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Assessment of the benefits of bispectral index monitoring for using volatile anaesthetic agents for anaesthesia

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Abstract
AIM: This study was done to compare the cost-effectiveness and utilization of volatile anaesthetic drugs, to ascertain the depth and adequacy of anaesthesia by using bispectral index monitoring in patients in general anaesthesia.
Material and Methods: In this prospective randomized controlled study, 64 patients of either sex between age group of 18-64 years (ASA I and II) were allocated into four groups.
Group 1:O2+N2O+Isoflurane+inj vecuronium 0.1 mg/kg+IPPV without BIS monitoring.
Group 2:O2 +N2O+Isoflurane+inj vecuronium 0.1mg/kg+IPPV with BIS monitoring
Group 3:O2+N2O+Sevoflurane+inj vecuronium 0.1mg/kg+IPPV without BIS monitoring
Group 4:O2+N2O+Sevoflurane+inj vecuronium 0.1mg/kg+IPPV with BIS monitoring
General anaesthesia was administered by usual method and maintained on O2+N2O+isoflurane/sevoflurane. All patients were monitored vitally every 10 mints interval. BIS monitoring is done in group 2&4 and BIS value was kept between 40-60. Requirement of inhalational agents and recovery time were calculated. Post-operative vital data, sedation scale and side effects were recorded.
Results: Recovery of patient was faster in BIS titrated group (Group II&IV) as compared to control group (Group I&III) (P<0.05).Total volume of volatile anaesthetic agent Isoflurane and sevoflurane used was significantly lower in BIS titrated group than control group (P<0.001). In BIS guided anaesthesia patient remained hemodynamically stable throughout surgery.
Conclusion: Titrating isoflurane and sevoflurane using BIS monitor decreased their utilization and contributed to a faster emergence from anaesthesia.

Keywords: Isoflurane, sevoflurane, BIS monitoring

1. Introduction

The bispectral (BIS) index, a derived value from the electroencephalograph (EEG), has been shown to be a quantifiable measure of the sedative and hypnotic effects of anesthetic drugs on the central nervous system (CNS) [9]. BIS monitoring provides a numerical array from 1 to 100 that has been reported to correlate with the central nervous system (CNS)-depressant effects of anesthetics [8]. A BIS range of 40 to 60 denotes an adequate level of anaesthesia. Thus BIS presents an evaluation of the depth of anaesthesia in surgical patients.

It should also be noted that titrating anaesthetic agents via BIS monitoring can decrease the total dose of hypnotic drugs mandatory for an acceptable depth of anesthesia [8]. A BIS value of 40-60 was chosen as the target for titrating the volatile anesthetics as BIS values of less than 60 have been reported to be associated with a low probability of recall and a high probability of unresponsiveness during surgery. A long period of deep hypnosis (usually defined as BIS < 40) may increase postoperative morbidity and mortality, knowledge of the BIS values at equipotent (i.e. equivalent MAC) concentrations of commonly used volatile anaesthetics is essential for balancing the analgesic and hypnotic components of anaesthesia [4].

Titration of volatile anaesthetics to a target BIS value would provide for a more rapid emergence in patients receiving Isoflurane and Sevoflurane with Nitrous oxide (N2O) for maintenance of general anaesthesia [9].

The present study had been carried out to assess the intraoperative hemodynamics and recovery profiles with Isoflurane and Sevoflurane anaesthesia by using BIS when compared with control groups [9].

2. Material and Methods

This Prospective Randomized Control Study was conducted in 64 patients of either sex belonging to ASA I & II between age group of 18 to 60 years scheduled for routine surgery under general anaesthesia.

Thorough pre-anaesthetic evaluation was carried out on the previous day and patients were explained regarding the procedure. Written informed consent was taken.

Patient refusal to participate in study, ASA grade III or higher, known neurologic, cardiovascular or metabolic diseases, psychiatric illness, impaired renal or hepatic function, body weight greater than 100% above the ideal,

history of alcohol or drug abuse were excluded from the study.

All patients were kept Nil by Mouth for 6-8 hours prior to anaesthesia. Injection Glycopyrolate 5-10 microgram/kg intramuscularly 30 minutes before induction was given as premedication. In addition to routine monitoring devices, the EEG signal was acquired using four electrodes applied to the forehead, with one 2 inches above nose, one above/adjacent to eyebrow, and one on the either temple between corner of eye and hairline in group 2 & 4.

In the operation theatre, after baseline monitoring of vital parameters, preoperative baseline BIS value was taken. Inj. Midazolam 50 microgram/kg was given intravenously. Preoxygenation was done with 100% oxygen for 3 min. General anaesthesia was administered with Inj. Fentanyl 1 microgram/kg, Inj propofol 2 mg/kg followed by Inj. Succinylcholine 1.5-2mg/kg. All patients were given IPPV with 100% O_2 and on achieving complete relaxation intubation was done with appropriate sized cuff portex endotracheal tube.

Patients were randomly divided in four groups and maintained accordingly.

Group 1: oxygen+ nitrous oxide+ isoflurane+ inj vecuronium 0.1 mg/kg + IPPV and no BIS monitoring.

Group 2: oxygen+ nitrous oxide+ isoflurane+ inj vecuronium 0.1 mg/kg + IPPV and BIS monitoring.

Group 3: oxygen+ nitrous oxide + sevoflurane+ inj vecuronium 0.1 mg/kg + IPPV and no BIS monitoring.

Group 4: oxygen+ nitrous oxide+sevoflurane+ inj vecuronium 0.1 mg/kg + IPPV and BIS monitoring.

Intraoperatively Pulse Rate, Blood Pressure, SpO_2 were recorded at 10 minute intervals till the end of surgery. Intraoperatively BIS monitoring done in group 2 and group 4 at every 10 minutes till extubation.

In control groups (Groups 1 and 3) concentrations of the volatile anesthetics were adjusted according to standard clinical practice (i.e., to maintain hemodynamic stability and avoid patient movement with the aim of achieving surgical plane of anaesthesia and a rapid recovery after surgery). In the

BIS-titrated groups (Groups II and IV), the volatile anesthetics were titrated to maintain a BIS value between 40 to 60, ideal for surgical plane of anaesthesia.

Reversal was done using Inj. Glycopyrrolate 0.008mg/kg and Inj Neostigmine 0.05mg/kg intravenously at the end of surgery.

Duration of anaesthesia and surgery was recorded. Recovery times at 1-min intervals from discontinuation of the inhaled anesthetics to awakening were determined [Opening of eyes, follows verbal command, orientation to time, place and person]. Patients were asked whether they recall any intraoperative events. Total dose of vecuronium (mg) required was recorded. Requirement of Isoflurane/Sevoflurane (ml/hr) was calculated by using Ehrenworth and Eisenkraft formula =3x FGF x Volume%

Post-operative SpO_2, Pulse, Blood pressure, sedation grade was recorded for every 15 minutes upto 120 minutes. Incidence of nausea and vomiting was recorded. Sedation was assessed by Richmond Agitation Sedation Scale. Statistical Analysis was done using Student t test, Newman-Keuls test, Chi-Square test and P values of less than 0.05 were considered statistically significant.

3. Results

There was no statistically significant difference between groups with regard to age, weight, sex, duration of surgery and duration of anaesthesia.

Table 1: physical parameters of the study Group

Particulars	Group I	Group II	Group III	Group IV	P value
	Mean± SD	Mean± SD	Mean± SD	Mean± SD	
Age (years)	31.18±10.31	30.5 ±9.15	33.87±11.32	29.75±7.59	P>0.05
Weight (kg)	55 ± 7.52	55.62±7.04	55 ± 9.13	58.75±6.95	P>0.05
Duration of surgery (min)	98.56 ±25.71	97.43±22.5	106.6±19.9	100.87±17.7	P>0.05
Duration of anesthesia (min)	111.87±28.57	108.1±23.1	116.8±20.8	108.1±17.21	P>0.05

Table 2: Intraoperative mean heart rate

Heart rate (per minute)	Group I (MEAN ±SD)	Group II (MEAN ±SD)	P value	Heart rate (per minute)	Group III (MEAN ±SD)	Group IV (MEAN ±SD)	P value
Baseline	84 ± 7.89	89 ± 7.33	P>0.05	Baseline	86.62 ± 11.09	87.25 ± 4.94	P>0.05
After Intubation	94.37 ± 7.16	98.75 ± 8.79	P>0.05	After Intubation	93.62 ± 10.35	99.12 ± 6.06	P>0.05
10 min	93.25 ±7.26	93.75 ± 7.26	P>0.05	10 min	91.75 ± 10.27	95.12 ± 5.41	P>0.05
20 min	90 ± 6.61	90.62 ± 6.68	P>0.05	20 min	89.87 ± 9.27	90 ± 4.95	P>0.05
30 min	85.87 ± 6.79	87.87 ± 6.63	P>0.05	30 min	87.37 ± 6.87	87.25 ± 6.48	P>0.05
40 min	83.87 ± 6.86	86.12 ± 6.94	P>0.05	40 min	85.75 ± 7.26	84.12 ± 5.43	P>0.05
50 min	82.62 ± 7.61	84.75 ± 4.78	P>0.05	50 min	83 ± 7.37	84.12 ± 5.63	P>0.05
60 min	83.12 ± 8.82	84.12 ± 5.67	P>0.05	60 min	83.12 ±8.48	82.12 ± 5.08	P>0.05
70 min	84.37 ± 8.04	85.12 ± 5.46	P>0.05	70 min	81.33 ± 7.95	83.12 ± 6.77	P>0.05
80 min	84.87 ± 8.48	83.57 ±7.96	P>0.05	80 min	82 ± 7.31	84.87 ± 5.26	P>0.05

90 min	86 ± 7.00	86 ± 6.68	P>0.05
100 min	83.77 ± 6.74	87.16 ± 5.99	P>0.05
120 min	82.33 ± 3.20	89 ± 7.48	P>0.05
130 min	82.8 ± 8.07	87.33 ± 7.02	P>0.05
140 min	85 ± 11.6	90 ± 8.48	P>0.05
150 min	77 ± 9.89	84 ± 00	P>0.05
After Extubation	89.12 ± 4.73	92.75 ± 5.45	P>0.05

No significant changes in pulse rate was observed perioperatively between Group I and II.

90 min	82.71 ± 7.98	88.12 ± 7.62	P>0.05
100 min	83.53 ± 7.66	88 ± 4.89	P>0.05
110 min	84.66 ± 6.34	88.44 ± 4.21	P>0.05
120 min	88.44 ± 6.98	90.57 ± 0.97	P>0.05
130 min	89.6 ± 6.22	94 ± 00	P>0.05
After Extubation	89.62 ± 7.12	92.75 ± 5.45	P>0.05

No significant changes in pulse rate was observed perioperatively between Group III and IV.

Gradual decrease in heart rate from basal value till 50 minutes in Group I, till 60 minutes in Group II &IV and till 70 minutes in Group III was observed intraoperatively which was not statistically significant(P>0.05). None of the patients observed bradycardia intraoperatively.

Baseline systolic blood pressure was 112.5 ± 8.56 mmHg in Group I and 109.37 ± 6.8 mmHg in Group II. So, baseline systolic blood pressure was comparable among both the groups (P>0.05).

Significant fall in systolic blood pressure from basal value was observed at 20minutes and 30 minutes in both the groups (P<0.05). Systolic blood pressure was significantly lower in Isoflurane control group (Group I) as compare to BIS titrated group (Group II) at 20 minutes and 30 minutes.

Baseline systolic blood pressure was 113.75 ± 8.85 mmHg in Group III and 108.75 ± 8.85 mmHg in Group IV. So, baseline systolic blood pressure was comparable among both the groups (P>0.05).

Systolic blood pressure was lower in Sevoflurane BIS titrated group as compare to control group intraoperatively which was not significant (P>0.05)

Baseline diastolic blood pressure was 73.75 ± 5 mmHg in Group I & III and 71.87 ± 4.03 mmHg was in Group II & IV.

No significant change in Diastolic Blood Pressure was observed perioperatively in isoflurane and sevoflurane Groups (P>0.05).

Table 3: Recovery Time

Time (min)	Group I	Group II	Group III	Group IV
Mean	13.31	10.68	10.87	8.5
SD	3.59	2.49	3.42	1.71
P value	P<0.05		P<0.05	

Recovery of patient after discontinuation of inhaled anaesthetic to awakening was 13.31 ± 3.59 minutes in Group I and 10.68 ± 2.49 minutes in Group II. Thus recovery from Isoflurane was earlier in BIS titrated group as compared to control group which was statistically significant (P< 0.05).

Recovery time from discontinuation of inhaled anaesthetic to awakening was 10.87 ± 3.42 minutes in Group III and 8.5±1.71 minutes in Group IV. Thus recovery from Sevoflurane was earlier in BIS titrated group as compared to control group which was statistically significant (P< 0.05).

The time to awakening and extubation was significantly shorter in the BIS-titrated groups compared with the control groups. Within the BIS-titrated groups, the time to awakening was significantly shorter in Group IV compared with Group II.

Table 4: Volume % of volatile anaesthetic agent utilised

Volume % of Volatile Anaesthetic (%)	Group I	Group II	Group III	Group IV
Mean	0.93	0.62	1.15	0.78
SD	0.13	0.08	0.27	0.25
P value	P< 0.001		P< 0.001	

Total volume of volatile anaesthetic agent Isoflurane used in Group I was 0.93 ± 0.13 % and in Group II was 0.62 ± 0.08 %. Thus usage of Isoflurane was significantly lower in BIS titrated group than control group. The statistical difference was highly significant (P< 0.001).

Total volume of Sevoflurane used was 1.15 ± 0.27 % in Group III and 0.78 ± 0.25% in Group IV. Thus usage of Sevoflurane was significantly lower in BIS titrated group than control group. The statistical difference was highly significant (P< 0.001).

Table 5: Requirement of volatile anaesthetic agent

Requirement of Volatile Anaesthetic (ml/hr)	Group I	Group II	Group III	Group IV
Mean	16.76	11.25	20.81	14.06
SD	2.34	1.54	4.87	4.65
P value	P< 0.001		P< 0.001	

Total requirement of Isoflurane utilised in Group I was 16.76 ± 2.34 ml/ hr while it was 11.25 ± 1.54 ml/hr in Group II. Thus usage of Isoflurane was significantly lower in BIS titrated group than control group. The statistical difference was highly significant (P< 0.001).

Cost of Isoflurane [7] in market is approximately 350 Rs. for 30 ml. So average cost of Isoflurane used per hour was 194.41 ± 27.14 Rs. in control group and 130.5 ± 17.86 Rs. in BIS titrated group. The difference is highly significant (P< 0.001). Thus BIS monitor is very cost effective.

Total requirement of Sevoflurane utilised in Group III was 20.81 ± 4.87 ml/hr while it was 14.06 ± 4.65 ml/hr in Group IV. Thus usage of Sevoflurane was significantly lower in BIS titrated group than control group. The statistical difference was highly significant (P< 0.001).

Cost of Sevoflurane [1] in market is approximately 8500 Rs. for 250 ml. So average cost of sevoflurane used per hour was 707.54 ± 165.58 Rs. in control group and 478.04 ± 158.1 Rs. in BIS titrated group. The difference is highly significant (P< 0.001). Thus BIS monitor is very cost effective.

Nausea and vomiting was observed in two patients (12.5%) in Group I and three patients (18.75%) in Group II. None of the patients had any other side effect in four groups.

4. Discussion

Intraoperative monitoring equipment should provide information that improves the administration of anaesthetic drugs and thereby provides more rapid recovery after surgery [5].

Hemodynamic responses are commonly used to judge the depth of anaesthesia, they do not necessarily correspond to purposeful motor responses to surgical stimuli [9]. The use of MAC as to titrate volatile anaesthetics can result in either underdosing or overdosing of an volatile anaesthetic. Further, end-tidal anaaesthetic monitoring does not improve intraoperative hemodynamic stability or decrease emergence times from general anesthesia [9].

The BIS monitoring device provides practitioners with information regarding the hypnotic component of the anaesthetic state [9]. BIS index has been shown to be a significant predictor of patient response to skin incision when isoflurane and sevoflurane were used as inhalational agents [9].

The bispectral index (BIS), a value derived from the electroencephalograph (EEG), has been proposed as a measure of anaesthetic effect [3]. To establish its utility, it is important to determine the relation among BIS, measured drug concentration, and increasing levels of sedation [3].

The BIS monitor actually improves the anaesthesia provider's ability to administer anaesthetic drugs (e.g., decreasing emergence times) and improves patient outcome (e.g., earlier discharge from the operating room, the PACU and the ambulatory facility) [9]. The BIS monitor has been found to predict recovery of consciousness from general anesthesia [9].

BIS values in a range of 40-60 have been proposed for producing adequate degree of hypnosis during anaesthesia [6]. The BIS is designed to reflect consciousness and memory formation rather than movement suppression [2]. In our study, BIS was maintained between 40 to 60 in Group II and IV.

At low concentrations of anaesthetic agent the predominant EEG determinant is arousal and the BIS is less agent specific [6]. This is consistent with the findings that BIS-awake values were similar between the agents [6]. As the concentration increases, the effects of arousal are less, and the effects of anaesthetics are greater and the BIS may be more agent-specific [6]. BIS reduces cost by reducing drug consumption [1].

In summary, Bispectral index monitoring is a useful device to ascertain the depth and adequacy of anaesthesia.

Titration of isoflurane and sevoflurane using the Bispectral index monitoring decreases utilization of both inhalational agents, is cost effective and contributes to a faster emergence from general anaesthesia.

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