

Comparison of Bispectral Index Values at Equal End Tidal Mac Values of Halothane and Isoflurane

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Abstract:

Atequi-MAC end tidal concentrations isoflurane produces less BIS values than halothane and the clinical consequence of this observation is that, at doses that cause similar degree of immobilization, isoflurane produces a greater depth of hypnosis than halothane.

KEYWORD: Bispectral index, Mac, halothane, EEG, Endtidal carbondioxide, isoflurane

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I. Introduction:

To study the anaesthetic action of a volatile agent, quantitative measurements of anaesthetic potency are essential. To this end, MAC has been defined which is the alveolar pressure of a gas at which 50% of humans do not respond to a surgical incision. This definition presupposes that equi-MAC concentrations of different anesthetics have a similar potency in suppressing spinal responses to painful stimuli, but anaesthetic agents vary in their relative hypnotic and immobilizing potentials. Measuring a surrogate end point such as a processed EEG value, like Bispectral index which incorporates different information from the raw EEG: power and frequency, β activation, and burst suppression integrated into a single number might be a better indicator of anesthetic depth than merely measuring delivered concentrations.

Theoretically, BIS and MAC measure 2 different components of anesthesia. MAC measures spinal response to pain and BIS measures the degree of hypnosis. Therefore, similar MAC concentrations of various anesthetic agents may produce dissimilar BIS values. The present study was designed to compare the BIS values at different MAC concentrations of Halothane and Isoflurane.

II. Method:

After obtaining institutional ethical committee approval and informed written consent, Eighty patients with ASA physical status I-II, scheduled for elective abdominal surgeries lasting >60min were randomly allocated into two groups receiving either Halothane (Group H) or Isoflurane (Group I). Patients with morbid obesity (weight >130% of IBW), uncontrolled hypertension or diabetes mellitus, impaired renal or hepatic function, or having history of drug or alcohol abuse were excluded.

All patients were fasted overnight and received diazepam 5 mg orally at night and 2 hr before surgery. On arrival in the operation theatre, routine monitoring of ECG, oxygen saturation and blood pressure was started. The BIS was recorded continuously with smoothing rate of 15sec. After obtaining base line values of heart rate, blood pressure and BIS, anaesthesia was induced with fentanyl 2 μ g/kg followed by propofol 2-3mg/kg till loss of verbal response. Tracheal intubation was facilitated with vecuronium 0.1 mg/kg. Anaesthesia was maintained with 66% N₂O in oxygen along with either Halothane or Isoflurane. The patients' lungs were mechanically ventilated to maintain an end-tidal CO₂ concentration of 32-35 mmHg. Total flow through asemicircle system was kept constant to 3L/min throughout the study period. The inspired and end-tidal concentrations of inhalational agents, oxygen and carbon-di-oxide were measured.

During the maintenance phase, 10 min after incision, the end-tidal concentration of inhalational anaesthetic was adjusted at 0.5 MAC for 10 min. When BIS values were stabilized, the inspired concentrations of halothane or isoflurane were increased from 0.5 to 1.0 MAC and then 1.5 MAC, and then decreased to 0.5 MAC in same graded manner. After each increment or decrement, the concentration was kept constant for 10 min, to reduce the difference between inspired and end-tidal concentration of inhalational anaesthetic to a minimum.

The inhalation agent was discontinued just before skin closure and the residual neuromuscular blockade reversed at the end of surgery. While the end-tidal concentration of the inhaled anaesthetic was decreasing, the patients were asked to open their eyes. The BIS value (BIS-awake) and end-tidal concentration of inhalational agent at eye opening was recorded. Patients were extubated and shifted to postoperative care unit for monitoring of vitals and recovery.

III. Statistical Analysis:

The data were collected and presented as mean \pm SD. Two sample unpaired student's t-test was used to compare demographic data and duration of surgery. Friedman two-way analysis of variance was applied to see the trends of BIS value in each group. Mann-Whitney U test was used to compare the BIS values between the two groups. P value <0.05 was considered significant.

IV. Results:

The demographic data and duration of surgery were comparable among groups (Table 1).

Table 1 Demographic data and duration of surgery

| VARIABLES | HALOTHANE Group | ISOFLURANE Group |
|---------------------------|-----------------|------------------|
| Age (yr) | 35.6 \pm 8.9 | 39.6 \pm 10.2 |
| Weight (kg) | 54.5 \pm 5.8 | 54.8 \pm 8.7 |
| Height (cm) | 154.9 \pm 5.4 | 155.5 \pm 8.2 |
| Sex (M : F) | 36 : 4 | 32 : 8 |
| ASA (I : II) | 34 : 6 | 36 : 4 |
| Duration of surgery (min) | 135 \pm 10.8 | 142 \pm 8.6 |

In both groups the pre-induction BIS values were between 96 and 98, and then decreased precipitously after induction.

The BIS values decreased significantly with increasing MAC concentrations during wash-in phase and increased significantly with decreasing MAC concentrations during wash-out phase in both the groups. However, for similar anaesthetic agent the BIS values were comparable at equi-MAC concentrations during wash-in and wash-out phases. The BIS values were 66.5 \pm 3.1 and 55.3 \pm 5.5 at 0.5 MAC, and 54.2 \pm 3.7 and 42.4 \pm 5.8 at 1 MAC in halothane and isoflurane groups respectively. At 1.5 MAC, BIS values were 40.1 \pm 5.2 and 34.7 \pm 4.5 respectively. BIS values were significantly ($P < 0.05$) lower in isoflurane group as compared to halothane group at each target MAC value during anaesthesia. However, BIS-awake did not differ between the halothane and isoflurane groups (89.6 \pm 4.2 vs 88.2 \pm 3.3). The time taken for awakening was 9.2 \pm 3.4 min in halothane group and 6.3 \pm 2.8 min in isoflurane group ($P < 0.05$).

Table 2 Comparison of BIS values at Equi-MAC value of HALOTHANE and Isoflurane

| MAC | HALOTHANE Group | ISOFLURANE Group |
|-------|-----------------|------------------|
| 0.00 | 96-98 | 96-98 |
| 0.5 | 66.5 \pm 3.1 | 55.3 \pm 5.5 |
| 1.0 | 54.2 \pm 3.7 | 42.4 \pm 5.8 |
| 1.5 | 40.1 \pm 5.2 | 34.7 \pm 4.5 |
| Awake | 89.6 \pm 4.2 | 88.2 \pm 3.3 |

BIS – Bispectral Index MAC – Minimum Alveolar Concentration

There was no significant difference in heart rate, mean arterial pressure, end-tidal carbon-di-oxide concentration and oxygen saturation in both groups at various MAC concentrations. At 1.5 MAC 3 patients in halothane group developed mild hypotension which was corrected by fluid administration. No other adverse effect was recorded in any group.

V. Discussion:

The results of our study showed that the BIS values were less during isoflurane anaesthesia than during halothane anaesthesia at equivalent MAC levels. Anesthetic agents variably affect the spinal mechanisms of immobility and cerebral mechanisms of hypnosis. This may account for the differences in the BIS values observed between agents at equi-MAC concentrations. This observation is probably consistent with the greater metabolic suppression caused by isoflurane and also its ability to produce a higher degree of brain electrical activity suppression than halothane¹. Halothane and isoflurane differently affect spectral power and median power of EEG. Halothane produces relatively fast EEG rhythms^{2,3} whereas isoflurane produces mainly slow

waves. Burst suppression pattern, which is an indicator of deep anesthesia, occurs with isoflurane⁴ and not halothane, at least not up to 2 MAC concentration⁵. These known differences in the effects of halothane and isoflurane on EEG are expected to influence the BIS value differently at a similar depth of anaesthesia. Another explanation for the difference in the BIS values observed lies in the components of anesthetic state measured by MAC and BIS. Movement to stimulus, as quantified by MAC, is a measure of the immobilizing effect of an anesthetic agent that involves spinal motor reflexes and has a poor correlation with the degree of hypnosis caused by the agent. In contrast, BIS has been designed to reflect consciousness and memory formation rather than immobilization and selectively measures the hypnotic or obtunding aspects of anaesthesia rather than the immobilizing action. The difference in BIS values between the two groups may be due to the different mechanism of anaesthetic action of the two agents. Halothane is known to have a greater analgesic and immobilizing effect (through its spinal action) as compared to isoflurane⁶. At low concentrations of anaesthetic agent the predominant EEG determinant is arousal and the BIS is less agent specific. This is consistent with the findings that BIS-awake values were similar between the agents. As the concentration increases, the effects of arousal are less, and the effects of anaesthetics are greater and the BIS may be more agent-specific⁷. In a previous study in children, Davidson et al, also reported significant low BIS values with isoflurane than halothane at 1MAC but not at awakening⁸.

BIS values in a range of 40-60 have been proposed for producing adequate degree of hypnosis during anaesthesia. In our study, the BIS values differed significantly between halothane and isoflurane at all the MAC concentrations investigated. The BIS value at 1 MAC of halothane (54.2 ± 3.7) was adequate for hypnotic effect. In contrast the BIS value at 1 MAC of isoflurane was 42.4 ± 5.8 , which shows the possibility that 1 MAC of isoflurane is more than enough for adequate hypnotic effect. This finding is consistent with the fact that the use of BIS monitoring for titration of anaesthetic agent reduces intraoperative isoflurane consumption⁹.

VI. Conclusion:

Atequi-MAC end tidal concentrations isoflurane produces less BIS values than halothane and the clinical consequence of this observation is that, at doses that cause similar degree of immobilization, isoflurane produces a greater depth of hypnosis than halothane.

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