International Journal of Research and Review
Vol.7; Issue: 4; April 2020
Website: www.ijrrjournal.com
Original Research Article *E-ISSN: 2349-9788; P-ISSN: 2454-2237*

A Clinical Study of the Utility and Efficacy of Monitoring Depth of Anaesthesia with Auditory Evoked Potentials and Its Use in Assessing Effect of Premedication with Oral Clonidine on Intraoperative Requirements of Inhalational Anaesthetics

Ajay Chandra[1], Ajit Kumar Singh[2], Maninder K Grewal[3], Anurag Garg[4], Vivek B Sharma[1]

[1]Associate Professor, [4]Sr. Resident,
Department of Anaesthesiology and Critical Care, Research and Referral, Army Hospital, Delhi, India. 110010
[2]Assoc Prof, Department Of Anaesthesiology and Critical Care, Command Hospital, Chandimandir, Panchkula, India. 134107
[3]Asst Prof., Department Of Anaesthesiology and Critical Care, Moolchand Hospital, New Delhi, India. 110010

Corresponding Author: Ajit Kumar Singh

ABSTRACT

Background: General anaesthesia (GA) reversibly depresses central nervous system (CNS) resulting in the loss of response and perception of all external stimuli. Against this background, this study was conducted in patients undergoing surgery under GA to stress that monitoring depth of anaesthesia with using Auditory Evoked Potentials helps dose reduction of volatiles and early recovery.
Materials and Methods: A total of 100 patients after applying exclusion and inclusion criteria, undergoing elective surgical procedures under GA, were enrolled in the study. They were divided randomly in three groups of Gp 1 - Control - 34, Gp 2- 33 and Gp- 3 Premedicated - 33. AEP monitor was used in Gp 2 and 3 to assess the depth of Anaesthesia and was compared with Gp 1 in terms of duration, dosage of isoflurane and recovery. Data recorded were analyzed using relevant statistical test.
Result: Patients in Gp 1, without AEP monitoring required higher doses of isoflurane (0.51%). In comparision to AEP monitored groups (B- 0.35(0.03) and Gp C-34(0.01) Vol%. The emergence (*e.g.*, awakening), orientation, and extubation times were significantly reduced in the AEP-monitored (*vs.* control) group (<0.05). The duration of recovery room stay was significantly reduced in the AEP-monitored (*vs.* control) group (<0.05). There were no differences between the two groups with respect to pain scores and opioid analgesic consumption. None of the patients reported recall of any intraoperative events.
Conclusion: Auditory evoked potential monitoring and premedication with an Agonist Clonidine reduces the volatile anaesthetic (Isoflurane) consumption compared to, standard monitoring to assess the depth of anaesthesia and helps in early recovery.

Key Words: *Isoflurane, Auditory Evoked Potential, awareness, Monitoring, BIS*

INTRODUCTION

General anaesthesia has been defined as a drug-induced reversible depression of the central nervous system (CNS) resulting in the loss of response to and perception of all external stimuli. It is not a single pharmacological process but a complex interaction of multiple stimuli, diverse responses, and the drug-induced probability of non-responsiveness to the

stimuli. The components of Anaesthetic state include unconsciousness, amnesia, analgesia, immobility, and attenuation of autonomic responses to noxious stimulation. Many complex surgical procedures would not be possible without the patient entering a state of general anaesthesia (GA).

An important contributing factor to inadequate GA was our limited ability to evaluate the levels of consciousness. In 1957, Woodbridge defined anaesthesia as having four components; sensory blockade, motor blockade, blockade of autonomic reflexes and loss of consciousness. [1]

As observed by Prys-Roberts, anaesthesia is non-responsiveness and the crux of the difficulty in defining non-responsiveness is that it cannot be measured directly. What can be measured is the patients' response to varied stimulations like, Does the patient respond to command? Does the response to incision suggest conscious perception? Does the heart rate or blood pressure go up in response to surgical manipulation or does the patient remember events, conversations, or pain? The "depth" of anaesthesia is determined by the stimulus applied, the response measured, and the drug concentration at the site of action that blunts responsiveness.

Assessment of depth of anaesthesia is fundamental to anaesthetic practice. Titrating the depth of anaesthesia with a careful balance of various drugs and inhalational agents basing on age, sex, surgical requirements and physical profile of the patients with constant monitoring of various vital physiological parameters real time is the utmost challenge faced by the anaesthetists and has constantly evolved over the decades.

The primary effort in constantly monitoring the depth of anaesthetic state is to minimize the incidence of anaesthetic awareness (AA) which is defined as postoperative recall of events experienced under general anaesthesia. Awareness during anaesthesia is an important clinical problem that sometimes results in disabling psychological sequelae for the patient including symptoms associated with posttraumatic stress disorder (PTSD). [2-8]

The first part of this clinical utility study was designed to test the hypothesis that the availability of the AAI value during Auditory evoked potential monitoring in the intraoperative period would reduce the volatile anesthetic (Isoflurane) gas consumption in comparison to standard clinical monitoring practices to assess the depth of anaesthesia. Secondary objectives were to evaluate the impact of AEP monitoring on the speed, quality of recovery and any incidence of awareness.

Study also assessed the role of premedication in reducing the volatile anaesthetic requirement while monitoring the depth of anaesthesia using auditory evoked potential monitoring. We used a-agonist clonidine as premedication in our study.

MATERIAL AND METHODS

After approval by the hospital ethical committee and informed consent 100 patients (ASA-1 & 2) undergoing elective laparoscopic general surgical/ gynaecological procedures at tertiary care centre of armed forces were enrolled.

Sample size was decided based on the previous studies and the observed beneficial response with the AEP monitoring at 95% confidence level, it was estimated that a minimum of 30 patients would be required in each group. Hence, we included just above 30 patients in each group with a confidence interval of 2 giving 90% power for the study.

These patients were randomly assigned using the computer generated random number tables to one of three study groups:

a) Group 1: Control (n - 34).No oral clonidine premedication and depth of anaesthesia monitored using standard clinical practices.
b) Group 2: AEP monitored (n - 33).No oral clonidine premedication, and depth of anaesthesia assessed using the AEP monitor.

c) Group 3: Clonidine + AEP (N – 33). Oral clonidine (150µg) premedication given and depth of anaesthesia assessed using the AEP monitor.

Exclusion criteria included weight less than 70% or more than 130% of ideal body weight, a history of central nervous system disease (*e.g.*, hearing disorders, seizures), chronic use of psychoactive medication, and any clinically significant cardiovascular, renal, hepatic, or endocrinologic disorders. Group 3 patients were given clonidine 150 μg po 90 min before induction. In the preoperative holding area, two AEP electrodes were placed on the forehead and one behind the left ear over the mastoid bone to all the patients of Group 2 and Group 3 , and acceptable contact impedance was confirmed when the electrodes were connected to the AEP monitor (A-line; Danmeter, Denmark).

All patients received 2 mg intravenous midazolam for premedication in the holding area. 3 lead ECG, NIBP, Pulse oximetry was applied to the patient on the OT table and a wide bore intravenous line established. The baseline values were based on the average of three consecutive readings before induction of anaesthesia. Body temperature (36-37.5ºC, pharyngeal temperature probe) was maintained constant.

The AAI values, as well as heart rate and systolic, diastolic, and mean blood pressure values were recorded at specific time intervals after entering the operating room and at 3- to 5-min intervals throughout the intraoperative period in the respective groups as required. The MLAEP were elicited with a bilateral click stimulus of 70 dB intensity and 2 ms duration. The AAI was automatically calculated based on the amplitude and latency of the MLAEP responses in the A-Line AEP monitor. The A-Line monitor recorded AAI index values nominally each 8 sec.

Anaesthesia was induced with 3-5 mg/kg intravenous Thiopental and 1–1.5mg/kg intravenous fentanyl, and tracheal intubation was facilitated with1.5 mg/kg intravenous succinylcholine. Fluid administration during induction of anaesthesia was aimed at providing adequate preload conditions throughout the study period. Anaesthesia was initially maintained with isoflurane, 1.5% inspired concentration, in combination with oxygen and nitrous oxide in the ratio of 1:2. The end-tidal carbon dioxide concentration was kept between 35 and 45 mmHg during the study period. The inspired isoflurane concentration was varied in increments of 0.2-0.4%, and intermittent bolus doses of 20 µg intravenous fentanyl and/or 5 mg intravenous labetalol were given to maintain hemodynamic variables within 15% of the baseline values. All patients received 4 mg IV Ondansetron for antiemetic prophylaxis.

At the end of the surgical procedure, residual neuromuscular block was antagonized with 2.5-3mg Neostigmine and 0.4-0.6mg Glycopyrrolate IV. Isoflurane was discontinued, and fresh oxygen was administered at a flow rate of 5 l/min until tracheal extubation. The isoflurane anesthetic requirement was calculated based on the average end-tidal concentrations recorded at 3-5 min intervals throughout the maintenance period.

In the AEP-monitored group, the inspired isoflurane concentration was titrated in 0.2-0.4% increments to maintain an AAI value between 15 and 20.

The targeted range for the AAI was based on earlier studies suggesting that values of 15-20 are associated with hypnotic effect site anesthetic concentrations. In the presence of an AAI value less than 20, 5 mg intravenous labetalol was administered to treat increases in blood pressure exceeding 15% of the baseline value, and 20 µg intravenous fentanyl was used to treat increases in heart rate exceeding 15% of the baseline value.

If the AAI was less than 15, the inspired isoflurane was decreased by 0.2-0.4%. If the acute autonomic response occurred in the presence of an AAI value of 20 or greater, the inspired isoflurane

concentration was increased in 0.2-0.4% increments.In the control group, the inspired isoflurane concentration was increased or decreased in 0.2-0.4% increments depending on whether the patient displayed clinical signs of inadequate or excessive anaesthesia, respectively. Acute hyperdynamic responses (*e.g.*, increases in mean arterial pressure and/or heart rate exceeding 15% of the baseline values) without other clinical signs of inadequate anaesthesia were treated with either 20 µg intravenous fentanyl or 5 mg intravenous labetalol, in the presence of an "adequate" hypnotic state as assessed using clinical signs (control group) or AAI level in the AEP group. Recovery times to awakening (*i.e.*, opening eyes in response to a verbal command), extubation, and orientation were continuously assessed (at approximately 1-min intervals after discontinuation of isoflurane).

Time to extubation was calculated as the time from cessation of isoflurane until the endotracheal tube was removed. Time to orientation was the time from cessation of isoflurane until the patient could state his/her name, date of birth, and location (city, state) when questioned by the blinded observer. Time to achieve a White fast-track score14 greater than 12 and a modified Aldrete score15 of 10 were continuously assessed (at 5- to 10-min intervals) by the PACU staff, VAS, sedation score and adverse events were recorded at 30 min, 60 min, 90 min and 120 min postoperatively.

To ensure proper blinding of the study, all the study parameters were calculated by a single anaesthetist, who was not aware about the intervention and the premedication given to the patient.
However, the duration of the stay in the PACU was calculated based on the actual clock times from admission until discharge from the PACU. The patients were discharged to the post-surgical ward when they met the standard PACU discharge criteria as assessed in the recovery room.

Finally, the occurrence of postoperative side effects (*e.g.*, pain, nausea, vomiting), the times to first "rescue" analgesic and/or antiemetic medication, and the total dosage of opioid analgesics required were recorded at the time of discharge from the PACU. Patients were queried about recall of intraoperative events.

The data was analyzed using the descriptive statistics (mean, standard deviation and range) and comparison between the groups was done using the one way ANOVA test of significance. A p-value of less than 0.05 was considered significant in all the tests and the data was analyzed using the Graphpad Prism software, Version 6.

RESULTS & OBSERVATIONS

A total of 97 patients were enrolled in the study and the patients are divided into three groups. The mean age of the study participants is 42.8±9.9 yr and the mean body weight is 62.4±7.8 kg. Of the 97 patients, 33 were randomized to the control group (Group 1) and the remaining 64 were randomized to the AEP-monitored group. The AEP monitored group is subdivided into two groups without (group 2) or with preanesthetic use of clonidine. The study groups were comparable with respect to their demographic characteristics, baseline AAI and hemodynamics values, and durations of surgery and anesthesia as shown in Table 1 and Figure 1.

Table 1. Comparison of baseline parameters and study findings between 3 groups.

Attributes	Group 1 (n=33)	Group 2 (n=32)	Group 3 (n=32)	P Value
Age	41.5 (9.6)	46.3 (11.1)	40.7(8.5)	0.0541
weight	62.2 (9.1)	61.2 (5.5)	63.5 (8.5)	0.5901
Heart Rate	90.5 (6.9)	86.2 (6.5)	79.6 (5.3)	<0.0001
SBP	132.2 (6)	126 (6.3)	113.2(8.1)	<0.0001
DBP	89.2 (6.5)	83.5 (5.05)	72.2 (3.8)	<0.0001
MAP	103.6 (5.9)	97.7 (5.2)	85.8 (4.4)	<0.0001
Iso	0.51(0.03)	0.35 (0.03)	0.34 (0.01)	<0.0001
Eye	6.03 (1.26)	4.9 (1.1)	4.87 (1.04)	<0.0001
Obeys	8.03 (1.26)	5.9 (1.1)	5.87 (1.04)	<0.0001
Extub	10.03 (1.26)	6.9 (1.08)	6.87 (1.04)	<0.0001
Surgery	60.5 (8.2)	58.6 (7.5)	61.2 (8)	0.3949
Anaesth	70.6 (9.2)	64.8 (7.4)	69.9 (8.1)	0.0119
AAI	-	15.8 (1.12)	15.5 (1.04)	0.2534

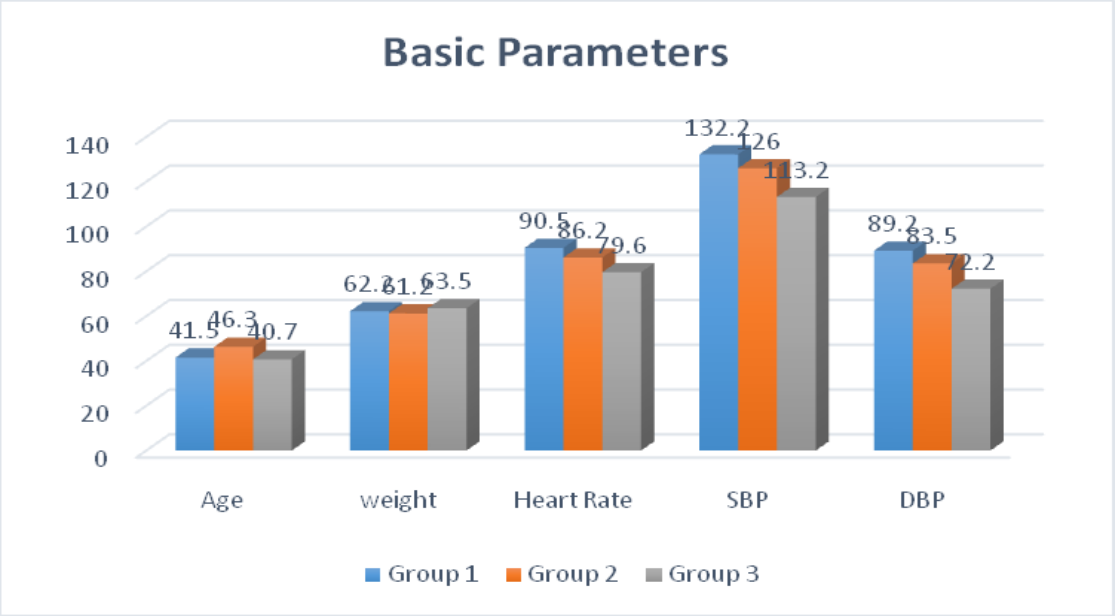


Fig 1- Demographic and Haemodynamic Profile

During surgery, the average hemodynamic variables were also similar in the study groups. However, the averaged AAI value during the maintenance period was not different between the groups.

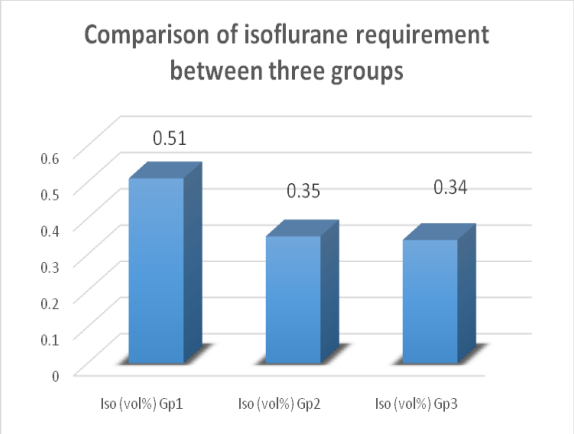


Fig 2. Comparison of isoflurane requirement between three groups.

The participants in group 2 had higher age when compared with other two groups. The emergence (*e.g.*, awakening), orientation, and extubation times were significantly reduced in the AEP-monitored (*vs.* control) group (Table 1). More importantly, the duration of recovery room stay was significantly reduced in the AEP-monitored (*vs.* control) group. There were no differences between the two groups with respect to pain scores and opioid analgesic consumption. At the 24-h follow-up evaluation, none of the patients reported recall of any intraoperative events.

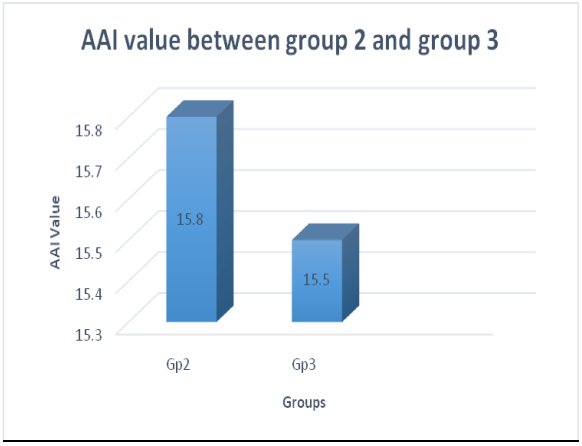


Fig 3. AAI value between group 2 and group 3.

Patients in group 1 who did not receive oral clonidine and were monitored normally had higher blood pressure, heart rate and higher dose of the isoflurane to achieve a good depth of anesthesia. The patients with AEP monitoring in both groups 2 and 3 showed good response with less doses of isoflurane. Following clonidine, mean inspiratory isoflurane concentration, necessary to render the patients unconscious and unresponsive to stimuli, could be reduced from 0.35(0.03) in group 2 with 0.34(0.01) Vol% in group 3 as shown in Figure 2. Patients without AEP

monitoring require higher doses of isoflurane up to 0.51%.

The addition of clonidine did not change the parameters significantly and the AAI was same between both the groups 2 and 3. Figure 3 showed that there is no significant difference between the groups using AEP monitoring with or without clonidine.

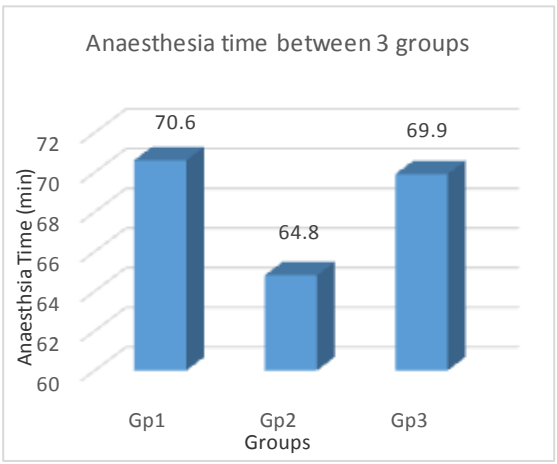
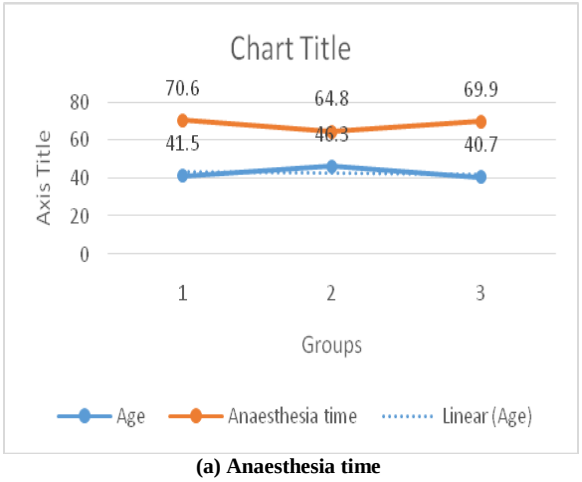


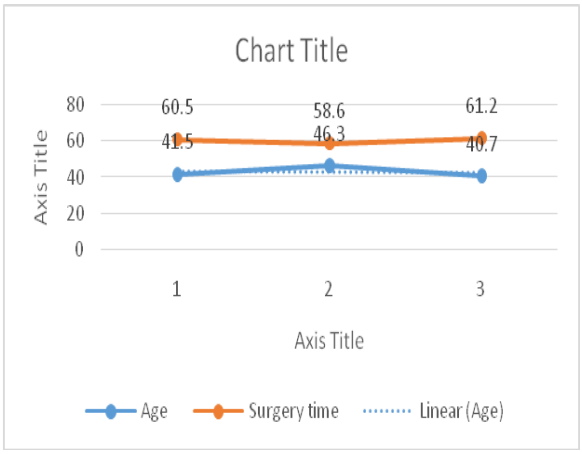
Fig 4. Anaethesia time between all 3 groups.

The anaesthesia time is significantly reduced in group 2 when compared with the others as shown in the Figure 4.

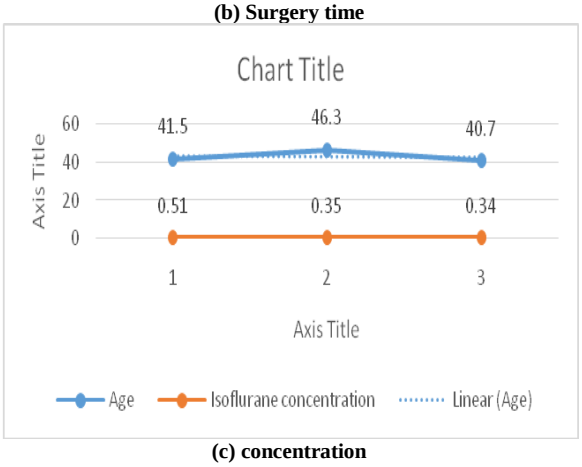
The correlation analyses were carried out between various study parameters to identify the factors associated with the observed changes using AEP monitoring and clonidine.



(a) Anaesthesia time



(b) Surgery time



(c) concentration

Figure 5. Correlation analyses between age and anesthesia time (a), surgery time (b) and isoflurane (c) concentration.

Our data pertaining to the entire study population did not show any correlation between the age of the patient and anaesthesia time Figure 5 (a), surgery time Figure 5 (b) and the requirement of isoflurane Figure 4 (c) respectively.

DISCUSSION

Our study findings suggest that AEP montitoring resulted in the better anaesthesia response in all the subjects. The premedication with clonidine did not give any further benefits in anaesthesia. The AEP monitor provides the anesthesiologist with information regarding the effect of anesthetic drugs on the MLAEP during sedation and general anesthesia. [9] Several clinical studies have suggested that the AAI can discriminate between the conscious and unconscious states, with higher awake AAI values compared with AAI values during general anesthetic states. [9-11]

Kurita *et al.* reported that, AAI can predict the depth of sedation and movement to skin incision during sevoflurane anesthesia. [12] Although Struys *et al* also found that the AAI could track the level of sedation and loss of consciousness with propofol but they found a poor predictive power with respect to movement in response to noxious stimuli. [9,13]

Analogous to the previously published studies with the electroencephalogram-based BIS® monitor (Aspect Medical Systems, Natick, MA) [11,14] and PSI4 monitor (Baxter Healthcare, Chicago, IL), this study demonstrated that the AEP monitor could improve the titration of maintenance anesthetic drugs by minimizing the time the AAI value was below 15. As expected, patients in the control group had received higher average concentrations of the volatile anesthetic. The availability of the AAI value influenced the anesthesiologist's use of the volatile anesthetic (isoflurane), opioid analgesic and sympatholytic drug during the maintenance period. This anaesthetic-sparing effect, helped in the AEP-monitored group, early surrogate recovery endpoints. [15]

The use of AEP monitor resulted in the faster arousal from the effects of anesthesia and also reduced the stay in recovery room. Earlier studies with the BIS® and PSI monitors have demonstrated that use of cerebral monitoring can lead to a faster emergence from anesthesia as a result of the anesthetic-sparing effect. Preliminary studies describing the impact of AEP monitoring on recovery times after anesthesia have yielded contradictory findings. [14-16]

The recent study by Maattanen *et al.* reported decreased desflurane consumption and faster emergence times after spine surgery with AEP monitoring when they maintained an AAI value of 20. However, they failed to demonstrate a benefit with respect to clinically meaningful recovery times. This may have been related to the fact that the duration of PACU stay can be influenced by institutional protocols that are unrelated to anesthesia. [17]

Interestingly, Assareh *et al.* used the AAI index to titrate sevoflurane during brief ambulatory surgery procedures and reported a decreased time to discharge even though the intraoperative anesthetic requirement was allegedly unchanged. [18]

The current study has demonstrated that the anesthetic and analgesic-sparing effects of AEP monitoring can lead to a clinically meaningful reduction in the duration of PACU stay and the incidence of PONV. In their recent editorial, Kalkman and Drummond suggested that use of cerebral monitors to reduce anesthetic drug use and expedite PACU discharge may result in increased autonomic stress responses and adverse outcomes (*e.g.*, myocardial ischemia, intraoperative awareness, purposeful movements during surgery). In our study, the intraoperative hemodynamic variables were similar in both study groups despite the AEP-monitored group's receiving less isoflurane and less fentanyl (compared to the control group). [19,20]

Previous studies have demonstrated that patient outcome is similar whether general anesthetic, opioid analgesic, or sympatholytic drugs were used to control acute stress responses during general anesthesia. There is a correlation between the duration of time during anesthesia that the BIS value was less than 45 and the incidence of adverse clinical outcomes in an elderly surgical population. Therefore, avoiding excessively deep levels of anesthesia by using sympatholytic drugs such as labetalol may actually have benefits beyond the early recovery period (*e.g.*, reduced PONV). It would seem that the availability of information regarding the patient's hypnotic state may lead to an increased use of drugs lacking in central nervous system depressant effects to control acute autonomic responses during general anesthesia. As a result, more purposeful movements may occur during surgery in non-paralyzed patients. It should be noted

that the presence of increased electromyographic activity during surgery can also interfere with the interpretation of the AAI. [20]

Practitioners are increasingly being required to provide economic data that justifies the use of new monitoring devices. Cerebral monitoring with an AEP device could potentially affect the cost of patient care by reducing anesthetic and analgesic drug use during surgery, as well as decreasing the need for medication to treat postoperative side effects (*e.g.*, pain, PONV). In addition, if patients emerged more rapidly from anesthesia, it might be possible to reduce turnover times in the operating room and allow additional cases to be performed. More important, by increasing the proportion of patients who could be fast tracked (*i.e.*, bypass the PACU), use of a cerebral monitor could reduce PACU and day-surgery personnel costs, as well as the need for overtime nursing staff. [21] A carefully performed cost–benefit analysis will be required to determine the future role of AEP monitoring in clinical practice.

The level of anaesthetic depth is routinely determined by clinical signs of analgesia and unconsciousness, as well as by depression of autonomic responses and muscle relaxation. Centrally, acting alfa agonists are known to reduce the intra-operative analgesic requirements by 45-75%. The present data does not support the findings from the previous investigators who favour the simultaneous use of clonidine in opioid and/or volatile anaesthesia to reduce narcotic and/or anaesthetic requirements. The reduction of drug requirements can be explained by reduced activation of cortical pyramidal cells, resulting from *a*, adrenoceptor activation within the locus coeruleus and/or subcortical centers by clonidine. [22]

The locus coeruleus was shown to be a major site of the hypnotic action of *a2* agonists in the central nervous system (CNS), since it contains the highest content of *a*, adrenoceptors in the brain. Being the centre of vigilance, the locus coeruleus also controls the entire CNS by multiple ascending and descending connections. Clonidine effects on ascending connections are corroborated by the data of the somatosensory evoked potentials. The central conduction time, the latency of the sensory impulse travelling from the upper cervical cord to the cortex, was prolonged. This suggests that clonidine rapidly crosses the blood brain barrier and accumulates within the brainstem, setting off a suppression of nonspecific afferent nerve volleys in sensory neurotransmission. The observed EEG slowing and cortical electrical power reduction following clonidine infusion in the present study can thus also be explained by the known brainstem action of clonidine, thus potentiating the underlying narcotic and volatile anaesthetic effects. Clonidine, however, had no significant effect on the cortical component (N,O-P25) of the SEP. This is in accordance with the presumption that there are no *a*, receptor sites within the cortex. [23]

Clonidine used as an adjunct to isoflurane-N,O/O, anaesthesia caused EEG changes, which represent a deepening of anaesthetic levels. The effects on the spinal component and the latencies of the SEP, but not that on the cortical and auditory evoked brainstem potentials, suggest a subcortical mode of action of clonidine. Volatile anaesthetic concentrations could significantly be reduced, while haemodynamic variables remained stable.

CONCLUSION

The first part of this clinical utility study was designed to test the hypothesis that the availability of the AAI value during Auditory evoked potential monitoring in the intraoperative period would reduce the volatile anesthetic (Isoflurane) gas consumption compared to, standard clinical monitoring practices to assess the depth of anaesthesia. Secondary objectives were to evaluate the impact of AEP monitoring on

the speed, quality of recovery, and any incidence of awareness.

The second part of the study was to use an alpha agonist like clonidine as a premedicant to assess its efficacy in reducing the volatile anaesthetic requirement while monitoring the depth of anaesthesia using Auditory evoked potential monitoring.

Conflict of Interest – Nil
Declarations - None
Funding -AFMRC Project

REFERENCES

1. Woodbridge PD. Changing concepts concerning depth of anaesthesia. Anaesthesiology1957; 18:536
2. Moerman N, Bonke B, Oosting J: Awareness and recall during general anesthesia. Facts and feelings. *Anesthesiology* 1993; 79:454-464.
3. Hobbs A, Bush G, Downham D: Perioperative dreaming and awareness in children. *Anaesthesia* 1988; 43:560-562.
4. Pollard R, Coyle J, Gilbert R, Beck J: Intraoperative awareness in a regional medical system. A review data. *Anesthesiology* 2007; 106:269-274.
5. ASA Advisory Committee: Practice advisory for intraoperative awareness and brain function monitoring: A report by the American Society of Anesthesiologists Task Force on Intraoperative Awareness. *Anesthesiology* 2006; 104:847-864.
6. Moerman N, Bonke B, Oosting J: Awareness and recall during general anesthesia. Facts and feelings. *Anesthesiology* 1993; 79:454-464.
7. Samuelsson P, Brudin L, Sandin R: Late psychological symptoms after awareness among consecutively included surgical patients. *Anesthesiology* 2007; 106:26-32.
8. Hutchinson R: Awareness during surgery. *Br J Anaesth* 1960; 33:463-469.
9. Struys MM, Jensen EW, Smith W, Smith NT, Rampil I, Dumortier FJ, Mestach C, Mortier EP: Performance of the ARX-derived auditory evoked potential index as an indicator of anesthetic depth. Anesthesiology 2002; 96:803–16
10. M, Gajraj RJ, Mantzaridis H, Kenny GN: Relationship between calculated blood concentration of propofol and electrophysiological variables during emergence from anaesthesia: Comparison of Bispectral Index, spectral edge frequency, median frequency and auditory evoked potential index. Br J Anaesth 1997; 78:180–4
11. Gajraj RJ, Doi M, Mantzaridis H, Kenny GN: Comparison of bispectral EEGanalysis and auditory evoked potentials for monitoring depth of anaesthesia during propofol anaesthesia. Br J Anaesth 1999; 82:672–8
12. Kurita T, Doi M, Katoh T, Sano H, Sato S, Mantzaridis H, Kenny GN: Auditory evoked potential index predicts the depth of sedation and movement in response to skin incision during sevoflurane anesthesia. Anesthesiology 2001; 95:364–70
13. David Miller, Sharon R Lewis, Michael W Pritchard et al. Intravenous versus inhalational maintenance of anaesthesia for postoperative cognitive outcomes in elderly people undergoing non-cardiac surgery. Cochrane Database Syst Rev. 2018 Aug; 2018(8): CD012317. Published online 2018 Aug 21.
14. Song D, Joshi GP, White PF: Titration of volatile anesthetics using bispectral index facilitates recovery after ambulatory anesthesia. Anesthesiology 1997; 87:842–8
15. Sharon R Lewis, Michael W Pritchard, Lizzy J Fawcett et al. Bispectral index for improving intraoperative awareness and early postoperative recovery in adults. Cochrane Database Syst Rev. 2019 Sep; 2019(9): CD003843. Published online 2019 Sep 26.
16. Wong J, Song D, Blanshard H, Grady D, Chung F: Titration of isoflurane using BIS index improves early recovery of elderly patients undergoing orthopedic surgeries. Can J Anaesth 2002; 49:13–8
17. Maattanen H, Anderson RE, Uusijarvi J, Jakobsson J: Auditory evoked potential monitoring with the AAITM-index during spinal surgery: Decreased desflurane consumption. Acta Anaesthesiol Scand 2002; 46:882–6
18. Assareh H, Anderson RE, Uusijarvi J, Jakobsson J: Sevoflurane requirements during ambulatory surgery: A clinical study with and without AEP-index guidance. Acta Anaesthesiol Scand 2002; 46:495–9

19. Kalkman CJ, Drummond JC: Monitors of depth of anesthesia, quo vadis? (editorial). Anesthesiology 2002; 96:784–7
20. Anthony G Messina, Michael Wang, Marshall J Ward, et al. Anaesthetic interventions for prevention of awareness during surgery. Cochrane Database Syst Rev. 2016 Oct; 2016(10): CD007272. Published online 2016 Oct 18. doi: 10.1002/14651858.CD007272.
21. Apfelbaum JL, Walawander CA, Grasela TH et al. Eliminating intensive postoperative care in same-day surgery patients using short-acting anesthetics. Anesthesiology 2002; 97:66–74
22. Ghignonme, Noec , Calvillo O, Quintin L. Anesthesia for ophthalmic surgery in the elderly: the effects of clonidine on intraocular pressure, perioperative hemodynamics and anesthesia requirement. *Anesthesiology* 1988; 68: 707-16.
23. Correa-Salce SR, Abinb C, Mazem. A hypnotic response to dexmedetomidine, an a,-agonist, is mediated in the locus coeruleus in rats. *Anesthesiology* 1992; 76 948-52.

How to cite this article: Chandra A, Singh AK, Grewal MK et.al. A clinical study of the utility and efficacy of monitoring depth of anaesthesia with auditory evoked potentials and its use in assessing effect of premedication with oral clonidine on intraoperative requirements of inhalational anaesthetics. International Journal of Research and Review. 2020; 7(4): 179-188.

******