	16.005	0.392
Group 2	16	94.69	13.475	
Duration of Anesthesia (in minutes)				
Group 1	17	86.94	15.139	0.567
Group 2	16	84.06	13.319	
Duration of Pneumoperitoneum-Trendelenburg (in minutes)				
Group 1	17	71.47	14.444	0.471
Group 2	16	68.13	11.673	

SD – Standard deviation

Table 2: Comparison of changes in regional cerebral oxygen saturation (rSO_2) at different positions

rSO_2	Group	*n*	Mean	SD	*P*
T_N	Group 1	17	68.85	1.466	0.058
	Group 2	16	69.84	1.423	
T_P	Group 1	17	70.97	1.452	0.000
	Group 2	16	67.91	1.186	
T_T	Group 1	17	74.21	1.160	0.000
	Group 2	16	65.72	1.251	
T_D	Group 1	17	70.71	1.261	0.000
	Group 2	16	64.06	1.263	

T_N – Neutral position, T_P – pneumoperitoneum, T_T – Trendelenburg position, T_D – Desufflation, SD – Standard deviation

Table 3: Comparison of changes in partial pressure of oxygen at different positions

PO_2 (mm Hg)	Group	*n*	Mean	SD	*P*
T_N	Group 1	17	249.18	16.905	0.010
	Group 2	16	235.13	12.154	
T_P	Group 1	17	253.53	16.272	0.016
	Group 2	16	238.94	16.659	
T_T	Group 1	17	257.47	10.730	0.000
	Group 2	16	238.56	15.996	
T_D	Group 1	17	247.12	16.624	0.108
	Group 2	16	238.31	13.647	

T_N – Neutral position, T_P – pneumoperitoneum, T_T – Trendelenburg position, T_D – Desufflation, PO_2 – Partial pressure of Oxygen, SD – Standard deviation

DISCUSSION

Cerebral oxygen saturation reflects the balance between cerebral oxygen supply and demand and it is affected by changes in blood oxygenation, CBF, Hb (g%), and $CMRO_2$.[11]

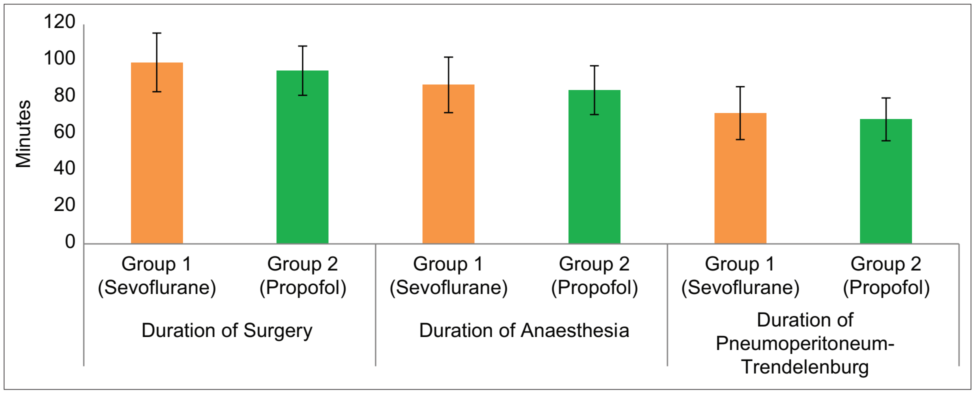

Figure 1: Comparison of durations between two groups

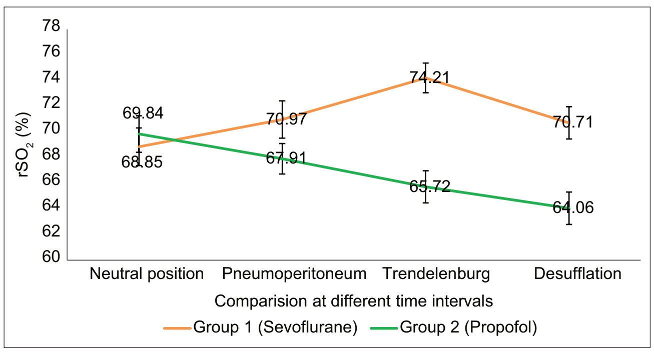

Figure 2: Line diagram showing the comparison of changes in rSO_2 at different positions. rSO_2 = Regional cerebral oxygen saturation

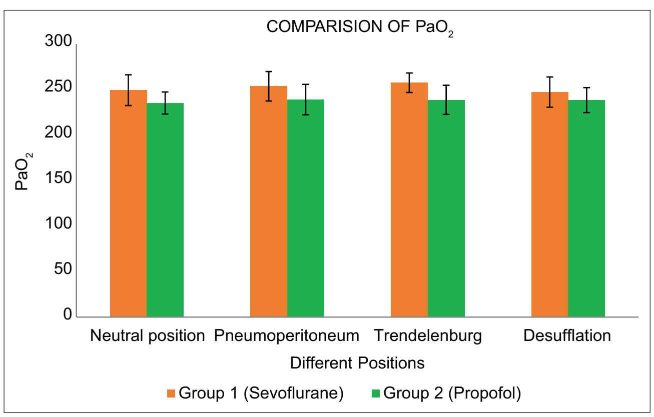

Figure 3: Comparison of changes in partial pressure of oxygen at different positions

NIRS allows continuous and noninvasive monitoring of regional rSO_2. Numerous clinical studies have demonstrated the ability of cerebral oximetry monitoring to detect changes in CBF and cerebral ischemia.[12-14]

Since the invention of NIRS, its application has been proven useful, especially in the perioperative period. It is an invaluable monitoring tool in measuring cerebral oxygenation in cardiac surgery (during deep Trendelenburg and other positions to facilitate surgery), aortic surgeries, carotid surgeries, thoracic, neonatal, and geriatric surgery. Its application in advanced cardiac life support is commendable after the return of spontaneous circulation. In critical care monitoring, rSO_2 decreased the length of tracheal extubation, shortens the ICU as well as hospital stay, improves postoperative outcomes, reduces mortality, and decreases postoperative neurological dysfunction.[19] If the rSO_2 is within the normal limit, it is implied that the outcomes will be good as there would be better cerebral oxygenation.

Two-thirds of the cerebral oxygen utilization is by the interneuronal signal transmission and hence neuropharmacological properties of each agent as well as the dose influences the rSO_2. The anesthetic agents which suppress the cortical activity like barbiturates, volatile agents, propofol, etc., increase the rSO_2, whereas the drugs such as benzodiazepines and opioids do not. Increasing doses of cortical suppressant drugs lead to an increase in rSO_2 and reverse in lighter planes of anesthesia. In the present study, this confounding factor was dealt with by maintaining the adequate depth of anesthesia with BIS.

The rSO_2 values were not affected if the mean blood pressure is within the autoregulatory range, i.e., 50–150 mmHg. In the present study, the blood pressure was maintained within the autoregulatory range of the brain. There are different studies showing the difference in adding of N_2O as pre-treatment or as co-administration. In the studies where pre-treatment with N_2O was given, the induction times were faster with sevoflurane (second gas effect) but there was no difference in the induction times when N_2O and sevoflurane were co-administered. In this study, the N_2O and sevoflurane were co-administered.[20-22]

The present study demonstrated that at steady-state conditions, sevoflurane anesthesia provides a significantly higher rSO_2 value after CO_2 pneumoperitoneum and surgery in the Trendelenburg position as compared to propofol anesthesia as supported by the study conducted by Kim *et al.*[23] who also found the rSO_2 values were significantly lower in the propofol group. Another study conducted by Doe *et al*.[24] on the effects of deep Trendelenburg and pneumoperitoneum in robotic-assisted prostatectomy found that the SjO_2 is significantly higher in the sevoflurane group compared to the propofol group. This is probably due to inhalation-based selective and regulated vasodilatation as desired in the different organ systems translating in a statically significant oxygenation in the brain, which was better in comparison to the propofol group and also due to increased $PaCO_2$ and $PaCO_2$-independent catecholamine release.[23] In the sevoflurane group, rSO_2 increased after pneumoperitoneum and the Trendelenburg position then gradually decreased to a value close to the baseline. In the propofol group, rSO_2 value did not change significantly after CO_2 pneumoperitoneum.

It is well known that patients with an increased ICP respond to inhaled anesthetics such as sevoflurane with a significantly higher $CBF/CMRO_2$ ratio and SjO_2 compared to they do after propofol.[25-27]

Since increased rSO_2 is observed in sevoflurane-based anesthesia, it translates into increased CBF and better cerebral protection during adverse positionings such as Trendelenburg position, insufflation, and desufflation (causing variation in thoracic venous return) than propofol-based anesthesia which is statistically significant ($P < 0.05$).

CONCLUSION

The sevoflurane group showed significantly higher rSO_2 values than the propofol group in gynecological laparoscopic surgery not only during pneumoperitoneum in the Trendelenburg position but also after desufflation of the abdomen in the neutral position. The present study is in contrast to the findings of the study conducted by Mielck *et al*.[25] who reported that one MAC sevoflurane reduced CBF and $CMRO_2$ by approximately 38% and 47%, respectively, compared with the awake state in cardiac patients. Vandesteene *et al*.[26] found that propofol at an infusion rate of 6 and 12 mg/kg/h decreased CBF by 28% and 39%, respectively, and $CMRO_2$ by 5% and 22%, respectively. Hence, such an increase in rSO2 with sevoflurane translates into better cerebral oxygen extraction (delivery) and better cognitive function after sevoflurane anesthesia in comparison with propofol in our present study. The $CBF/CMRO_2$ ratio can be maintained during sevoflurane-based anesthesia but reduced during propofol anesthesia. The present study was conducted on the Asian population in the Indian subcontinent whose demography and genetic profile are completely different from the population taken by other studies. A larger multicentric trial involving a higher sample size would reinforce the finding of the current study undertaken by the authors with profound solidarity.

Data availability statement

The data that support the findings of this study are available from the Dr. Sandeep Kumar Kar (corresponding author), Dr. Atul Aman, Dr. Samarendra Nath Samui, Dr. Pavan Kumar Dammalapati (author), upon reasonable request.

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Conflicts of interest

Dr. Sandeep Kumar Kar, an editorial board member at *Taiwan Journal of Medical Sciences*, had no role in the peer review process of or decision to publish this article. The other authors declared no conflicts of interest in writing this paper.

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