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Relationships between bispectral index, implicit memory, dream recall and minimum alveolar concentration in blended anaesthesia

Abstract

Objective: The aim of this study was to estimate relationships between Bispectral Index and awareness and the possibility to reduce halogenate administration during blended anaesthesia.

Methods: An epidural catheter was placed and an bolus of 7-10 mg of levobupivacaine 0,5% and 30 mcg of sufentanil injected. Anaesthesia was induced with propofol 2 mg/kg and cis-atracurium 0.15 mg/kg and fentanil 2 mcg/kg. Analgesia was carried out with levobupivacaine (0.125%) and sufentanil (1 mcg/ml) in epidural infusion. During anaesthesia, patients listened two stories at 1 and 0.5 MAC of sevoflurane. Cardiovascular parameters and BIS were continuously recorded. Patients were interviewed to detect awareness 24 h after awakening. To identify differences between patients with and without implicit memory or/and dreaming recall, the Fisher exact test was applied for independent quantitative variables and the Mann-Whitney test for quantitative variables (p=0.05) and also Cohen's d.

Results: 32 patients were enrolled. There were not events of explicit memory. Seven patients (21.9%) showed dream recall; two (6.3%), presented implicit memory for the story played a 0,5 MAC.

Conclusion: Maintaining Bispectral Index values within the range recommended for general anaesthesia, did not permit to avoid unconscious memory formation. Therefore, it should be suppose that, the end-tidal concentration of volatile anesthetics, to maintain the loss of consciousness during blended anaesthesia, is higher than 50% of MAC for sevoflurane.

Keywords: awareness, consciousness monitors, anesthesia, epidural

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Introduction

The decreased responsiveness to stimulation defines the depth of anaesthesia which is a balance between effects of anaesthetic drugs and surgical stimulations. Awareness is a rare occurrence with an incidence of 0,1-0,2 %,[1] defined as postoperative recall of events occurring during general anaesthesia. This memory can be traumatic and may result in developing a chronic posttraumatic stress disorder (PTSD) in more than half of subjects.[2] Some cases of awareness are caused by inadequate anesthesia and are potentially avoidable through the assessment of depth of hypnosis by an intraoperative monitoring, especially when muscle relaxants are used. In order to prevent awareness, anaesthesiologists often use larger amounts of anaesthetics which leads to prolonged ventilation and post-operative sedation. Also we have to consider that "deep" anaesthesia is associated with increased 1-year mortality. During the last decade, an increasing number of monitor systems were developed to assess the depth of anesthesia.

The Bispectral Index (BIS), one of these devices, through a proprietary algorithm, elaborates EEG and provides an index of hypnotic level. A range between 40 and 60, during surgery, permits both to prevent awareness and reduce the dose of anesthetic agent administered. The aim of this study was to estimate the relations between Bispectral Index values and explicit or implicit memory and dreams during two different minimal alveolar concentration (MAC) of sevoflurane in patients undergoing blended anaesthesia for major abdominal surgery and if a deep analgesia, like epidural analgesia, reduces the requests of halogenated to avoid awareness.

Methods

Permission was obtained from the local Ethical Committee (Ethical Committee IDA1044/2001 and ClinicalTrial.gov ID NCT01800578). Written informed consent was obtained from 32 patients (26 men and 6 women), native Italian speakers, aged 18-70 years (mean, 63±5), with American society of anaesthesiologist physical status I-II, scheduled for elective major abdominal surgery. Exclusion criteria included: refusal of placement of epidural catheter, neurological or psychiatric diseases, hearing impairment, use of drugs known to affect central nervous system, coagulopathy, heart conditions, infections, allergy to local anaesthetics, liver or renal disease. Patients did not receive any preanaesthetic medication. Before the induction of general anaesthesia, an epidural catheter was placed at T6-T10 level After a dose test of lidocaine 2% 3ml, 7-10 ml of Levobupivacaine 0, 5% with 30 µg of sufentanil diluted in 10 ml of normal saline was administered. After founding sensory block at fourth thoracic dermatome, a BIS sensor was applied to the patient's forehead.

General anesthesia was induced with propofol 2 mg/kg IV, and fentanyl 2 µg /kg IV, and tracheal intubation was facilitated with cisatracurium 0, 15 mg/kg IV. Sevoflurane was also used for the maintenance of anaesthesia. After skin incision, an epidural infusion, at 5 ml/h, of levobupivacaine 0,125% and sufentanil 1 µg/ml was started through a 275 ml infusor system. Hemodynamic parameters

(noninvasive arterial pressure, heart rate) and BIS were recorded while patients were awake (baseline), immediately after the induction until the emergency from anaesthesia every 15 min.

During surgery, sevoflurane minimal alveolar concentration was regulated at the beginning at 1 MAC and after at 0, 5, however greater than MAC awake. During the steady- state at different MAC, one of two stories was played three times to patients. The first audiotape, that contained a passage of the story "Puss in boots" was played at 1 MAC, and the second, whit a passage of "Pinocchio", was played a 0,5 MAC. Each audiotape contained also four keywords related to each story, repeated four times. The duration of single tape was three minute and during that BIS and hemodynamic parameters were recorded every minute.

After 24 h, patients were interviewed by an anesthetist blind to the content of the audiotape.

Explicit memory was assessed using an interview pertaining to:

a. The last memory before falling asleep

b. The first memory after waking up

c. Dreams or other experiences during surgery.

Nondeclarative memory was investigated using a story-related free association test,[3–5] in which subjects were asked to respond with " the first thing that comes to mind " to a series of words associated with the contents of the recording. The test proved to be positive, when the patient, after listening to one of key words, related to the story he had heard during anaesthesia, retold something about the story without conscious recall. In case of dreams, the patient was asked to describe feelings and content.

Statistical analysis

Mean and Standard Deviation (SD)/median and Interquartile Range (IQR) and absolute and relative frequencies were used to describe the sample with respect to quantitative and qualitative variables respectively. In order to identify differences between patients with and without implicit memory or/and dreaming recall, the Fisher exact test was applied for independent quantitative variables (gender) and the Mann-Whitney test was used for quantitative variables (age, Bispectral Index (BIS); heart rate (HR), Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP)). Cohen's d was used also. The significance level was set at p=0.05. SPSS version 12.0 was employed to perform the analysis.

Results

The study started on September 2005 and finished on February 2009. Four patients were excluded because of protocol violation. The sample was composed of 32 subjects, 26 (81.3%) male and 6 (18.7%) female. The mean age of the sample was 62.7 (SD 5.6; Minimum 53 Maximum 71). During general anaesthesia, in all patients, BIS was maintained between 40 and 60, avoiding values > 60 and MAC of halogenate was higher than MAC awake. There were not events of explicit memory: patients did not remember something happened during surgery. The last memory before falling asleep and the first memory after waking up were, respectively, previous induction and following emergency. Seven patients (21.9%) showed dream recall. Two patients told about the content of dream that was, in the first case, related at the own work and in the other nonspecific whit a pleasant atmosphere. There were not dreams suggestive of intraoperative memory formation.

Only two patients (6.3%), during the free association test, presented implicit memory for the story of "Pinocchio" that was played a 0, 5 MAC (BIS mean 41 during surgery; listening mean BIS 49). As far as the univariable analysis is concerned, results are shown in Table 1. Statistical differences did not result in demographic data, BIS, blood pressure and heart rate between the subgroups of implicit memory dreaming recall/ no implicit memory during anaesthesia and also during audiotapes listening.

Table 1 Results

	Without implicit memory and or dreaming recall (24)	With implicit memory and/or dreaming recall (8)	p	Cohen's d
Gender				
Male	19 (79.2%)	7 (87.5%)	1	
Female	5 (20.8%)	1 (12.5%)		
Age	63 (13)	61 (9)	0.82	
Mean BIS	46 (9)	41 (11)	0.45	0.25
Post-induction BIS	43 (15)	49 (24)	0.51	0.17
Mean HR	66 (14)	57 (12)	0.06	0.81
Post-induction HR	66 (17)	63 (18)	0.54	0.31
Mean SBP	102 (8)	104 (13)	0.78	0.07
Post-induction SBP	115 (23)	115 (32)	0.4	0.38
Mean DBP	62 (9)	64 (9)	0.75	0.08
Post-induction DBP	70 (12)	67 (25)	0.98	0.37

Discussion

In August 2010 a review on Minerva Anestesiologica indicates that awareness "is still viewed as an important problem for which solutions are being actively sought".[6] Recall is the patient's ability to report previous events that occurred during general anaesthesia and results a relatively uncommon complication of anaesthesia. Different stages of awareness should be defined: conscious awareness with explicit recalls with pain; conscious awareness with explicit recalls without pain; conscious awareness without explicit recall and possible implicit recall; subconscious awareness without explicit recall and possible implicit recall; no awareness. Risk factors for awareness during general anaesthesia are: light anaesthesia, history of awareness, some types of surgery (caesarean delivery, cardiac surgery, trauma surgery), chronic use of central nervous depressants, young age, obesity, inadequate anaesthesia delivery systems, insufficient knowledge about awareness, and misuse of electroencephalographic activity monitors.[7]

Patients with awareness during general anaesthesia have a variety of experiences: auditory perceptions pain and/or paralysis, inability to communicate, helplessness, and terror. The evaluation of explicit

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memory is important to avoid chronic posttraumatic stress disorder (PTSD). Implicit memory instead establishes changes in behaviour and performance without the ability to recall events causing these changes.[8] Actually the most common system, used to assess the depth of hypnosis, is monitoring autonomic signs (sweating, tachycardia, hypertension). However observation of autonomic signs, and also the calculation of the PRST-score, does not seem a perfect indicator of depth anaesthesia adequacy but should be used to help intraoperative consciousness assessment.[9] Additionally a potent inhaled anesthetic agent is incorporated in the majority of general anesthetics management, and concentrations of exhaled anesthetic are routinely measured.

The minimum alveolar concentration (MAC) is the concentration of anesthesia required to prevent 50% of subjects from moving in response to a noxious surgical stimulus.[10] When the end-tidal anesthetic-agent concentration (ETAC) is approximately 0.33 MAC, 50% of subjects do not respond appropriately to oral commands and maintaining the ETAC greater than 0.7 MAC during surgery decreases the incidence of awareness.[11] A large number of devices, used for monitoring anaesthesia depth, are available and Bispectral index (BIS) is one of these. Bispectral index (BIS) was introduced as a measure of consciousness by algorithmic analysis of a patient's electroencephalogram during general anesthesia that it records from a four electrodes frontotemporal montage. So the bispectral index is a statistically, empirically derived parameter composed of time and frequency domain, and high order spectral subparameter.[12] Bis generates a dimensionless number from 0 (EEG silence) to 100 indicating the patient's level of consciousness. Numerous studies reported BIS wide ranges during different phases of anaesthesia: baseline 80-98; after induction 37-70; during surgery, 20-58; at emergency or end of surgery 42-96 and during recovery 64-96. Some studies reported a reduction in the incidence of awareness using BIS monitoring.[13] in contrast whit other that does not found the same results.[14] In October 2012 was published on *Anesthesiology* a randomized controlled trial of unselected surgical patients and by a post hoc analysis, seems that a protocol based on BIS monitoring reduced the incidence of definite or possible intraoperative awareness compared with routine care.[15] Although, there are studies reporting decreased drug consumption, such as Song et al.[16] and Liu et al.,[17] other studies did not find any significant difference in analgesic consumption and anaesthetic gas delivery, such as Lindholm et al., who reported no impact on drug dosing and gas delivery using BIS, with fentanyl and sevoflurane anaesthesia.[18] The aim of this study was to estimate the relations between Bispectral Index values and explicit or implicit memory or dreams during two different minimal alveolar concentration (MAC) of sevoflurane in patients undergoing blended anaesthesia for major abdominal surgery and if a deep analgesia, like epidural analgesia, reduces the requests of halogenated to avoid awareness.

This management provides better analgesia and is associated with fewer cases of postoperative respiratory failure with no significant differences in mortality, length of stay in hospital, or other morbidity variables.[19] So with the use of BIS, to avoid light anaesthesia, this study tried to evaluate the presence of memory process using 1 and 0,5 MAC of sevoflurane. Patients in this study were surgically stimulated when they were listening to the audiotape at two different MAC. After 24 h, patients were interviewed because some studies demonstrate that specific information, learning during anaesthesia, is remembered if tested no later than 36h.[20] The important result of this study is the absence of differences between BIS and hemodynamic parameters, during every stages of general anaesthesia, in patients with and without implicit memory or dream recalls. Then the maintaining of BIS values within the range recommended for general anaesthesia, did not permit to avoid unconscious memory formation. So, in accord to previous studies, the unconscious learning seems to occur also during periods of deep anaesthesia4, not only during light hypnosis, and to be facilitated by surgical stimulation. On the other hand, dreaming is an experience that patients remember and that, they believe, occurred during anaesthesia. Often dreaming is pleasant, and related to habitual life (family, work). This phenomenon results more common in younger, female, more anxious patients and ASA status I-II patients.[21] Dreaming, in this study, was reported by 21, 9% of patients, this is consistent with results of previous studies in which, however, patients were tested immediately after emergency from anaesthesia.[22]

In accord with Samuelsson et al.,[23] we did not find any relationships between dreams recall and patients' characteristic or between dreams and BIS values. To analyze the contents of dreams results important to determine if there is a relationship with external events; in this case dreams could be a "dreams-like process" and a risk factor for develop a posttraumatic stress syndrome3. All patients of this study had pleasant dreaming not related to surgery. Dreams did not seem to influence patient satisfaction.

The secondary outcome of this study was to analyze the possibility of a reduction of sevoflurane MAC during blended anaesthesia. Some studies support the hypothesis that epidural anesthesia with lidocaine reduces by 34% the amount of volatile general anesthetic required for adequate depth of anesthesia and so the use of volatile agents during combined epidural - general anesthesia techniques can be reduced by the inhibition of tonic afferent spinal signaling to the brain.[24] So two audiotapes were presented during the stady state at 1 and 0, 5 MAC. It should be noted that, despite adequate BIS level listening (mean BIS 49), the implicit memory process was occurred only for the story presented a 0, 5 MAC. Therefore, based on our results, it should be suppose that, the end-tidal concentration of volatile anesthetics, to maintain the loss of consciousness during blended anaesthesia, is higher than 50% of MAC for sevoflurane.

The occurrence of intraoperative recall, despite BIS values characteristics of hypnosis and adequate anesthetic depth, is still reported in the literature. Effectively Bis results influenced by different anesthetics, electrical equipement, specific clinical conditions, abnormal EEG patterns and neuromuscular blockers.[25] When implicit memory tasks or hypnosis are employed, traces of unconscious memory of intraoperative auditory information can be shown in 20-30% of the patients. These observations are of important clinical relevance, because the unconsciously recalled information about the intraoperative procedure may have a negative influence on the patient's postoperative recovery and well-being. Hypnotic state fluctuation is a factor proposed to explain implicit memory without explicit recall. Maybe the BIS limitation in correlates with implicit memory, can be explain with the time to update that can range from 14 to 155 seconds.

Another explanation is that subcortical structures, involved with the mechanism of implicit memory, are not detected by EEG and consequently by the BIS. In conclusion, BIS results useful in detecting explicit memory that is more sensitive than implicit to the effects of all anaesthetic agents and can result in developing a chronic posttraumatic stress disorder (PTSD). On the other hand, BIS values, registered throughout anaesthesia, even if below 60, results unable to correlate and predict dream recall and implicit memory. Also it is unlikely that a single method will be found to measure hypnosis

reliably for all patients and all anaesthesia management. Therefore BIS 60 can result excessive and can only suggest a low probability of implicit memory in blended anaesthesia but it cannot exclude it totally. Although this finding remains to be proven in a large number of patients, to determined the state in which events can be processed in the form of implicit memory, it results very interesting for further researches.

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Conflicts of interest

The authors declare there is no conflict of interests.

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