Review Article

Comparison of bispectral index and end tidal anaesthetic gas concentration guided protocols on recovery profile for desflurane based general anaesthesia in adult surgical patients

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ABSTRACT

Background: Early recovery is a major goal after anaesthesia and various techniques have been used to monitor adequate depth of anaesthesia while ensuring rapid recovery. Our study attempts to compare bispectral index (BIS) with end tidal anaesthetic gas concentration (ETAG) guided protocols for anaesthesia depth for recovery after desflurane anaesthesia.

Methods: Eighty American Society of Anaesthesiologists (ASA) I and II patients were randomly divided into 2 groups of 40 each. Group B (40 patients) were monitored intraoperatively using BIS guided technique and Group E (40 patients) using ETAG guided technique. After induction, maintenance of anaesthesia was done with oxygen/nitrous oxide (50:50) and desflurane mixture. In group B, desflurane was titrated to maintain a BIS value of 40-60 and the display of ETAG values were hidden. In group E desflurane was titrated to MAC value of 0.7 - 1.2 and BIS values on the monitor were hidden. Time from discontinuation of desflurane till time to eye opening, response to verbal commands and tracheal extubation were recorded and hemodynamic variations in both groups were also noted.

Results: Time to eye opening in BIS vs ETAG group was 7.44 ± 1.52; 6.53 ± 2.47 (mins), Time to response to verbal commands (10.16 ± 2.02; 8.58 ± 3.27 (mins) and time to tracheal extubation (11.43 ± 2.15; 10.47 ± 3.54 (mins)) was comparable between both the groups.

Conclusion: BIS and ETAG guided protocols are comparable for early recovery after desflurane anaesthesia and hemodynamic variations associated with both are similar.

Key Words: Airway extubation, bispectral index monitor, desflurane, end tidal anaesthesia gas concentration.

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INTRODUCTION

Rapid recovery is a desirable goal after general anaesthesia. It is associated with better clinical outcome and utilisation of hospital resources[1]. There is optimisation of theatre time and workforce, hence improving operating room cost and efficiency with reduced ICU and hospital stay. Maintaining adequate depth of anaesthesia and at the same time ensuring fast track recovery requires a fine balance. To this end, intraoperative operative techniques to monitor depth of anaesthesia have evolved. There are various somatic and clinical parameters, and devices available for the anaesthetists to monitor the depth of anaesthesia and facilitate early recovery. Some of them are Bispectral Index (BIS), end tidal anaesthetic gas (ETAG) monitoring, EEG monitoring, AEP Monitoring, narcotrend monitor, cerebral state monitor, entropy etc...[2, 3].

The most common metric used is the concept of minimum alveolar concentration (MAC), which has led to the monitoring of end tidal anesthetic gas (ETAG) concentration to ensure adequate level of unconsciousness while using inhaled anesthetics. ETAG monitoring is done using a gas analyzer which works on the principle of infrared absorption. It measures the alveolar concentration of the anaesthetic agent and thus ETAG is an indirect measurement of cerebral activity which is based on the hypothesis that the brain concentration of the anesthetic agent is in equilibrium with the expired lung concentration. To obtain the MAC that is being delivered to the patient, ETAG concentration is divided by MAC of that particular inhalation gas[4].

BIS, which is an EEG based measure of cerebral activity, has also been used to monitor depth of anaesthesia. It is an empirically derived, statistically based complex parameter that is composed of a combination of time domain, frequency domain and high order spectral sub parameters. It integrates several disparate descriptors of the EEG into a single variable, based on a large volume of clinical data to synthesize a combination that correlates assessments of sedation and hypnosis, and is insensitive to the specific anaesthetic or sedative agent chosen. The BIS correlates

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well with the level of the responsiveness and provides an excellent prediction of the level of consciousness. A BIS score of 40 to 60 indicates appropriate anaesthetic for surgery, whereas a score of less than 40 denotes a deep hypnotic state. To prevent anaesthesia awareness while allowing for a decrease in the administration of anaesthetic agents, it is advisable to target a range of BIS values between 40 and 60.

Usage of BIS has reduced anaesthetic requirement and may permit better titration of inhaled anesthetic agents according to patient requirements thus reduce recovery time[4, 5].

Although time to recovery is influenced by patient factors, duration of surgery etc., anaesthetic technique and drugs used play a critical role. Anaesthetists need to choose appropriate agents to reduce time to extubation and recovery. Desflurane's blood gas partition coefficient is low (0.42). The relative low solubility of desflurane allows it to be rapidly eliminated after it is discontinued and hence, as compared to isoflurane or sevoflurane, it is the agent of choice whenever early recovery is desired. All of the advantages that are offered by desflurane for early recovery can be magnified if we can monitor and reduce its intraoperative requirement and thus promote early recovery[6].

While BIS has been used to monitor depth of anaesthesia and recovery frequently, there are very few studies which have compared it to ETAG to assess which of the two can achieve recovery earlier. Thus, we decided to conduct this study to compare the recovery profiles of bispectral index guided and end tidal anaesthetic gas concentration guided protocols for desflurane-based general anaesthesia in adult surgical patients.

METHODOLOGY

A randomized comparative study was conducted in eighty adult patients of either sex, belonging to ASA grade I and II after taking ethical approval from institutional ethical committee and also after obtaining patients consent for the procedure. Pregnant patients, patients with any psychiatric illness or on psychoactive medication, those with known or suspected EEG abnormalities like epilepsy, neurosurgery patients, history of drug or alcohol abuse, BMI > 30kg/m^2 and surgical duration less than 60 minutes or more than 180 mins were excluded from the study.

Sample size was calculated based on a study by Sudhakaran et al, in which it was observed that emergence time (eye opening) in BIS group was 5 ± 2.12 min as compared to ETAC group was 5.1 ± 1.53 min. Taking these values as reference, the minimum required sample size with 80 % power of study and 5 % level of significance is 53 - 59 patients in each study group. For finite sample size taking population as 80, due to time constraint and non-availability of patients due to Covid 19, total sample size calculated is 80. So total sample size taken was 80 (40 per group).

Patients were randomly divided into two groups of 40 each using block randomization technique. Group B (40 patients) was managed using BIS guided technique. Group E (40 patients) was managed using the ETAG guided technique. BIS values were not shown in the ETAG group and vice versa, that part of the monitor screen was covered with a piece of paper so that the reading was not visible.

Preanaesthetic evaluation was done in all patients the day before surgery. In the operation theatre, all the ASA standard monitors were attached which included 5 lead ECG, pulse oximetry and non-invasive blood pressure (NIBP), baseline values recorded and monitored throughout surgery. For BIS monitoring “QUATRO” BIS sensor was used. The electrodes were placed on frontal temporal region and the values were recorded. End-tidal desflurane concentration (ETAG) was monitored on the anaesthesia gas monitor using technology based on infrared absorption.

IV access was secured and Ringer Lactate infusion started. Patients received midazolam 0.02 mg/kg and fentanyl 2 μg/kg intravenously. Induction of anaesthesia was done with propofol 2 mg/kg I.V. and trachea intubated after neuromuscular block using vecuronium bromide 0.1 mg/kg. Maintenance of anaesthesia was done with oxygen/nitrous oxide (50:50) and desflurane mixture at a rate of 2 lit/min. EtCO2 was maintained between 30 - 35 mmHg. Intraoperatively, intermittent doses of vecuronium were given to maintain the neuromuscular blockade.

Desflurane was given according to the group to which the patient had been allocated. In group B, desflurane was titrated to maintain a BIS value of 40 - 60 and the display of ETAG values were hidden. In group E desflurane was titrated to MAC value of 0.7 - 1.2 and BIS values on the monitor were hidden. Any tachycardia, hypertension, sweating, or lacrimation during the maintenance period were defined as inadequate anaesthesia and were treated with fentanyl 0.5 g/kg intraoperatively. Desflurane was stopped at the end of skin closure and fresh gas flow was increased to 10 lit/min. After onset of spontaneous respiration, residual neuromuscular blockade was reversed using neostigmine (0.05 mg/kg) and glycopyrrolate (0.01 mg/kg). Extubation was done when patient responded to verbal commands, had sustained head lift for more than 5 seconds and was able to maintain adequate SpO_2. Any tachycardia, hypertension, sweating or lacrimation during the intraoperative period were defined as inadequate anaesthesia and were treated with fentanyl 0.5 g/kg intraoperatively.

Time from discontinuation of desflurane till eye opening, response to verbal commands and tracheal extubation were recorded. Intraoperative hemodynamic parameters (pulse, mean BP and SpO_2) were recorded every 15 mins intraoperatively until the patient was shifted to the recovery room.

STATISTICAL ANALYSIS

Data analysis was done using Statistical Package for Social Sciences (SPSS) version 21.0. Categorical variables were presented in number and percentage (%) and continuous variables were presented as mean ± SD and median. Normality of data was tested by Kolmogorov-Smirnov test. If the normality was rejected, then nonparametric test was used.

Statistical tests were applied as Quantitative variables and compared using Unpaired t-test/Mann-Whitney Test (when the data sets were not normally distributed) between the two. Qualitative variables were compared using Chi-Square test /Fisher's exact test.

A p value of < 0.05 was considered statistically significant.

RESULTS

Both groups were well-matched in terms of age, weight, height, gender, and ASA status. There was no statistically significant difference between the two groups in terms of duration of surgery and anaesthesia Table 1, Figure 1.

Table 1: Demographic profile of study subjects:

	BIS guided Group (n = 40)	ETAC guided Group (n = 40)	*p* value
Mean age in years (mean ± SD)	38.10 ± 12.28	39.92 ± 11.82	0.50
Mean Height (cm) (mean ± SD)	153.30 ± 4.21	154.30 ± 4.74	0.32
Mean Weight (kgs) (mean ± SD)	60.75 ± 9.77	62.55 ± 9.29	0.40
Gender			0.36
Male	14	18	
Female	26	22	
ASA			0.55
I	32	34	
II	8	6	
Duration of surgery (min) (mean ± SD)	130.23 ± 28.31	127.28 ± 26.94	0.48
Duration of anaesthesia (min) (mean ± SD)	149.28 ± 27.99	145.03 ± 27.05	0.24

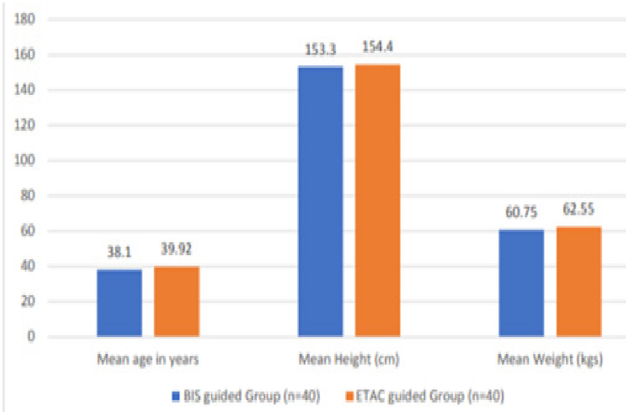

Figure 1: Demographic profile of study subjects.

Interpretation: The distribution of age, height and weight was comparable between BIS and ETAG groups ($P < 0.05$).

After induction, the mean BIS value, which was 98 at baseline, fell to 40. BIS value in group B was kept between 40 and 60 throughout the period of surgery Table 2, Figure 2.

Table 2: BIS value of study subjects at different interval:

BIS value	Mean ± SD
Preop	95.45 ± 1.63
15 minutes	53.38 ± 4.69
30 minutes	51.10 ± 4.34
45 minutes	51.35 ± 3.96
60 minutes	49.0 ± 4.87
75 minutes	49.20 ± 4.85
90 minutes	50.24 ± 5.34
105 minutes	49.39 ± 5.78
120 minutes	48.80 ± 3.48
135 minutes	48.68 ± 3.48
150 minutes	49.76 ± 3.33
165 minutes	50.71 ± 2.69
180 minutes	53.50 ± 2.12
Postop (immediatey after extubation	95.77 ± 1.86

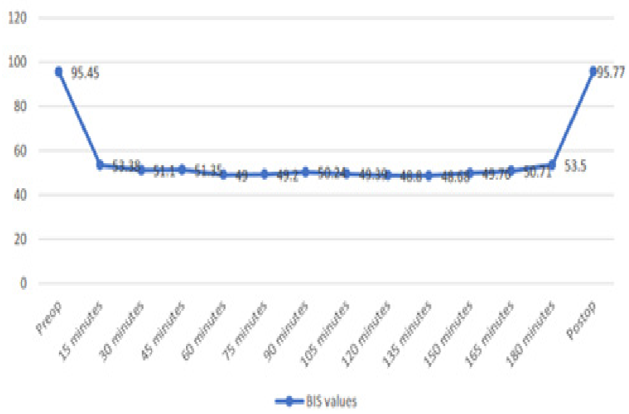

Figure 2: BIS values of study subjects at different intervals.

Interpretation: Mean of preoperative BIS value of study subjects was 95.45 ± 1.63. Intraoperative BIS values ranged between 40 - 60. Mean BIS values after extubation was 97.77 ± 1.86.

Interpretation: Mean of preoperative BIS value of study subjects was 95.45 ± 1.63. Intraoperative BIS values ranged between 40 - 60. Mean BIS values after extubation was 97.77 ± 1.86.

Time to eye opening in BIS vs ETAG group was 7.44 ± 1.52; 6.53 ± 2.47 (mins), time to response to verbal commands (10.16 ± 2.02; 8.58 ± 3.27 (mins)) and time to tracheal extubation was 11.43 ± 2.15; 10.47 ± 3.54 (mins) which was comparable between both the groups Table 4, Figures 4, 5, 6.

No significant difference in hemodynamic parameters between the groups was seen throughout the period of study.

Table 3: ETAG values of study subjects at different interval:

ETAG values	Mean ± SD
Preop	0
15 minutes	0.75 ± 0.14
30 minutes	0.86 ± 0.09
45 minutes	0.88 ± 0.09
60 minutes	0.91 ± 0.08
75 minutes	0.93 ± 0.11
90 minutes	0.85 ± 0.26
105 minutes	0.93 ± 0.08
120 minutes	0.93 ± 0.08
135 minutes	0.91 ± 0.08
150 minutes	0.90 ± 0.09
165 minutes	0.97 ± 0.05
180 minutes	0.9
Postop (immediately after extubation)	0

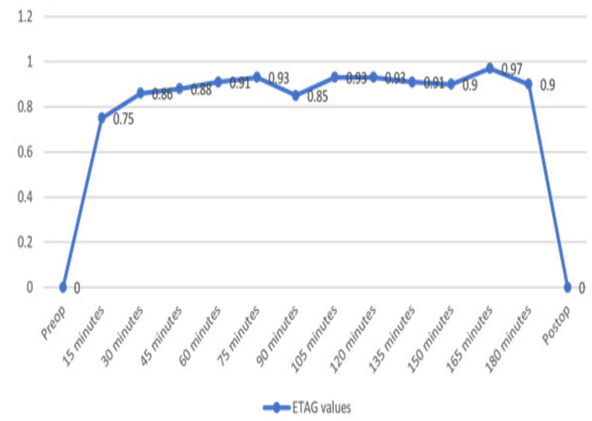

Figure 3: ETAG value of study subjects at different intervals.

Interpretation: Mean baseline ETAG values of study subjects was 0. Intraoperative ETAG values increased till they reached the predetermined study range. They ranged between 0.7 - 1.2 throughout the intraoperative period until stopping the inhalational agent.

Table 4: Comparison of recovery times between both groups:

	BIS guided Group	ETAC guided Group	*p* value
Time in minutes to eye opening (mean ± SD)	7.44 ± 1.52	6.53 ± 2.47	0.22
Time in minutes to response to verbal commands (mean ± SD)	10.16 ± 2.02	8.58 ± 3.27	0.10
Time in minutes to tracheal extubation (mean ± SD)	11.43 ± 2.15	10.47 ± 3.54	0.28

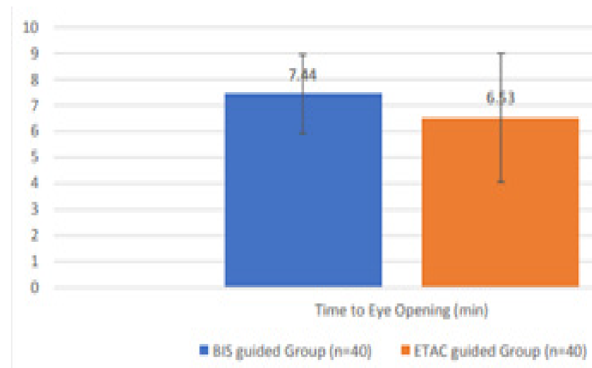

Figure 4: Comparison of time to eye opening (min) between both groups at different intervals.

Interpretation: Time of eye opening (mins) between BIS and ETAG group was 7.44 ± 1.52 (mins) and 6.53 ± 2.47 (mins) respectively. There was no statistical difference between both the groups with *P* value of 0.22.

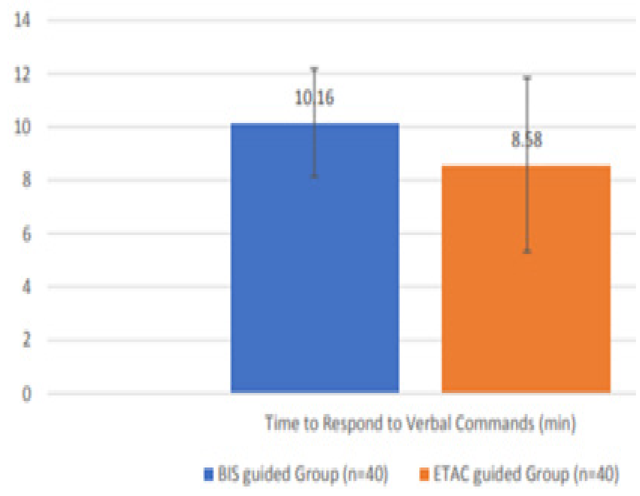

Figure 5: Comparison of time to respond to verbal commands (min) between both groups at different intervals.

Interpretation: Time to response to verbal commands (mins) between BIS and ETAG group was 10.16 ± 2.02 (mins) and 8.58 ± 3.27 (mins) respectively. Both BIS and ETAG are comparable and there was no statistical difference with *P* value of 0.10.

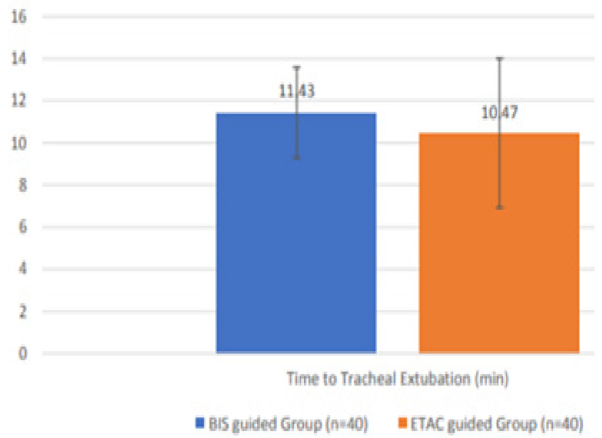

Figure 6: Comparison of time to tracheal extubation (min) between both groups at different intervals.

Interpretation: Mean time to tracheal extubation (mins) between BIS and ETAG group was 11.43 ± 2.15 and 10.47 ± 3.54 respectively. Both BIS and ETAG are comparable with $P < 0.05$.

DISCUSSION

While MAC (and indirectly ETAG) is the most frequently used guide for titration of volatile anesthetics in clinical practice, it mainly describes the immobilizing potency of the anesthetic agent Table 3 and Figure 3. EEG-derived BIS is more specific and aids the anaesthetist in tailoring the anaesthetic dose to specific patient physiology, is simple to read, may assist with reducing the chance of being conscious during surgery and reduces the duration for emergence and recovery[7 - 10]. It also ensures adequate depth of anaesthesia, while facilitating early recovery. Therefore, in our study we compared two anesthetic protocols based on bispectral index (BIS) and end tidal anaesthetic gas concentration (ETAG), on recovery profile for desflurane based general anaesthesia in adult surgical patients.

In our study, the two groups were comparable with respect to age, gender distribution, height, weight and ASA physical status. The duration of surgery and duration of anaesthesia was similar in both groups and hence could not affect the results.

Mean time for eye opening in BIS and ETAG guided protocol groups was 7.44 ± 1.52 vs 6.53 ± 2.47 minutes respectively, which was similar. Mean time for verbal response in BIS (10.16 ± 2.02 mins) and ETAG (8.58 ± 3.27 mins) was comparable. The mean time for tracheal extubation between BIS group (11.43 ± 2.15 mins) and ETAG group (10.47 ± 3.54 mins) was comparable with no statistically significant difference between the two groups. Hence recovery time for both BIS guided or ETAG guided protocols was similar in both groups. ($P > 0.05$).

Similar results have been observed in some other studies. Sudhakaran R et al. investigated recovery characteristics such as time to tracheal extubation using BIS monitoring or ETAG monitoring, vs standard monitoring in desflurane based spine surgeries. They observed that time to tracheal extubation between BIS-guided anaesthesia was comparable to ETAG-guided anaesthesia (6.34 ± 2.22 vs 6.51 ± 1.78 mins)[4].

Villafranca et al. carried out a study on sevoflurane or desflurane-assisted fast-track heart surgery. They came to the conclusion that anaesthesia management based on BIS does not significantly improve the likelihood of earlier tracheal extubation in patients undergoing fast-track cardiac surgery as compared to management based on ETAC (*P* value - 0.643). The patient's features and perioperative course have a greater impact on the choice to extubate the trachea than the assignment to BIS or ETAC monitoring[11].

Likewise, Chaudhuri et al conducted a randomized control study to compare BIS and ETAG for monitoring recovery from sevoflurane anaesthesia. Time to extubation and time to recovery was not significantly different in both groups and they concluded that both BIS and ETAG are comparable for monitoring recovery[12].

Bradley A Fritz et al conducted a study on postoperative recovery with bispectral index versus anaesthetic concentration guided protocols and also concluded that BIS-guided protocol was not faster than an ETAG guided procedure in recovery from surgery in patients who were at high risk for awareness[13].

In contrast to our study, some studies did not find recovery after the BIS and ETAG groups comparable. In a trial using halothane, Jain et al. discovered that the extubation time was considerably lower in the ETAG-guided group (5.29 ± 1.51 min) than in the BIS-guided group (9.63 ± 3.02 min). Their results were different from our study possibly because the inhalation agent used was different and recovery from halothane is slow compared to desflurane. Halothane causes higher BIS values than any other inhalational drug when MAC values are equal[2]. Some studies also found that the recovery was earlier in BIS monitored group than the ETAG monitored group.

Persec *et al.* used sevoflurane and observed that the time for tracheal extubation was significantly shorter in BIS group than compared to ETAG (17.5 min vs. 75 min, $p < 0.001$)[14]. Their results could be different from our study because the agent used was different (sevoflurane), and sample size (45 patients) and the duration of the study was shorter (6 months) compared to our study. Extubation times were also significantly lower in the BIS monitored group compared to the ETAG monitored group for sevoflurane, according to research by Shukla *et al.,*[15].

Our study has certain limitations. Body mass index, blood loss, temperature, fluid and electrolyte balance are other factors that may affect recovery from general anaesthesia but these weren't considered in this study. Age of patients was limited to 18 - 65 years and only ASA Grade I - II were taken. Hence these results might not be applicable to the pediatric and geriatric age groups or patients with comorbidities. The sample size taken was small and more patients need to be evaluated. Future research can take these factors into consideration and evaluate which protocol-based technique of anaesthesia, allows faster recovery from desflurane and would be more useful in these subgroups of patients.

CONCLUSION

This study concluded that intraoperative use of BIS and ETAG guided protocols are both comparable in terms of achieving early recovery after desflurane anaesthesia.

MAIN POINTS

- Rapid recovery is a desirable goal after General Anaesthesia.
- Various techniques have been used to monitor depth of anaesthesia and ensure rapid recovery.
- Our study attempts to compare BIS with ETAG based protocols for recovery after desflurane anaesthesia.
- We concluded BIS and ETAG are comparable in achieving early recovery after desflurane anaesthesia.

CONFLICT OF INTEREST

There are no conflicts of interest.

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