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RESEARCH ARTICLE

USE OF SEVOFLURANE DURING ELECTIVE CESAREAN SECTION: A COMPARISON WITH ISOFLURANE FOR GENERAL ANESTHESIA

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ABSTRACT

BACKGROUND: General anesthesia is needed for caesarean section in situations such as obstetric emergencies (eclampsia, acute fetal distress etc) or when spinal anesthesia is contraindicated (patient refusal, thrombocytopenia etc). Regardless of indication, it is desirable to keep dose of volatile anesthetics to a minimum so as to decrease their effects on the neonate without causing a risk of awareness in the mother. **OBJECTIVES:** To compare efficacy of Sevoflurane 1% and Isoflurane 0.5% as inhalational anesthetic for maintenance of general anaesthesia in cesarean section. **PARTICIPANTS:** 50 term parturients with ASA II and III planned for elective LSCS under general anesthesia. **METHODS:** Patients were divided into two groups. Group A received 1% sevoflurane with N₂O for maintenance of anesthesia while group B received 0.5% isoflurane with N₂O. Bispectral Index (BIS), HR, NIBP, SpO₂, EtCO₂ and Et_{sevo}/Et_{iso} were recorded at 16 designated points throughout the procedure. Post-operatively patients were interviewed for any recall of intraoperative events. **RESULTS:** From the time of skin incision until uterine closure, average values for BIS were higher for group A (Sevoflurane 1%) than for group B (Isoflurane 0.5%) but values in both groups were below 60. From abdominal mopping till the end of procedure, values for group A continued to be higher than that for group B and values in group A reached above 60 in some patients. None of the patients had any intraoperative awareness as confirmed by post-operative interviews. **CONCLUSIONS:** Isoflurane 0.5% with N₂O for maintenance of general anesthesia seems to be adequate for preventing intraoperative awareness during LSCS under while Sevoflurane 1% may be inadequate for maintenance of anesthesia in some patients.

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INTRODUCTION

Amnesia and unconsciousness are important aspects of anesthetic state and these are achieved by a use of hypnotic and amnesic drugs (Crowder, 2013). Awareness with recall after surgery under general anesthesia is an infrequent but well described adverse outcome. Intraoperative awareness occurs in 1 to 2 per 1000 operations under general anesthesia (0.1% to 0.2%), an occasionally occurring critical event (Bischoff, 2000). It is a cause of significant concern to patient (Ghoneim, 2000). A significant proportion of the patients with confirmed intraoperative awareness fulfill the criteria for PTSD on follow up (Leslie et al., 2010).

This high incidence of severe long-term psychological sequelae reinforces the need for preventing intraoperative awareness (Mashour, 2010). Caesarean section carries a high risk of awareness, especially in the period prior to neonatal delivery, again possibly leading to post traumatic stress disorder. This is largely due to the use of low concentrations of volatile agent and the complete avoidance of opioid analgesia prior to delivery of the neonate. The objectives of general anesthesia for cesarean section are to keep mother and fetus adequately oxygenated, while limiting fetal drug transmission and maintaining maternal comfort. Crawford called this conflict "the dilemma of obstetric anesthesia and analgesia" and said it epitomized the challenge and the attraction of the

specialty (Crawford, 1984). Evaluation of hemodynamic parameters and subjective clinical signs such as movement, sweating and lacrimation is the routine approach for determining adequacy of general anesthesia. The availability of new technology to assess various aspects of anesthesia depth has led us to evaluate the efficacy of the general anesthesia we currently use. Some the techniques for monitoring electrical activity of brain are Electroencephalogram, Compressed Spectral Analysis, Cerebral function analysis monitor (CFAM), Bispectral Index (BIS), Narcotrend, Visual Evoked Potential etc (Shander, 2018; Sinha, 2007). BIS is a proprietary algorithm (Aspect Medical Systems, Natick, MA) that converts a single channel of frontal EEG, obtained from a sensor applied to patient's forehead, into an index of hypnotic level. To compute the BIS, several variables derived from the EEG time domain (burst suppression analysis), frequency domain (power spectrum, bispectrum: inter-frequency phase relationships) are combined into a single index of hypnotic level. The BIS score varies from 0 (EEG silence) to 100 (fully alert person) (Chung *et al.*, 2004). After induction, general anesthesia is most frequently maintained with a volatile anesthetic agent like Isoflurane, Sevoflurane (which is nearly 2/3rd in potency compared to Isoflurane), Halothane etc with or without N₂O. Use of volatile anesthetics with 50% N₂O is preferred in cesarean section to decrease volatile anesthetic concentration needed as volatile anesthetics cause both, a decrease in uterine blood flow, and uterine muscle contractility (Lertakyamane, 1999).

METHODOLOGY

After approval from the institutional review board 50 patients of ASA II and ASA III scheduled for elective cesarean section under general anesthesia were included in the study. A written informed consent was taken from the patients for participation in the study. Patients with the history of mental diseases or anticipated difficult intubation and high risk patients like placenta accreta, placenta previa and PIH were excluded from the study. Patients were divided randomly into 2 groups of 25 patients each – Group A and Group B. All patients were pre-medicated with Inj Pantoprazole 40 mg IV and Inj Metoclopramide (10 mg IV) 1 hour prior to surgery. Pre-anesthetic evaluation was done and noted down. In the operating room after securing IV line using 16G cannula, standard multichannel monitor for monitoring baseline non-invasive blood pressure (NIBP), heart rate (HR), oxygen saturation (SPO₂), end tidal carbon dioxide (ETCO₂) and electrocardiogram (ECG) were connected. After that, BIS electrodes were kept in place and connected to BIS monitoring equipment. A BIS reading was taken for each patient 3 minutes prior to induction which served as baseline in both groups. After 3-5 minutes of pre-oxygenation in 10-15 degree left lateral tilt, general anesthesia was induced by giving Inj Propofol (1.5-2.5mg/kg IV) and Inj rocuronium (0.6-1.2 mg/kg IV) and patients were intubated using cuffed PVC endotracheal tube. Anesthesia was maintained with nitrous oxide in oxygen and sevoflurane 1% in group A. In group B nitrous oxide in oxygen was used with 0.5% isoflurane. Muscle relaxation was maintained using 5mg boluses of Inj rocuronium as needed. After fetal delivery and clamping of cord, Inj Oxytocin 5U bolus with an infusion of 15U in 500ml Normal Saline (as needed and asked by obstetrician) was given and analgesia given using IV Inj Fentanyl 100 µg and Inj Morphine 0.1 mg/kg.

Small drops in BP were treated with Inj ephedrine 6mg IV boluses and Inj atropine 0.6mg, Inj epinephrine 100000:1 and Inj Nor-epinephrine 80µg/ml were kept ready for emergencies. Volatile anesthetic was stopped at the start of skin closure and Nitrous Oxide was stopped at the end of skin closure. The patients were then ventilated with 100% O₂ at 8L/min. Reversal of muscle relaxation was achieved using Inj Neostigmine (60mcgm/kg) and Inj Glycopyrolate (10mcgm/kg). Extubation was done when patients were fully conscious and responding to commands. Non invasive blood pressure, heart rate and SpO₂ were continuously monitored as well as end tidal concentration of sevoflurane/isoflurane (Et_{sevo}/Et_{iso}), nitrous oxide, carbon dioxide (EtCO₂). The BIS was measured and recorded at following 16 designated points of sequential events during general anesthesia:

- Baseline (3 minutes before induction).
- After giving Propofol when patient became unresponsive to verbal command.
- Laryngoscopy
- After intubation.
- Skin incision.
- Retraction of rectus muscle.
- Uterine incision.
- Fetal delivery.
- Uterine closure.
- Abdominal mopping.
- Peritoneal closure.
- Subcutaneous closure.
- Cessation of volatile anesthetic.
- Skin closure.
- After giving reversal.
- Eye opening.

All the patients were interviewed for intra operative/post operative recall of events like

- Could the patient be alerted during surgery?
- Did patient recall any event during surgery?
- Did the patient have any dreams during surgery?
- Did the patient hear any conversation during surgery?

STATISTICAL ANALYSIS: The recorded data regarding both Group A (sevoflurane 1%) and group B (sevoflurane 1.5%) was compiled and entered in a spreadsheet (Microsoft Excel) and then exported to data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables were expressed as Mean ±SD and categorical variables were summarized as frequencies and percentages. Graphically the data was presented by bar and line diagrams. Student's independent t-test or Mann-Whitney U-test, whichever feasible, was employed for comparing continuous variables. Chi-square test or Fisher's exact test, whichever appropriate, was applied for comparing categorical variables. Variables have been discussed at 5% level of significance and P-value of less than 0.05 was considered statistically significant. All P-values were two tailed.

RESULTS

Summary of the observations is given in the following paragraphs: The two groups were similar with respect to average age of patients, weight of patients and gestational age.

Table 2 and Figure 1 show the average values for BIS at each of the 16 designated points in both group A (sevoflurane 1%) and group B (isoflurane 0.5%). Initial fall in BIS till the time of intubation was followed by steady rise throughout the procedure in both groups. Till intubation the difference in BIS in the two groups was not significant. From the time of skin incision until uterine closure, average values for BIS were higher for group A (39.20, 41.92, 45.64, 47.88, 51.72 at skin incision, retraction of rectus muscle, uterine incision, fetal delivery, and uterine closure respectively) than for group B (32.72, 34.88, 39.52, 41.76, and 45.56 respectively) but values in both groups were below 60. The difference was statistically significant. From abdominal mopping till the end of procedure, values for group A continued to be significantly higher (55.28±4.93 at abdominal mopping, 57.20±4.43 at peritoneal closure, 59.60±3.43 at subcutaneous closure, 61.64±4.46 at cessation of volatile anesthetic, and 61.44±2.95 at skin closure) than that for group B (47.76±5.08, 50.12±5.39, 50.48±4.91, 52.52±4.93, 53.20±4.96 at abdominal mopping, peritoneal closure, subcutaneous closure, cessation of volatile anesthetic, and skin closure respectively) and **some** values in group A reached above 60. During the procedure, difference between the average values for the two groups was lower (6.12) at fetal delivery, but thereafter the difference slightly increased (7.52 at abdominal mopping). This indicates that sevoflurane 1% with 50 % N₂O might be inadequate to produce sufficient hypnosis during cesarean section. Table 3 shows the pattern of heart rate in the two groups during the procedure. Difference between the two groups was not significant. In both groups, three spikes in heart rate were noted – after giving Propofol, after intubation, and at fetal delivery. Other than these, heart rate was stable in both groups. Systolic BP in the two groups is given in Figure 3. Difference between the two groups was statistically insignificant. Both groups showed a fall in SBP after giving Propofol and at fetal delivery to a similar extent.

Result of post-op interview:

| Intra operative recall of events | Result |
|--|--------|
| 1. Number of patients which could be alerted during surgery. | Nil |
| 2. Number of patients who recall any event during surgery. | Nil |
| 3. Number of patients who had any dreams during surgery. | Nil |
| 4. Number of patients who heard any conversation during surgery. | Nil |

None of the patients in either of the two groups had incidence of uterine atony or intractable bleeding after fetal delivery that could not be controlled by use of Inj Oxytocin or Inj Methylergometrin.

DISCUSSION

Amnesia and unconsciousness are important aspects of anesthetic state and these are achieved by a use of hypnotic and amnesic drugs. Awareness with recall after surgery under general anesthesia is an infrequent but well described adverse outcome. Intraoperative awareness occurs in 1 to 2 per 1000 operations under general anesthesia (0.1% to 0.2%), an occasionally occurring critical event. The prevalence is higher in cardiac surgery, obstetric and major trauma cases. Cesarean section carries an especially high risk of awareness, especially in the period prior to neonatal delivery due to rapid sequence induction, avoidance of opioids before delivery, and low concentration of inhalational anesthetics as well as physiological high output state in pregnancy causing wider distribution of drugs and hence their decreased potency, possibly leading to awareness. This is largely due to the use of

low concentrations of volatile agent and the complete avoidance of opioid analgesia prior to delivery of the neonate. Traditional method of keeping volatile anesthetics at 0.5 MAC due to risk of excessive neonatal depression and uterine atony doesn't seem to provide adequate depth of anesthesia (Crawford, 1984; Paech, 2008; Zand *et al.*, 2014). With these things in consideration, we conducted this study in Department of Anesthesiology and Critical Care, SKIMS Srinagar to compare 1% Sevoflurane with 0.5% Isoflurane in lower segment cesarean section as inhalational anesthetics for maintenance of general anesthesia. In this study, 50 parturients scheduled for cesarean section electively under general anesthesia were included and divided into two groups of 25 patients each. Group A received 1% Sevoflurane while group B received 0.5% Isoflurane with 50% N₂O in oxygen for maintenance of anesthesia. Bispectral index (BIS), heart rate (HR), blood pressure (BP), oxygen saturation (SpO₂), end-tidal carbon dioxide (ETCO₂), and end-tidal anesthetic concentration (ET_{sevo}/ET_{iso}) were measured at 16 designated points throughout surgery. Both groups were similar with respect to average age, weight, and gestational age of the patients. Based on the trends of BIS, we can divide the general course of anesthesia into three phases both in group A and in group B:

- Induction to intubation.
- Intubation to fetal delivery.
- Fetal delivery to end of anesthesia.

Induction to intubation: Mean BIS in group A before induction was 91.56, and in group B it was 89.56. In group A, after giving Propofol, at laryngoscopy and at intubation, average BIS values were 36.24±17.70, 32.12±6.24, and 32.32±6.90 respectively. In group B, values at these points respectively were 31.36±12.34, 30.20±7.85, and 30.08±7.21. Difference between the two groups was not statistically significant (p-value>0.05). This is expected as the procedure and the use of drugs was similar in the two groups up till the point of intubation. No patient in either of the two groups had a BIS reading of more than 60. Average fall in BIS after giving Propofol was 55.32 in group A and 58.20 in group B, (more than 50% fall in BIS in both groups). These results are in accordance to the study conducted by Gürses E *et al* in 2004 titled "Assessing Propofol Induction of Anesthesia Dose Using Bispectral Index Analysis." in which fall in BIS post-induction was more than 50% with mean BIS values being 33.4±11.9 which is close to the values we observed in our study (Gürses *et al.*, 2014).

Mean heart rate and BP in both groups showed a similar trend with slight tachycardia and 20-25% fall in systolic BP after giving Propofol. This can be due to the sympatholytic effect of Propofol with decrease in Blood Pressure possibly leading to mild reflex increase in heart rate. This finding is similar to a previous study by Lim HK *et al* who noted that increase in heart rate is seen when induction of anesthesia is done using IV Propofol injection (Lim, 2000). Also a more significant increase in heart rate accompanied by increase in BP was seen on intubation. Baseline heart rate in group A was 84.60±9.96 beats/min, and in group B it was 81.96±9.06 beats/min. After intubation, average heart rate in group A was 100.72±8.20 beats/min, while in group B it was 100.64±7.41 beats/min. This can be explained by strong sympathetic stimulation caused by laryngoscopy and intubation. Systolic BP (SBP) also showed similar trend in both groups.

Table 1. Showing average duration of surgery (minutes) in the two groups

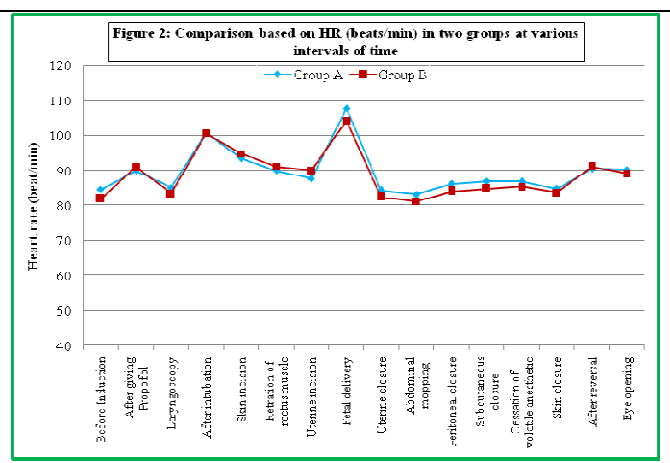
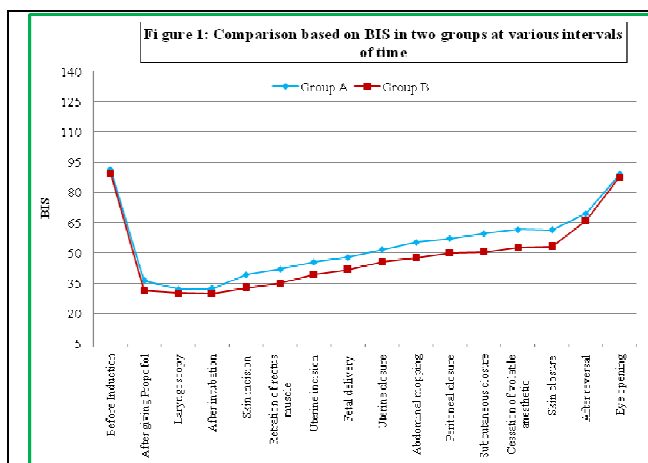
| Duration of surgery (Minutes) | N | Mean | SD | Range | P-value |
|-------------------------------|----|------|-------|-------|---------|
| Group A | 25 | 46.4 | 5.767 | 39-58 | 0.726 |
| Group B | 25 | 45.9 | 5.464 | 32-55 | |

*Statistically Significant Difference (P-value<0.05)

Table 2. Comparison of BIS in the two groups at various intervals of time

| Time interval | Group A | | Group B | | P-value | Difference in BIS |
|----------------------------------|---------|-------|---------|-------|---------|-------------------|
| | Mean | SD | Mean | SD | | |
| Before Induction | 91.56 | 4.60 | 89.56 | 5.34 | 0.162 | 2.00 |
| After giving Propofol | 36.24 | 17.70 | 31.36 | 12.34 | 0.264 | 4.88 |
| Laryngoscopy | 32.12 | 6.24 | 30.20 | 7.85 | 0.343 | 1.88 |
| After intubation | 32.32 | 6.90 | 30.08 | 7.21 | 0.267 | 2.24 |
| Skin incision | 39.20 | 7.21 | 32.72 | 5.30 | 0.002* | 6.48 |
| Retraction of rectus muscle | 41.92 | 7.87 | 34.88 | 5.23 | <0.001* | 7.04 |
| Uterine incision | 45.64 | 6.68 | 39.52 | 5.28 | <0.001* | 6.12 |
| Fetal delivery | 47.88 | 6.56 | 41.76 | 4.08 | <0.001* | 6.12 |
| Uterine closure | 51.72 | 3.94 | 45.56 | 4.40 | <0.001* | 6.16 |
| Abdominal mopping | 55.28 | 4.93 | 47.76 | 5.08 | <0.001* | 7.52 |
| Peritoneal closure | 57.20 | 4.43 | 50.12 | 5.39 | <0.001* | 7.08 |
| Subcutaneous closure | 59.60 | 3.43 | 50.48 | 4.91 | <0.001* | 9.12 |
| Cessation of volatile anesthetic | 61.64 | 4.46 | 52.52 | 4.93 | <0.001* | 9.12 |
| Skin closure | 61.44 | 2.95 | 53.20 | 4.96 | <0.001* | 8.24 |
| After reversal | 69.44 | 5.35 | 66.24 | 4.58 | 0.028* | 3.20 |
| Eye opening | 88.92 | 3.35 | 87.64 | 3.28 | 0.179 | 1.28 |

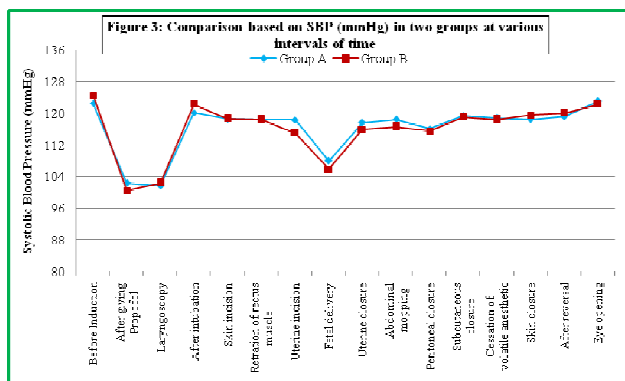
| Time interval | Group A | | Group B | | P-value |
|----------------------------------|---------|------|---------|------|---------|
| | Mean | SD | Mean | SD | |
| Before Induction | 84.60 | 9.96 | 81.96 | 9.06 | 0.332 |
| After giving Propofol | 90.00 | 7.14 | 91.04 | 6.54 | 0.594 |
| Laryngoscopy | 85.16 | 4.87 | 83.52 | 5.80 | 0.285 |
| After intubation | 100.72 | 8.20 | 100.64 | 7.41 | 0.971 |
| Skin incision | 93.48 | 6.30 | 94.84 | 6.26 | 0.448 |
| Retraction of rectus muscle | 90.00 | 4.66 | 91.20 | 4.72 | 0.370 |
| Uterine incision | 87.76 | 4.68 | 90.08 | 5.30 | 0.107 |
| Fetal delivery | 107.84 | 7.71 | 104.28 | 7.12 | 0.096 |
| Uterine closure | 84.28 | 5.65 | 82.40 | 5.27 | 0.230 |
| Abdominal mopping | 83.20 | 5.26 | 81.08 | 3.74 | 0.107 |
| Peritoneal closure | 86.24 | 4.68 | 84.08 | 3.76 | 0.079 |
| Subcutaneous closure | 86.96 | 4.04 | 84.76 | 4.10 | 0.062 |
| Cessation of volatile anesthetic | 86.92 | 5.02 | 85.40 | 5.46 | 0.311 |
| Skin closure | 84.80 | 5.69 | 83.68 | 4.65 | 0.450 |
| After reversal | 90.60 | 6.88 | 91.12 | 4.69 | 0.756 |
| Eye opening | 90.36 | 5.85 | 89.16 | 5.26 | 0.449 |



EtCO₂ after intubation in group A was 37.64±4.68 while in group B it was 35.72±3.90. No patient had hypocapnia or hypercapnia in either of the two groups.

Intubation to fetal delivery: Between these two points the difference between the two groups in average BIS readings were statistically significant.

In group A, at skin incision, retraction of rectus muscle, uterine incision and fetal delivery, mean BIS values respectively were 39.20±7.21, 41.92±7.87, 45.64±6.68, and 47.88±6.56. In group B, at these points of observation, values were 32.73±5.30, 34.88±5.23, 39.52±5.28, and 41.76±4.08 respectively. These readings showed significant difference between the two groups (p-value<0.05).



None of the patients in either of the two groups had incidence of uterine atony or intractable bleeding after fetal delivery that could not be controlled by use of Inj Oxytocin or Inj Methylergometrin.

However, none of the patients in either of the two groups had any of the readings above 60 which would have signified intraoperative awareness. On fetal delivery, both groups showed a similar and significant fall in BP (mean systolic BP decreasing from 116.62 mmHg at uterine incision to 106.88 mmHg after fetal delivery) along with sharp rise in heart rate (from mean HR of 88.92 beats/min at uterine incision to 105.56 beats/min after fetal delivery). This was expected due to routine use of IV bolus Inj Oxytocin after fetal delivery which decreases vascular tone and systemic vascular resistance and also decreases venous return due to decrease in venous tone. As shown in previous study by Bhattacharya S *et al* titled "Oxytocin administration during cesarean delivery: Randomized controlled trial to compare intravenous bolus with intravenous infusion regimen", they concluded that IV bolus Oxytocin leads to significant fall in MAP and rise in heart rate. These hemodynamic changes are short lived and easily controlled by IV boluses of Inj ephedrine (Bhattacharya, 2013).

Fetal Delivery to end of anesthesia: Mean BIS values of group A at uterine closure, abdominal mopping, peritoneal closure, subcutaneous closure, skin closure, and cessation of volatile anesthetic respectively were 51.72 ± 3.94 , 55.28 ± 4.93 , 57.20 ± 4.43 , 59.60 ± 3.43 , 61.44 ± 2.95 , 61.64 ± 4.46 . Thus by the time of abdominal mopping, some values tend to reach above 60 and by the time of skin closure, mean BIS was also above 60 in the 1% sevoflurane group, which might indicate inadequate anesthesia. However, post-operative interview for recall did not reveal any incidence of awareness in any of the patients in either of the two groups. This can be explained by the fact that after cord clamping, for analgesia Fentanyl (along with morphine) were administered and Fentanyl causes decrease in awareness without equivalent decrease in BIS. A study published in BJA by Lysakowski C *et al* concluded that in patients with use of Propofol for induction, μ -agonist opioids increase the hypnotic effect clinically without reflecting this increased hypnosis on BIS measurements.¹⁸ Our results were also similar to those of another study by Hadavi SMR *et al* in 2013 on adequacy of general anesthesia in cesarean section using Bispectral Index. In this study too, analgesia was provided using Fentanyl (without use of morphine). They also noted BIS readings above 60 in a number of patients. However, all the patients had BIS of less than 70. And intraoperative awareness was not present as confirmed by post-operative interviews (Hadavi, 2013). Another possible explanation of higher values of BIS despite absence of intraoperative awareness is the use of nitrous oxide. Although, nitrous oxide does have additive effect on MAC and

decreases consciousness as a result, it has been shown to have a paradoxical effect of increasing BIS. GD Puri in 2001 noted the observation of increase in BIS values on administration of nitrous oxide along with volatile anesthetics which decreased below 60 on discontinuation of nitrous oxide (Puri, 2001). Similarly Rajeeb Kumar Mishra *et al* noted that nitrous oxide use results in higher BIS, especially when used with Sevoflurane (Mishra, 2017). On the other hand, values of mean BIS in group B at uterine closure, abdominal mopping, peritoneal closure, subcutaneous closure, skin closure, and cessation of isoflurane were 45.56 ± 4.40 , 47.76 ± 5.08 , 50.12 ± 5.39 , 50.48 ± 4.91 , 53.20 ± 4.96 , and 52.52 ± 4.93 respectively. As can be seen, all the values were well below our upper target of BIS value of 60. This confirms the results of previous study by Gambling D *et al* in which they concluded that 0.5% isoflurane was successful in maintaining BIS below 60 throughout the procedure (Gambling, 1995). After cessation of sevoflurane/isoflurane, as expected, BIS values rose sharply and reached 88.92 ± 3.35 in group A and 87.64 ± 3.28 in group B at the time of eye opening. Difference between the two groups was not statistically significant (p -value > 0.05). By the time of uterine closure, the tachycardia experienced on fetal delivery/Oxytocin injection settled in both the groups. Thereafter the heart rate and BP in the two groups remained stable with no sudden changes seen in either of the two groups and no statistically significant difference seen. Mean heart rate and BP at uterine closure, abdominal mopping, peritoneal closure, subcutaneous closure, skin closure, cessation of volatile anesthetic, after reversal and at eye opening were similar in both groups. SpO₂ and EtCO₂ remained normal in both the groups at all these points and no sudden changes or statistically significant difference was observed. No significant difference was seen in the overall duration of surgery. None of the patients in either of the two groups had any significant intraoperative event that could be attributed to differential use of volatile anesthetic like uterine atony or intractable uterine bleeding not controlled by routinely used drugs like Oxytocin or Methylergometrine.

CONCLUSION

While clinically both Isoflurane 0.5% and Sevoflurane 1% generally appear to be adequate for preventing intraoperative awareness during general anesthesia when used in combination with 50% nitrous oxide in O₂, Sevoflurane 1% may occasionally prove insufficient as evident by BIS values rising above 60 in some patients during later parts of surgery. Further research is needed on this topic.

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