Awareness: Where do we stand?

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Awareness during general anesthesia is potentially an important issue for adults, infants and young children. In October of 2004, the Joint Commission on Hospital Accreditation (JCAHO) issued a sentinel alert regarding anesthesia awareness (Issue 32, October 6, 2004). For the past number of months, the ASA Task Force has been holding meetings to craft a consensus statement regarding the need (if any) of monitoring awareness during anesthesia. Frequently, these types of consensus statements do not adequately address the needs of children. Because of concerns regarding the pediatric aged patient, the preverbal status of young children, an insufficient amount of peer-reviewed scientific and medical literature regarding pediatric awareness during anesthesia, and the reliability of awareness monitors (regardless of design or manufacturer) to predict or reduce the incidence of awareness in children, the Society for Pediatric Anesthesia held a one-day forum in which a small group of physicians and scientists were gathered to address the issue of awareness in children and also to discuss what, if any, direction the Society may want to take regarding this issue. During this one-day forum, the following issues were addressed:

(1) Awareness during anesthesia in children with regard to incidence and impact
(2) The developmental aspects of the EEG and the anesthetic effects on the adult and pediatric EEG
(3) The limitations of cerebral monitoring devices
(4) The relationships of integrating EEG data with drug pharmacology

In addition, two break out sessions were held, which focused on (1) current technology—can it be made to work, and (2) what type of studies should be/could be done to further advance the field. This presentation will primarily focus on (1) awareness during anesthesia in children (2) the relationship of integrating EEG & monitoring devices with drug pharmacology.

I. Awareness during anesthesia

Awareness during anesthesia has become an important concern for both patients and physicians. Unintentional awareness during general anesthesia occurs when a patient becomes cognizant of some or all the events during surgery and has direct recall of these events. For purposes of discussion, awareness will be used in the context of the patient's being able to recall the events. That is, the ability to have a memory of such events.

The frequency of awareness in anesthesia has ranged between 0.1 to 0.2% of adult patients undergoing anesthesia. The incidence of awareness in the United States appears similar to the incidence reported in other areas of the world. Traditional clinical monitors such as at rest blood pressure during anesthesia, the use of benzodiazepines and the use of end-tidal gas monitoring are not necessarily useful in preventing awareness. In addition, awareness is not always reported immediately after the surgery. Thirty-five to 50% of cases are reported during delayed interviews (one week to one month later).

In adults, higher incidences of awareness have been reported in patients undergoing Cesarean section, cardiac surgery or treatment for trauma. Awareness under anesthesia in children is even more difficult to quantify. The vivid imaginations of children, the difficulty in separating fantasy from reality, the ability to extract information without being suggestive, make quantification of awareness in children difficult. There are no published case reports of awareness in children and few published studies. In 1973, McKire reported an incidence of 5% but some of the patients were only anesthetized with nitrous oxide. More recently, Davidson, in a study involving 864 children, determined the incidence of awareness in children 5 to 12 years of age to be 0.8%. This is a 4- to 8-fold increase reported in adults. Is there something different in children that predisposes them to awareness? At equivalent MAC concentrations of sevoflurane and desflurane, BIS and entropy measurements are greater in children. Are children more likely to retain information during relatively deeper levels of anesthesia? In addition, in children can one extract information regarding intraoperative awareness without influencing the results?

II. Integrating EEG monitoring devices with drug pharmacology

Devices that monitor anesthetic effect generally process, acquired evoked responses from auditory stimuli or process brain electrical activity. The auditory evoked potentials are electrical responses of the brainstem, auditory pathways and auditory cortex that result from auditory stimulation. Anesthetic agents affect the brainstem responses very little, while early cortical responses, also known as mid-latency responses, have an increase in latency and a decrease in amplitude as a result of increasing concentrations of anesthetic agents. Although descriptive reports of the use of auditory evoked responses have been published, there are no randomized control trials (RCT) that have evaluated its role on intraoperative awareness.

Numerous commercial monitors that process spontaneous EEG and electromyographic activity are available. Entropy monitor, narcotrend monitor, patient state analyzer, SNAP index, Danameter, cerebral state monitor, process the EEG data and compute a value that is reflective of the patient's hypnotic state. Although there are many publications regarding their clinical use, there are no randomized control trials with these services that have evaluated intraoperative awareness.

The BIS monitor also uses EEG data and by combining in a proprietary algorithm involving burst suppression data and frequency domain data, complex electrical patterns are transformed into a single value that is reflective of the patient's hypnotic state. A large number of BIS studies have been published that correlate age, anesthetic agents, and drug concentration to the BIS value. In addition, RCT have also been published regarding the use of BIS and intraoperative awareness.

Although BIS has been shown to reduce the incidence of awareness in adults and decrease the anesthetic requirements in patients, nonetheless, issues involving specific drug effect and patient variability create significant limitations in its use. Because drug use alters the brain's state, different drugs effect BIS differently in spite of the fact that the patient's level of sedation may be the same. Increasing amounts of ketamine, for example, will increase a patient's level of sedation. However, the BIS values will remain unchanged. Nitrous oxide, an anesthetic agent frequently administered to decrease the anesthetic requirements of patient inhaled anesthetic agents appears to have little effect on BIS. Opioids decrease BIS but not in a predictable dose dependent way. Inhaled anesthetic agents have a dose dependent effect on BIS but the interpatient variability is large. BIS values of 50 have been observed with sevoflurane concentrations ranging from 0.5% to 2.5%. Large variability has also been associated with propofol. BIS values of 50 and less have been observed with plasma concentrations that range from 1 to 10 mcg/ml.

Neuromuscular blocking agents, when administered without any hypnotic agent or anesthetic to awake volunteers profoundly affected the BIS. Messier and colleagues demonstrated that in awake volunteers administered only alcuronium and succinylcholine, the BIS resembled a well-sedated patient.

The irony of EEG monitoring for awareness is that the monitor is sensing changes in the cortex. Sleep is a non-waking state with preserved brainstem arousability, and coma is a non-waking state with absent brainstem arousability. In patients with impaired cerebral reactivity, distortion and disappearance of normal EEG patterns; along with the appearance of abnormal patterns occur. In addition, slowing of posterior alpha, from upper alpha to lower alpha frequencies, into the theta range occurs. Also, in these patients frontal beta slows from the upper range to the lower range, and even into the alpha range.

What if awareness is a subcortical function? Classic endpoints for awareness generally assess patient movement, performance and memory tests. Advances in neuroimaging suggest that the thalamus, a subcortical structure, may be involved in awareness during anesthesia. If sleep is a non-waking state with preserved brainstem arousability, and coma is a non-waking state with absent brainstem arousability, may be the future monitoring in anesthesia will access both cortical and subcortical activity.

For children, the issue of determining intraoperative awareness is compounded by the issues of when and how one extracts such information. It is well documented that most cases of awareness are discovered days to weeks after the event. For children, behavior changes are frequent following surgery. Is postoperative behavioral change a function of intraoperative awareness?

As one tries to determine whether awareness occurs, how frequent is it, and what the psychosocial implications for the patient may be, at present, in children we are left with black box solutions. The present day monitors are imprecise, and maybe the best that can be achieved is to describe awareness as a phenomenon and determine if certain types of interventions (monitors) can reduce the incidence without really knowing how the true mechanism is involved.

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