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Original Research Article

# Role of Bispectral Index (BIS) Monitoring Vs End Tidal Anesthetic Gas Concentration in Predicting Recovery Time and Extubation in Surgeries Performed Under General Anesthesia

**Alok Kumar[1], Vinod kumar Verma[2], Nidhi Arun[3]**

[1]PG Student, Department of Anesthesiology & Critical Care Medicine, Indira Gandhi Institute of Medical Sciences, Patna, Bihar, India

[2]Professor, Department of Anesthesiology & Critical Care Medicine, Indira Gandhi Institute of Medical Sciences, Patna, Bihar, India

[3]Associate Professor, Department of Anesthesiology & Critical Care Medicine, Indira Gandhi Institute of Medical Sciences, Patna, Bihar, India

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**Corresponding author: Dr. Nidhi Arun**
**Conflict of interest: Nil**

**Abstract**

**Aim:** The aim of the present study was to compare the effect of BIS versus end tidal anesthetic gas (ETAG)-guided anesthesia on time to tracheal extubation in surgeries performed under general anesthesia.

**Methods:** The present double blind randomized controlled study was conducted in the Department of Anesthesiology & Critical Care Medicine, Indira Gandhi Institute of Medical Sciences, Patna, Bihar, India. The study protocol, informed consent form (in Hindi & English) and case report form (CRF) were submitted to the ethical committee of Indira Gandhi Institute of Medical Sciences, Patna for approval. Study was done after taking approval from institute ethical committee. Written informed consent was taken from each participant of the study. The data was collected between – Pre induction time to extubation.

**Results:** Maximum patients were 7 (23.33%) and 10 (33.33%) in 37-46 years and 47-56 years respectively in both the groups. The females were predominant than males in both the groups. In group A, there were 18 (60%) females and 12 (40%) males and in group B there were 24 (80%) females and 6 (20%) males. In group A, 18 (60%) patients were in ASA I and 18 (60%) patients were in ASA II according to ASA grade.

**Keywords:** Bispectral index, early extubation, end‑tidal anesthetic gas concentration



## Introduction

In this era of newer inhalational anesthetic agents, halothane is still in use in developing countries, due to its low cost, compatibility of halothane vaporizer with all kinds of anesthesia workstations and even Boyle's apparatus. [1] The low incidence of hepatitis is to be weighed against the cost‑effectiveness of the drug. For such reasons, complete replacement of halothane with other costlier volatile agents from developing nations including India may not be possible or appropriate.

[2] A recent survey studying anesthesia practice in our country showed significant use of halothane. [3] Early tracheal extubation after general anesthesia is a desirable goal as it is associated with decreased Intensive Care Unit (ICU) length of stay (LOS), hospital LOS, and thus, the potential for improved recovery and decreased resource utilization. While intraoperative anesthetic techniques have evolved to emphasize fast track recovery, [4] the role of brain monitoring in extubation has not been well studied. Bispectral index (BIS) monitoring has been used to monitor the depth of anesthesia [5] and might also permit improved accuracy of titration of anesthetic doses to individual patient requirement; therefore, may have relevance regarding reducing recovery time.

BIS gives a continuous assessment of patient with minimal stimulation and also enables titration of drug, whereas the ETAG concentration criteria relates to brain activity through concentration of anesthetic agent expired in lungs assuming it to be in equilibrium with brain concentration. About 50% of the participants do not respond to oral commands at ETAG equivalent to 0.33 times of minimum alveolar concentration (MAC) (MAC awake) and distressing (auditory) stimuli are not internalized at twice MAC–awake. [6] The B‑Unaware and BAG‑RECALL trials had reported no difference in awareness incidence with anesthetic protocol based on BIS range (40–60) and anesthetic protocol based on ETAG concentration (MAC range 0.7–1.3. [7,8]

Early tracheal extubation after general anesthesia is a desirable goal as it is associated with decreased Intensive Care Unit (ICU) length of stay (LOS), hospital LOS, and thus, the potential for improved recovery and decreased resource utilization. While intraoperative anesthetic techniques have evolved to emphasize fast track recovery, [9] the role of brain monitoring in extubation has not been well studied. Bispectral index (BIS) monitoring has been used to monitor the depth of anesthesia [5] and might also permit improved accuracy of titration of anesthetic doses to individual patient requirement; therefore, may have relevance regarding reducing recovery time.

The primary objective of the present study was to compare the effect of BIS versus end tidal anesthetic gas (ETAG)-guided anesthesia on time to tracheal extubation in surgeries performed under general anesthesia. The secondary objectives of the study was (a)Role of BIS monitoring in predicting recovery time and extubation in surgeries performed under general anesthesia. (b) To look for the role of BIS in reducing the incidence of awareness and measure the depth of anesthesia. (c) To measure the impact of BIS on hemodynamic parameters, consumptions of drugs and recovery time.

## Materials and Methods

The present double blind randomized controlled study was conducted in the Department of Anesthesiology & Critical Care Medicine, Indira Gandhi Institute of Medical Sciences, Patna, Bihar, India. The study protocol, informed consent form (in Hindi & English) and case report form (CRF) were submitted to the ethical committee of Indira Gandhi Institute of Medical Sciences, Patna for approval. Study was done after taking approval from institute ethical committee. Written informed consent was taken from each participant of the study. The data was collected between – Pre induction time to extubation. After obtaining written informed consent, the patients were randomized by computer-generated random table numbers inserted into an envelope and assigned into two groups:

**In group A**- BIS monitoring was initiated, and patients awake BIS were recorded,

then continuously monitored and BIS was maintained between 40 to 60.

**In group B-** BIS monitoring was not be done. Depth of anesthesia was maintained by keeping MAC between 0.7 to 1.3 MAC. (MAC values of nitrous considered being additive; so, we took total MAC as measure of end tidal anesthetic concentration concentration).

Patients were graded according to ASA classification.

The sample size (n) is calculated according to the formula n=Z2* P* (1-P)/e2 Where Z =, 1.96 for a confidence level (α) of 95%, P= Proportion

(Expressed as a decimal), e=margin of error Z= 1.96, P=0.04, e= 0.05 n=1.962*0.04 * (1-0.04)/0.052 n = 0.1475/0.0025=59.007 n=60

The sample size is equal to 60, 30 in both the groups.

**Inclusion criteria:**

1. Patients of ASA physical status I and II
2. Patients between 18-60 years of age of either
3. Elective surgery of different types
4. General anesthesia
5. Patients willing to participate.

**Exclusion criteria:**

1. Patients' refusal to participate.
2. Patients with traumatic brain injuries, memory impairments, psychosis, or known or suspected EEG abnormality.
3. Patients with neuromuscular disorders.
4. Uncooperative patients
5. Psychiatric patients
6. Patients with chronic abuse of psychoactive medication
7. Patients undergoing neurosurgery.
8. Patients who will need post-operative ventilation.
9. Any intraoperative events which can delay extubation like hypertension requiring inotrope massive blood loss or hypothermia.

**Intervention and data collection methods:**

On arrival in operation theater, patient's weight, fasting status, consent and pre anesthetic checkup record (PAC) was checked. Standard monitoring like non-invasive blood pressure (NIBP), SPO2, heart rate (HR), end tidal gas concentration (ETCO2), ECG and temperature was done, and base line parameters will be recorded. A good intravenous assess was secured. Now patients were randomly divided into two groups based on computer generated random numbers.

In all patient's general anesthesia was administered by standard uniform technique. After pre oxygenation all patients were induced by propofol (2mg/kg), morphine (0.1 mg/kg) and vecuronium (0.1mg/kg) was used as neuromuscular blocking agent in all patients. Trachea was intubated with appropriate size cuffed endotracheal tube and secured after confirming Bilateral air entry. Anesthesia was maintained with oxygen, nitrous oxide, isoflurane with intermittent positive pressure ventilation (IPPV). Morphine tops up and paracetamol infusion (15mg/kg) over 10 minutes will be used as intra-operative analgesic. All vital parameters were recorded at every 15 minutes intervals, till patients were shifted from OT.

After last skin suture, all anesthetic agents were stopped and after onset of spontaneous respiration, residual muscular blockade was reversed with neostigmine (0.05 mg/kg) and glycopyrrolate (0.01mg/kg). Extubation was done when-

(a) Patient follow verbal commands.

(b) Can lift head ≥5 seconds.

(c) Generate adequate tidal volume (6 mg/kg) and will maintain $SpO_2$ > 95%

Time between discontinuation of anesthetic agents and extubation was recorded as tracheal extubation time as primary outcome. Patients' variables, type

of surgeries, duration of surgery, peri-operative vital parameters, BIS, MAC (ETAG Concentration) and any intra-operative and immediate postoperative complications was recorded and managed.

**Timing of rescue analgesia**

Analgesics were avoided until demand by the patient. The time interval for the first analgesic consumption was noted.

**Anaesthesia protocol**

- Functional anaesthesia system was checked thoroughly (evaporators, infusion pumps, fresh gas flow and intravenous lines) have been verified to reduce the risk of intraoperative awareness.
- General anaesthesia has three components: amnesia, analgesia and muscle relaxation. The anaesthetist monitors the depth of anaesthesia by administering three types of drugs: hypnotics, to cause and maintain unconsciousness; analgesics, for inhibiting pain; and muscle relaxants, to block the muscle reactions. The dosages of these drugs are titrated to meet the specific needs of each patient. Patients are premedication with midazolam (2mg) administered intravenously.
- A standardized anaesthetic technique applied: induction with fentanyl (2 mcg / kg / dose), propofol (2 mg / kg), and vecuronium bromide (0.1 mg / kg) followed by maintenance therapy with O2, N2O and isoflurane. ECG, heart rate, blood pressure, SpO2, end-tidal isoflurane concentration, BIS, and clinical signs of lack of depth of anaesthesia (movement, sweating, tearing, coughing, and jerk) is continuously controlled and recorded.
- Bispectral index (BIS) commercialized by (Covidien BIS loc 2 channels) was connected via electrodes to the patient's forehead and is a signal derived from the electro-encephalographic activity of the patient.
- Bispectral Index (BIS) commercialized by (covidien BIS loc 2 channel). is attached via electrodes to the patient's forehead after preparation of the skin of the patient by cleaning the forehead with the alcohol to provide good electrical contact and exhibit a signal that is derived from the electro-encephalographic activity of the patient.
- BIS value ranges from 0-100. A BIS value of 0 as EEG silences, while close to 100, the value of a fully awake adult. Values between 40 and 60 indicates an adequate level of anaesthesia recommended by the manufacturer.
- BIS signal is near to 100 at the start of the operation when the patient is conscious and falls to about 50 after the induction stage when the patient loses consciousness.
- The BIS monitor allows the anaesthesiologist to detect excessively high or low hypnosis and consequently to adapt the titration of the anaesthetic agents to avoid unsafe states.
- Changes in anaesthetic delivery led by the presence of clinical signs in relation to the BIS value. If the patient had hypertension or tachycardia and BIS value was> 60, was isoflurane level increased. If BIS values were in the target range of 50-60, then fentanyl administered. If the BIS value <50 then isoflurane was reduced, and the patient is monitored for lack of pain relief. In the control group, anaesthetist could change anaesthesia management, at its discretion, based on the patient's needs.
- BIS Monitoring started before anaesthesia induction and during surgery. The monitoring was discontinued when patients were extubated and then time of tracheal extubated was noted.

- An end-tidal agent monitor was used.

**Outcomes**

**Primary outcome measure**

- Comparison of time of tracheal extubation in both groups

**Secondary outcome measures**

- Anaesthetic inhalational agent consumption
- Time to eye opening (either voluntary or in response to request
- Time to discharge from the PACU
- Intra-operative medications consumption
- Postoperative Nausea and vomiting (PONV)

**Statistical Analysis**

All the data were analyzed using SPSS package (Stata, version 26.0 SPSS INC, Chicago, IL, USA) for windows. The data were presented as descriptive statistics for continuous variables and percentage for categorical variables and was subjected Chi-square test, t test & Anova test. Other values were represented in number, proportions (%) and mean ± SD.

**Results**

**Table 1: Age wise distribution of Subjects**

| Age group (in yrs.) | Group A | | Group B | | P. Value |
|---|---|---|---|---|---|
| | N0. | % | N0. | % | |
| 18-26 | 4 | 13.33% | 1 | 3.33% | 0.946 |
| 27-36 | 6 | 20% | 7 | 23.33% | |
| 37-46 | 7 | 23.33% | 10 | 33.33% | |
| 47-56 | 7 | 23.33% | 7 | 23.33% | |
| >56 | 6 | 20% | 5 | 16.66% | |
| Total | 30 | 100% | 30 | 100% | |
| Mean ± SD | 43.30±13.47 | | 44.20±11.82 | | |

In the present study, maximum patients were 7 (23.33%) and 10 (33.33%) in 37-46 years and 47-56 years respectively in both the groups.

**Table 2: Gender wise distribution of Subjects**

| Gender | Group A | | Group B | | P. Value |
|---|---|---|---|---|---|
| | N0. | % | N0. | % | |
| Male | 12 | 40% | 6 | 20% | <0.001 |
| Female | 18 | 60% | 24 | 80% | |
| Total | 30 | 100% | 30 | 100% | |

In the present study, females were predominant than males in both the groups. In group A, there were 18 (60%) females and 12 (40%) males and in group B there were 24 (80%) females and 6 (20%) males.

**Table 3: ASA Grade distribution in groups**

| ASA Grade | Group A | | Group B | |
|---|---|---|---|---|
| | Number | % | Number | % |
| I | 18 | 60% | 12 | 40% |
| II | 12 | 40% | 18 | 60% |
| Total | 30 | 100% | 30 | 100% |

In group A, 18 (60%) patients were in ASA I and 18 (60%) patients were in ASA II according to ASA grade.

**Table 4: Heart Rate (bpm) of different groups in different time interval**

| Heart Rate (bpm) | Group A | Group B | 't' test | P-value |
|---|---|---|---|---|
| | Mean ± S. D | Mean ± S. D | | |
| Baseline | 82.03±8.62 | 81.42±7.44 | 0.356 | 0.725 |
| 15 min | 87.80±14.10 | 85.60±4.46 | 0.886 | 0.383 |
| 30 min | 78.23±10.29 | 85.16±9.13 | -2.944 | 0.006 |
| 45 min | 82.56±15.54 | 82.93±9.16 | -0.121 | 0.905 |
| 60 min | 76.83±15.10 | 83.06±12.34 | -1.912 | 0.066 |
| 75 min | 71.20±12.16 | 79.36±8.13 | -2.891 | 0.007 |
| 90 min | 72.40±7.92 | 85.66±14.25 | -4.495 | <0.001 |
| 105 min | 75.43±7.40 | 84.53±12.41 | -3.481 | 0.002 |

The heart rate (bpm) showed more fluctuations in group A as compared to group B.

**Table 5: Systolic Blood Pressure (mmHg) of different groups in different time interval**

| Systolic Blood Pressure (mmHg) | Group A | Group B | 't' test | P-value |
|---|---|---|---|---|
| | Mean ± S. D | Mean ± S. D | | |
| Baseline | 123.76±10.84 | 124.40±9.49 | -0.217 | 0.829 |
| 15 min | 116.43±7.99 | 122.73±11.96 | -2.518 | 0.018 |
| 30 min | 111.36±14.13 | 129.10±11.54 | -5.200 | <0.001 |
| 45 min | 121.60±17.40 | 131.83±17.03 | -2.414 | 0.022 |
| 60 min | 112.63±8.03 | 135.30±16.78 | -7.064 | <0.001 |
| 75 min | 109.50±10.77 | 136.63±13.02 | -9.232 | <0.001 |
| 90 min | 108.53±13.90 | 139.90±14.79 | -7.314 | <0.001 |
| 105 min | 113.70±7.23 | 137.80±6.59 | -11.997 | <0.001 |

**Table 6: Diastolic Blood Pressure (mmHg) of different groups in different time interval**

| Diastolic Blood Pressure (mmHg) | Group A | Group B | 't' test | P-value |
|---|---|---|---|---|
| | Mean ± S. D | Mean ± S. D | | |
| Baseline | 74.73±5.88 | 75.30±7.96 | -0.288 | 0.776 |
| 15 min | 75.16±8.26 | 81.86±10.14 | -3.007 | 0.005 |
| 30 min | 73.93±13.89 | 84.76±9.65 | -3.805 | 0.001 |
| 45 min | 82.33±13.45 | 86.16±17.60 | -1.120 | 0.272 |
| 60 min | 75.03±1.04 | 93.10±13.08 | -7.391 | <0.001 |
| 75 min | 72.40±10.35 | 93.10±15.68 | -6.157 | <0.001 |
| 90 min | 68.86±9.61 | 89.83±14.08 | -6.343 | <0.001 |
| 105 min | 74.56±5.08 | 89.46±10.39 | -6.719 | <0.001 |

The systolic and diastolic blood pressure showed few variations in group B as compared to group A and showed significant difference at 60-105 minutes. SPO2 (%) and EtCO2 of different groups didn't show any significant results.

**Table 7: BIS of Group A in different time interval**

| | Group A (BIS) | 't' test | P-value |
|---|---|---|---|
| | Mean ± S. D | | |
| Baseline | 96.50±2.09 | 52.076 | <0.001 |
| 15 min | 51.96±5.77 | 49.292 | <0.001 |
| 30 min | 52.00±5.31 | 53.562 | <0.001 |
| 45 min | 50.96±5.83 | 47.803 | <0.001 |
| 60 min | 52.03±5.64 | 50.464 | <0.001 |
| 75 min | 53.76±3.90 | 75.487 | <0.001 |
| 90 min | 62.76±1.71 | 200.375 | <0.001 |
| 105 min | 84.83±4.57 | 101.465 | <0.001 |

BIS of Group A showed significant difference in different time interval.

**Table 8: ETAG of Group B in different time interval**

| | Group B (ETAG) | 't' test | P-value |
|---|---|---|---|
| | Mean ± S. D | | |
| Baseline | 0 | 0 | 0 |
| 15 min | 1.07±0.098 | 60.074 | <0.001 |
| 30 min | 1.08±0.128 | 46.230 | <0.001 |
| 45 min | 1.07±0.103 | 56.967 | <0.001 |
| 60 min | 1.07±0.132 | 44.376 | <0.001 |
| 75 min | 1.00±0.112 | 49.080 | <0.001 |
| 90 min | 0.68±0.156 | 23.837 | <0.001 |
| 105 min | 0.06±0.037 | 10.134 | <0.001 |

ETAG of Group B showed significant difference in different time interval.

**Table 9: Time of Tracheal Extubation from discontinuation of volatile inhalation agent distribution in groups**

| Tracheal Extubation time | Group A | Group B | P. Value |
|---|---|---|---|
| | Mean ± S. D | Mean ± S. D | |
| | 7.20±2.17 | 9.63±2.15 | **0.001** |

The Time of Tracheal Extubation from discontinuation of volatile inhalation agent with 7.20±2.17 and 9.63±2.15 (mean ± S. D) in group A and Group B respectively with significant difference.

## Discussion

Recovery from anesthesia is a critical period from the perspective of both physiological stability and patient satisfaction. Hence, early extubation is desirable. Of the total 60 patients 30 patients were assigned to the routine control group and 30 patients to the BIS group. Tasneem Waleed Tarayrah (2017) [10], showed no case of awareness was reported in the BIS-guided group but 4 reports (13.3%) in the control group (P=0.035), BIS-guided anesthesia decreased awareness by 13.3% (95% CI (1.3%26.4%). The most common forms of awareness were auditory perceptions, tactile perception and the sense of paralysis.

We observed a statistically significant difference in occurrence of awareness between patients undergoing routine care during surgery (4 out of 30, 13.3%) and patients monitored by a BIS device during surgery (0 out of 30, 0%) (P=0.035). BIS guided anesthesia decreased awareness by 13.3% (95% CI (1.3%-26.4%). These results are in agreement with previous findings. [11,12] The results of the current study are consistent with the earlier findings of Chen et al. showed that the use of the BIS-guided anesthesia significantly reduced the incidence of awareness from 0.65% to 0.14% when compared with the control group. [13]

In our study, we compared the time to tracheal extubation into two groups of patients receiving either BIS- or ETAG-guided titration protocol for isoflurane-based general anesthesia. Our study is consistent with a study of Sebel, et al. [14] from the US which showed that an incidence of intraoperative awareness of about 0.1% to 0.2% of patients undergoing general anesthesia.

Avidan et al. (2008) [15] compared a BIS-based anesthesia administration protocol and a protocol based on measurement of end tidal anesthetic gas (ETAG) and investigated reduction of anesthesia consciousness. They found that anesthesia

consciousness was similar between both groups.

We have considered isoflurane for maintenance in our study. Equal MAC of various volatile anesthetic agents may produce different BIS values. Gupta et al. found that at equi-MAC sevoflurane produces lower BIS values as compared to isoflurane, reflecting an agent-specific effect and a deficiency in BIS algorithm for certain agents and their interplay. [16]

The effect of halothane on EEG is different from other inhalational agents. Schwab et al. studied the effect of sevoflurane and halothane on BIS values. They concluded that sevoflurane causes a greater decrease in BIS values as compared to halothane at equal MAC multiples. They found that mean BIS value was 54 ± 7 with halothane as compared to 34 ± 6 with sevoflurane at 1 MAC. [17]

Punjasawadwong et al. [18] reported BIS-guided anesthesia reduced the requirement for volatile anesthetics by 0.65 times of standardized mean difference of MAC equivalents. Similarly, Ibraheim et al. [19] found significantly lower sevoflurane consumption in BIS group (mean sevoflurane consumption per hour was 15.66 ± 4.04 mL liquid in BIS group vs. 19.60 ± 3.94 mL liquid in non-BIS group, $P < 0.05$). Aimé et al. [20] reported BIS-guided anesthesia required 29% less sevoflurane than non-BIS guided anesthesia, the consumption was estimated by weighing sevoflurane vaporizers before and after anesthesia. Another study conducted by Basar et al. [21] reported that BIS-guided anesthesia reduced sevoflurane usage by 4.37% and 2.19 mL.h−1 was saved. [22]

## Conclusion

BIS-guided anesthesia (BIS kept at 40-60) reduced the risk of awareness and time of tracheal extubation as compared to routine care. BIS monitoring reduces the usage of volatile anesthesia consumption and the time of discharge from the Post Anesthetic Care Unit. BIS monitoring boosts the quality of patient care and should be an element of the standardized clinical practice in operating room settings.

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