Original Article

Comparison of bispectral index and end-tidal anaesthetic concentration monitoring on recovery profile of desflurane in patients undergoing lumbar spine surgery

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ABSTRACT

Background and Aims: Several techniques have evolved over time to monitor depth of anesthesia and ensure enhanced recovery. This randomized double-blinded trial was designed to compare bispectral index (BIS) or end-tidal anaesthetic concentration (ETAC) monitoring on the recovery characteristics of patients undergoing thoracolumbar spine surgeries. **Methods:** Seventy American Society of Anesthesiologist I–II patients of either sex were randomized to Group B – BIS-guided protocol, Group E – ETAC-guided protocol, or Group S – Standard protocol. After intravenous induction, anaesthesia was maintained with desflurane in O_2/N_2O (50:50) mixture. In BIS, ETAC and Standard groups, inspired end-tidal desflurane concentration was varied to achieve BIS of 45–55, 0.8–1.0 age-corrected minimum alveolar concentration, and haemodynamic parameters within 20% of the baseline, respectively. Time to eye opening (emergence time, the primary outcome), time to extubation, and time to name recall from the discontinuation of the anaesthetic agent were recorded. Incidence of nausea, vomiting, and total analgesic consumption was noted for 24 h. **Results:** Emergence time (mean ± SD) in ETAC (5.1 ± 1.53 min) and BIS (5.0 ± 2.12 min)-guided groups was significantly lower than Standard group (7.5 ± 2.90 min). Extubation time in ETAC (6.3 ± 2.22 min) and BIS-guided group (6.5 ± 1.78 min) was significantly lower than Standard group (9.0 ± 3.20 min) ($P < 0.001$). Time to achieve fast track score of more than 12 was significantly less in BIS-guided group (13.12 ± 2.59 min). **Conclusion:** ETAC-guided anaesthesia is comparable to BIS-guided anaesthesia in achieving early recovery.

Key words: Bispectral index, desflurane recovery profile, end tidal anaesthetic concentration, lumbar spine surgery

INTRODUCTION

Early neurological assessment is essential in patients undergoing spine surgery.[1] Rapid and smooth recovery from anaesthesia is essential to achieve this goal. Use of short-acting anaesthetic agents and monitoring the depth of anaesthesia are the two options available to enhance recovery. Use of short-acting inhalational agents is promising as the effects are short-lived and early emergence can be targeted. Desflurane has gained wide popularity because of its low blood gas solubility and emergence characteristics.[2]

Over the years, various methods have evolved to monitor the depth of anaesthesia. Haemodynamic responses to laryngoscopy, endotracheal intubation, or skin incision were used to assess the depth of anaesthesia initially.[3] Subsequently, various

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electroencephalography (EEG) and processed EEG parameters were used to relate clinical depth of anaesthesia and its impact on recovery. Although initial studies questioned the use of cerebral monitoring as an adjuvant to clinical monitoring,[4] current data suggest that there is decreased incidence of awareness with the use of these monitors during general anaesthesia.

Bispectral index (BIS) is the most commonly used method for cerebral monitoring. BIS is a complex parameter composed of a combination of time domain, frequency domain, and higher order spectral components derived from clinical data. BIS values range from 0 to 100; 0 signifies that there is no detectable brain activity, while a value of 100 signifies a fully awake state.[5] Several studies have been conducted to assess the effect of BIS monitoring on recovery profile in patients receiving general anaesthesia with desflurane. While few studies demonstrated the earlier emergence from general anaesthesia with the use of BIS monitoring,[6-8] others showed that use of BIS for titration of general anaesthetic agents during the maintenance of anaesthesia did not decrease the emergence time.[9,10]

Monitoring the end-tidal concentration of anaesthetic gases delivered by the anaesthesia delivery system can give essential information about the alveolar concentration of the anaesthetic agent. End-tidal anaesthetic concentration (ETAC) monitoring involves the use of a gas analyzer, which works on the principle of infrared absorption.[11] End-tidal agent concentration is divided by minimum alveolar concentration (MAC) of a particular inhalational agent to give a value of MAC being delivered to the patient. 50% of subjects do not respond to oral command at ETAC equivalent to 0.33MAC (MAC awake) and distressing (auditory) stimuli are not internalized at twice MAC-awake (about 0.7 MAC).[12] In a recent multicenter evaluator blinded trial, authors reported lower incidence of awareness in patients receiving ETAC-guided anaesthesia at a target MAC of 0.7–1.3.[13] However, other clinical signs that can be correlated with depth of anaesthesia such as awakening, recovery, and discharge from post anaesthesia care unit (PACU) were not recorded in this study.[14] However, the exact role of these monitoring techniques in lumbar spine surgeries remain uncertain. Hence, we planned this randomized double-blinded study to compare the effect of ETAC monitoring on recovery profile of patients receiving desflurane anaesthesia with BIS monitoring and standard clinical practice in subjects undergoing lumbar spine surgeries. We hypothesized that maintenance of general anaesthesia by titrating volatile anaesthetic to target ETAC or BIS would facilitate recovery in patients undergoing thoracolumbar spine surgeries

METHODS

After approval from institutional review board of our institute, this prospective randomized double-blinded study was conducted over a period of 18 months [July 2011 to December 2012]. Seventy consecutive subjects undergoing lumbar spine surgeries and having American Society of Anesthesiologist (ASA) I, II patients of both gender aged 20-60 years were screened for eligibility. Two patients refused to consent to participate in the study. Sixty-eight patients were recruited in the study after obtaining written informed consent. Patient with psychiatric illness, clinically significant cardiovascular, respiratory, hepatic and renal disease, long-term drug, or alcohol abuse were excluded.

All patients underwent detailed preanaesthetic check-up a day before surgery. Any neurological deficits found were recorded. No premedication was given. Prior to induction, patients were randomized to one of the three groups after picking a sealed envelope generated by randomized computer sequence: Group B – BIS-guided anaesthesia, Group E – ETAC-guided anaesthesia, and Group S – Standard anaesthesia practice. Intravenous access was secured with 18 G cannula and patients preloaded with 5–10 ml/kg normal saline. Continuous electrocardiography, non-invasive blood pressure and pulse oximetry were attached and baseline vitals recorded. BIS sensor Xp (Aspect Systems, Norwood, USA) was placed on frontotemporal region as per manufacturer's instructions and values were noted. ETAC concentration was measured using Datex multigas analyzer CAiOV module. The infrared gas analyzer was calibrated before start of each case using Datex-Ohmeda airway module calibration gas stock number 755583. Anaesthesia was induced with morphine 0.1 mg/kg and propofol 1.5–2 mg/kg. Trachea was intubated after giving 0.1 mg/kg vecuronium. In all the three groups, anaesthesia was maintained with intermittent doses of vecuronium and desflurane in O_2/N_2O (50:50) mixture at a flow of 2 l/min. Patients were mechanically ventilated to maintain an $EtCO_2$ in the range of 30–35 mmHg. Neuromuscular blockade was maintained with intermittent doses

of vecuronium to keep train-of-four count of 2. In group S, administration of anaesthetic was based on maintaining haemodynamic variables within 20% of preinduction baseline value. The desflurane concentration was adjusted to achieve a BIS value of 45–55 in group B. The desflurane concentration was adjusted to achieve a target age-corrected combined MAC of 0.8–1 in ETAC group. All patients received diclofenac 1.5 mg/kg and 4 mg ondansetron 15 min before the end of procedure. Prior to skin closure, 30 ml of 0.25% bupivacaine was infiltrated subcutaneously. Patients were turned supine after the surgery. Both agents were discontinued and flow increased to 10 l/min. Residual neuromuscular blockade was reversed with neostigmine 0.05 mg/kg and glycopyrrolate 0.01 mg/kg. The trachea was extubated after adequate reversal of neuromuscular blockade and on return of spontaneous respiration.

The BIS values, ETAC concentrations, MAC, and haemodynamic parameters (heart rate, noninvasive blood pressure) were recorded in all the three groups at every 1 min during induction and emergence. They were noted at intervals of every 5 min during rest of intraoperative period by a second independent investigator (JK). In group S, administration of anaesthetic was based on maintaining haemodynamic variables within 20% of preinduction baseline value.[4] Both BIS value and ETAC concentration were not displayed to the attending anaesthesiologist in this group (S). The desflurane concentration was adjusted to achieve a BIS value of 45–55 in group B. Display of ETAC values was hidden in this group for the purpose of blinding. The desflurane concentration was adjusted to achieve a target age-corrected combined MAC of 0.8–1.[15] For blinding, display of BIS values was hidden in this group. At the start of skin closure, desflurane concentration was adjusted to lowest target MAC maintained throughout surgery, i.e., 0.8 MAC in ETAC group and to lowest BIS target value of our protocol, i.e., 55 in BIS group. In the Standard protocol group, desflurane was reduced as much as clinically judged possible without allowing for movement or intraoperative awakening.

Any hypertension, tachycardia, patient movement, grimacing, lacrimation, or sweating during the maintenance period were defined as inadequate anaesthesia. In groups B and E, any sign of inadequate anaesthesia despite the target value was treated with fentanyl 0.5 μg/kg. In the S group, inadequate anaesthesia was treated by adjusting the desflurane concentration in steps of 0.5 vol% as necessary. If this was judged insufficient, fentanyl 0.5 μg/kg was given.

Time to spontaneous respiration, time to eye opening, time to obey verbal command, extubation time, and name recall were assessed every 20 s during emergence by a blinded investigator (JW). Emergence time was measured as the time between discontinuation of anaesthetic agent and opening of eyes (spontaneously or on verbal commands). Extubation time was measured as the time from discontinuation of anaesthetic agent till extubation.

Postoperatively, all patients were assessed for recovery using Wright Fast-track Criteria [Annexure 1].[16] A minimal score of 12, with no score <1 in any category was needed for these patients to bypass PACU. Time to achieve target score from turning off the anaesthetic agent was noted. Pain was assessed using verbal rating scale 0–10, 0 being no pain, 1–3 mild, 4–6 moderate, and 7 or more as severe pain. Paracetamol 1 g intravenously was given eight hourly. Morphine 3 mg was given as rescue analgesic if pain score ≥3. Postoperative nausea vomiting (PONV) was treated with 10 mg of intravenous metoclopramide. All patients who met the recovery criteria were transferred to phase II recovery room in the wards. Patients were followed up for 24 h. Time to first rescue analgesia, any incidence of PONV, and total analgesic consumption during this period were recorded. After 24 h, all patients were interviewed for intraoperative awareness using Modified Brice Interview.[17]

The sample size was calculated based on a previous report by White *et al.*, who demonstrated the mean time to eye opening as mean (±SD) of 9 (±4) minutes using standard clinical monitoring with haemodynamic parameters and 6 (±3) minutes with BIS, to titrate desflurane. Therefore to detect a 30% decrease in time to awakening using either BIS or ETAC, we required a sample size of 21 patients in each group with a power of 80% at $\alpha = 0.05$ and beta error of 0.2.[8] We planned to enroll seventy patients anticipating possible dropouts. Statistical analysis was carried out using Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL, version 17.0 for Windows). Normality of the data was checked by measures of Kolmogrov Smirnov tests of normality. Categorical data was analyzed using Chi-square test. Continuous data were analyzed by one-way analysis of variance (ANOVA) with Student–Newman–Keuls test for multiple comparisons as appropriate and compared using the

repeated measures ANOVA. The relationship between BIS and ETAC values (MAC) during the maintenance was analyzed using Pearson correlation and linear regression to determine the correlation coefficients (r value). All tests were two-tailed with statistical significance defined as $P < 0.05$; data are presented as mean ± SD.

The primary endpoint was to study the effect of BIS and ETAC monitoring on emergence time after desflurane anaesthesia. Other secondary outcomes were time to extubation, time to name recall from the discontinuation of the anaesthetic agent, the time to discharge from PACU, postoperative analgesic requirement, and awareness after 24 h.

RESULTS

We enrolled 68 subjects meeting our inclusion criteria, of which five patients were excluded from the study after enrolment In two patients BIS monitoring was lost intraoperative period -one each in S and E group. Whereas in three patients, there was protocol deviation in the maintenance of BIS or ETAC target values. Data were analyzed for 63 patients ($n = 21$ in each group) [Figure 1].

Demographic data were comparable in all the three groups [Table 1]. Emergence time, extubation time, and time to name recall were significantly less in Groups E and B as compared to Group S [Table 2]. Time to achieve fast track score of more than 12 was significantly less in Group B (13.12 ± 2.59 min, $P = 0.01$). Though the time was decreased in Group E as compared with Group S, it did not reach statistical significance. The emergence characteristics and coughing were also comparable in all the three groups [Table 2].

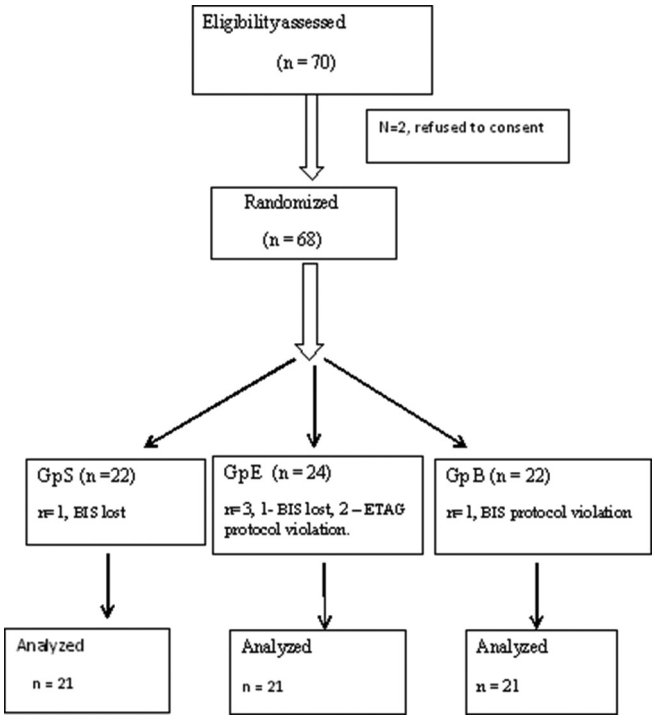

Figure 1: Consort flowchart

Mean BIS and MAC values of all the 63 patients during maintenance phase were 37.44 ± 6.09 and 0.80 ± 0.18, respectively. Average end-tidal desflurane was not significantly different in the three groups (Group S 3.04 ± 0.49%; Group E 2.86 ± 0.42%; and Group B 2.92 ± 0.46%). Average BIS values were also not significantly different in Groups S (46.43 ± 6.54), E (48.11 ± 5.08), and B (49.67 ± 1.81). For repeated measures of ANOVA, values of BIS and ETAC after 10 min of induction were taken as baseline. The BIS values in Group S were significantly lower than Groups E and B at 15 min (46.71 ± 10.01; 53.10 ± 5.79; 53.10 ± 5.79), 20 min (47.43 ± 7.19; 53.33 ± 7.27; 50.38 ± 4.94), and 45 min (46.30 ± 7.12; 48.38 ± 8.39; 52.38 ± 4.36) (P value < 0.05). Also, just before turning off the anaesthetic agents, the BIS values were significantly low in Group S (51.05 ± 7.29) as compared with Group E (56.62 ± 5.86) and Group B (58.43 ± 4.791) ($P < 0.001$). The mean BIS and mean ETAC values of all the 63 patients at the time of emergence were 79.41 ± 7.05 and 0.25 ± 0.24, respectively [Figures 2 and 3].

Table 1: Patient demographics

	S (n=21)	E (n=21)	B (n=21)	P
Age (years)	40.38±13.12	38.10±13.47	42.05±12.81	0.62
Sex* M/F	16:5	12:9	13:8	0.40
Weight (kg)	69.81±13.10	65.52±13.39	69.00±10.64	0.50
ASA* (I)/(II)	15:6	17:4	18:3	0.50
Duration of anaesthesia (min)	110.48±30.84	108.14±25.06	113.90±34.34	0.8
Duration of surgery (min)	80.00±30.75	72.67±25.58	81.29±32.14	0.59

Data expressed as mean±standard deviation, ANOVA. P<0.05 significant. *Data expressed as ratio, χ^2-test

Table 2: Recovery time and emergence characteristics

Emergence (min)	S (n=21)	E (n=21)	B (n=21)	P
Emergence time	7.55±2.90*	5.06±2.12	5.17±1.53	0.00
Extubation time	9.06±3.20*	6.34±2.22	6.51±1.78	0.00
Time to name recall	10.17±3.55*	7.46±2.48	7.70±2.00	0.00
Fast track time (min)	17.89±5.46*	15.03±6.25	13.12±2.59	0.01
#Coughing (0/1/2)	12/6/3	17/4/0	12/8/1	0.19
#Agitated/calm/sedated	3/16/2	0/20/1	4/17/0	0.18

Group B vs. Group S, post hoc using Student Newman keuls test. *P<0.05 significant. #Data expressed as ratio, χ^2-test

A total of 2301 data points were evaluated from total of 63 patients. Each data point represented a BIS–age-corrected MAC sampling pair. A weak negative correlation ($r = -0.217$) was found between BIS and MAC [Figure 4]. Figure 4 shows the three-dimensional distribution of ETAC from the range of 0.6–1.2 and BIS from the range of 44–56.

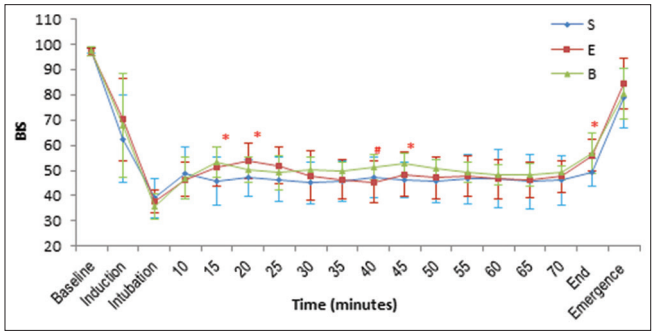

Figure 2: Perioperative bispectral index (BIS) values at various time points of anaesthesia. (B – BIS-guided protocol group, E– ETAC-guided protocol group, S – Standard protocol group)

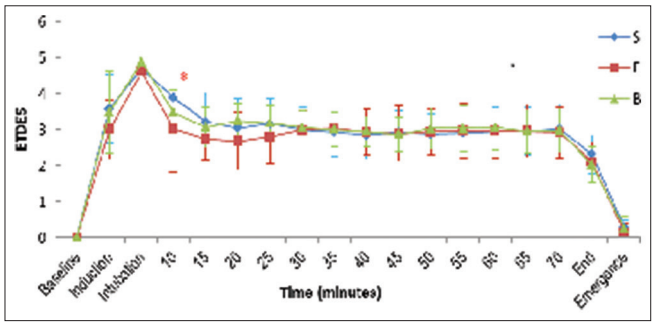

Figure 3: End-tidal Desflurane Concentration (ETDES) values at various time points of anaesthesia. (B – BIS-guided protocol group, E– End-tidal anaesthetic concentration or ETAC-guided protocol group, S – Standard protocol group)

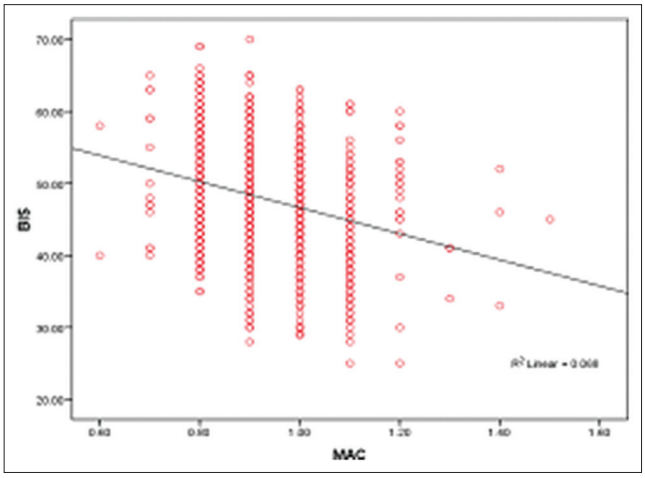

Figure 4: Scatter diagram showing correlation between Bispectral Index (BIS) and Minimum alveolar concentration (MAC) maintenance phase. (B – BIS-guided protocol group, E– ETAC-guided protocol group, S – Standard protocol group)

The BIS values were found within the target range of 45–55 in 74.54% of time in Group B as compared with 42.80 and 46.35% in Groups S and E, respectively. On the other hand, the MAC values were within the range of 0.8–1.0 in 62.63, 76.90, and 77.50% of the time in Groups S, E, and B, respectively. Significant correlation was found between the percentages of times BIS and MAC were maintained within the target range ($P < 0.05$ with $r = 0.554$).

The baseline HR and MAP were comparable in all the groups. The average HR and MA*P* values in the maintenance period were comparable between the three groups. No patient required fentanyl intraoperatively. Time to first rescue analgesia was not statistically different in all the three groups. Mean morphine requirement during the intraoperative period was 5.43 ± 1.12 mg, while it was 6.81 ± 2.705 mg in the postoperative period. There was no significant difference in incidence of nausea and vomiting between all the three groups. Only one patient in Group S had nausea. No patient had anaesthesia awareness when interviewed postoperatively after 24 h.

DISCUSSION

We conducted this study to evaluate the effect of ETAC or BIS monitoring on recovery characteristics after desflurane-based general anaesthesia in patients undergoing spine surgery and compare it with standard clinical practice. Our results showed that both BIS and ETAC-guided anaesthesia were associated with significant reduction in emergence time, extubation time, and time to name recall. BIS-guided anaesthesia was also associated with decrease in time to discharge from PACU.

A variable reduction in emergence time has been reported in previous studies.[6-8] While we found an emergence time of 5.17 ± 1.53 min with the use of BIS monitoring, Song *et al.* reported it at 2.8 ± 1.2 min and White *et al.* at 9 ± 4 min.[6,8] This can be attributed to the different anaesthetic regimens and BIS targets adopted by the different studies. Song *et al.* targeted BIS of 60 and allowed 20% variation of haemodynamic parameters from the baseline.[6] White *et al.* maintained BIS in the range of 50–60 and allowed 15% variation of haemodynamic parameters from the baseline.[8] We targeted BIS of 45–55 and allowed 20% variation in cardiovascular parameters from the baseline. End-tidal anaesthetic gas concentrations monitoring has become a part of modern-day low-flow anaesthesia. ETAC of

inhaled anaesthetics is an indirect measure of their brain concentration at stable anaesthetic depth. Monitoring of ETAC for guiding depth of anaesthesia was initially questioned by Song *et al*. in their study on BIS for recovery and titration of volatile anaesthetics.[6]

Wang *et al*. evaluated the impact of ETAC monitoring on recovery profile of patients undergoing elective surgery with isoflurane anaesthesia and did not find any reduction in emergence time.[18] This can be attributed to two reasons. First, although end-tidal gas concentrations were available to the anaesthesiologist in the study, cardiovascular parameters were targeted to monitor depth of anaesthesia. Secondly, resident anaesthesiologists were instructed to maintain a clinically acceptable depth of anaesthesia rather than administering lowest possible concentration required to maintain a MAC of 0.8.

Kreurer *et al*. conducted a study to define relationship between BIS values and desflurane effect-site concentrations and to assess the ability of effect-site concentration on predicting clinical endpoints such as eye opening.[19] Authors reported better prediction of spontaneous eye opening with the use of effect-site concentration rather than with the use of BIS.

Avidan *et al*.[13] recently conducted a study to determine whether BIS-guided anaesthesia was better than ETAC-guided anaesthesia in preventing awareness in patients undergoing high-risk surgery with inhalational anaesthesia. According to BAG-RECALL protocol, 6000 patients were allocated to receive anaesthesia guided by BIS or ETAC monitoring.[20] BIS-guided protocol did not show superiority over ETAC protocol. Further, ETAC monitoring was associated with decreased incidence of awareness. In our study, we found a significant reduction in emergence time, extubation time, and time to name recall with the use of ETAC monitoring. The latter clinical predictors which can be correlated with anaesthetic depth were not studied by Avidan. Though not adequately powered, none of the patients in our study complained of awareness at 24 h of follow-up.

Similar to the previous studies,[7,8] our study showed significant decrease in time to discharge from PACU with the use of BIS monitoring. Time to discharge from PACU was decreased in ETAC monitored group also, though it did not reach statistical significance. Recart *et al*. reported that a Fast score of >12 was achieved in 30 ± 22 min in BIS-guided group.[7] Lesser time taken to discharge from PACU in our patients [13.12 ± 2.5 min] can be attributed to the use of morphine and infiltration of wound site before closure. This resulted in increased time to first rescue analgesia. Also, all our patients received a score of 2 for pain component of fast track scoring.[21] Laparoscopic surgeries are associated with increased incidence of PONV as compared to spine surgeries.[6-8] Administration of ondansetron to all our patients would have contributed to early PACU discharge.[22]

As ETAC represents anaesthetic concentration in brain after equilibrium has been achieved, there would be an initial delay in attaining this equilibrium. We censored the data for initial 10 min after intubation with a purpose to achieve this equilibrium. Average ETAC and BIS values were not significantly different in any of the three groups. However, BIS values 5 min before turning off the anaesthetic agent were significantly low in Group S. Delivery of higher anaesthetic agent in order to prevent movement while making the patient supine from prone position in the absence of any depth of monitoring devices might have been attributed to delayed emergence in Group S.

Our study showed a weak negative correlation ($r = -0.227$) between BIS and age-corrected MAC during maintenance phase. Also, we found minimal changes in BIS value over a MAC range of 0.8–1.2, suggesting that the same value of BIS might be associated with different ETAC concentration. Two inferences can be made from these results. Firstly, both the BIS and ETAC might not respond to changes in hypnosis in a similar fashion. Secondly, increasing the concentration of inhalational agents causes a progressive increase in depth of anaesthesia, which is not reflected by a corresponding decrease in BIS values. Whitlock *et al*. recently studied the relationship between BIS values and ETAC concentration in more than 1000 patients. Authors reported a poor correlation of BIS with ETAC and found that BIS was insensitive to clinically significant changes in ETAC and shows interindividual variability.[23]

However, there are few limitations in our study. As continuous monitoring of blood concentrations of intravenous anaesthetic agents is not possible, the results of this study cannot be extrapolated to patients who receive total intravenous anaesthesia. Another limitation of our study is that we used N_2O in place of medical air as medical air was not available in our setup. Variable results have been reported in the

literature about effects of nitrous oxide on BIS. Few studies have reported decrease in BIS with addition of N_2O to anesthetic agents,[24,25] while others found no effect of N_2O on the BIS.[26]

CONCLUSION

We conclude from our study that ETAC-guided anaesthesia is comparable to BIS-guided anaesthesia in achieving early recovery and can be used as an alternative method to monitor depth of anaesthesia in patients who receive nitrous oxide and desflurane as a component of their anaesthetic regimen.

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Conflicts of interest
There are no conflicts of interest.

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ANNEXURE 1: WRIGHT'S FAST-TRACKING CRITERIA

Parameters score

I. Level of consciousness
   Awake and oriented – 2
   Arousable with minimal stimulation – 1
   Responsive only to tactile stimulation – 0

II. Physical activity
   Able to move all extremities on command – 2
   Some weakness in movement of extremities – 1
   Unable to voluntarily move extremities – 0

III. Haemodynamic stability
   Blood pressure of 15% of baseline – 2
   Blood pressure of 30% of baseline – 1
   Blood pressure of 50% of baseline – 0

IV. Respiratory stability
   Respiratory rate 10–20 breaths/min, able to breathe deeply – 2
   Tachypnea with good cough – 1
   Dyspneic with weak cough – 0

V. Oxygen saturation status
   Maintains value 90% while breathing room air – 2
   Requires supplemental oxygen to maintain saturation 90% – 1
   Saturation <90% with supplemental oxygen – 0

VI. Postoperative pain assessment
   No or mild discomfort – 2
   Moderate-to-severe pain controlled with intravenous analgesics – 1
   Persistent moderate-to-severe pain – 0

VII. Postoperative emetic symptoms
   No or mild nausea with no active vomiting – 2
   Transient vomiting or retching controlled with intravenous antiemetics – 1
   Persistent moderate-to-severe nausea and vomiting – 0