Depth of Anesthesia Monitoring – Have we progressed in 150 years?

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The challenge of adequately assessing depth of anesthesia has been with us since the earliest days of our specialty. In 1847 John Snow wrote “The question may be asked whether the medical man can always determine in what degree of etherization the patient is, and by that means estimate correctly whether or not he is liable to pain. I am not sure that he always can, by the mere observation of the patient.” Although much progress has been made in the intervening 153 years, and more recently at an exponential rate, the question and the answer remain unchanged. How best to “observe the patient” is a question fraught with philosophical, physiological and technical challenges.

Do We Know What We Are Trying to Monitor?

The intraoperative surgical experience brings together three different individuals - the patient, the surgeon, and the anesthesiologist. Each has a somewhat different view on what constitutes adequate anesthesia. The anesthesiologist likely thinks in terms of a triad - unconsciousness (hypnosis), analgesia and muscle relaxation. Although the three are to a great extent pharmacologically separable, it has become apparent that from the perspective of anesthetic depth they are quite intricately interwoven.

The development of an objective monitor of adequate anesthetic depth requires a widely accepted definition or gold standard to which the devices can be compared. Unfortunately, in clinical practice there is a heterogeneous group of outcomes that clinicians regard as indicating adequate anesthesia. These include (1) awareness or recall which may be explicit (conscious or spontaneous) and implicit (subconscious or needing to be specifically triggered); (2) Hemodynamic responses, e.g. heart rate and blood pressure changes to surgical stimuli; (3) Movement in response to noxious stimuli, which is how MAC is defined; (4) Response to spoken command, which includes the isolated forearm technique. Most clinicians and patients seem willing to regard a lack of spontaneous recall of intraoperative events (explicit memory) and without any indicators of implicit recall, e.g. nightmares, as an acceptable working definition of an adequate depth of anesthesia having been achieved.

As to the other potential end points mentioned above, it is clear that there is a very poor
correlation between changes in heart rate and blood pressure and any other outcome parameter and awareness. Similarly, the vast majority of individuals who are able to follow commands during experimental paradigms that allow for awakening during anesthesia do not in fact have any recall of the event (if there is no pain associated).

The Incidence of Awareness

There has been a gradual progression to better standardization of questionnaires and assessment instruments although this is still very much an evolving area. Recent surveys indicate that the incidence is in the order of 0.1-0.2% of the surgical population. It would appear that in comparison to earlier, perhaps more unreliable studies, that the incidence has progressively decreased. The data indicate that the incidence is higher and that pain and post traumatic stress disorders are more common when muscle relaxants are used.

How Can We Prevent Awareness?

Historically, and still the most commonly used, is simply to administer anesthetics at relative overdose concentrations. The progressive development of shorter acting and more titratable anesthetics and potent analgesics has greatly facilitated this phenomenon. A refinement of this approach has been the development of ways to monitor end tidal anesthetic concentration and thereby estimate the brain concentration. The development and popularization of pharmacokinetic models of intravenous anesthetic administration have similarly facilitated this approach whereby population-based models are used to estimate the amount of drug required.

However, none of the above approaches guarantees that every individual is adequately anesthetized. Hence the desire for objective monitors. Furthermore, there is the hope that such monitors would not only prevent awareness but would also result in cost saving by greatly limiting the use of drug overdose as a management strategy.

Monitoring

What Are The Characteristics of the Ideal Monitor?

The ideal monitor would:
1) Show changes that are independent of the anesthetic agent.
2) Show graded changes with changing drug concentrations, both on increasing and decreasing concentration, both while conscious and once unconscious.
3) Not be influenced by non-anesthetic agents.
4) Fluctuate with changing noxious stimulation.
5) Not be influenced by physiological changes e.g. blood pressure.
6) Not have overlapping values at different depths of anesthesia, especially at the transition from awake to anesthetized.
7) Indicate change to unconsciousness/lack of awareness with a high degree of sensitivity and specificity.

**EEG based monitors**

Over the past 70 years there have been attempts to use the EEG as a monitor of anesthetic depth. With increasing depth of anesthesia the EEG does show a common progression from low amplitude and high frequency through high amplitude and low frequency to isoelectricity. However the raw EEG is too complex for the untrained and interpretation is too non-specific and inconsistent. Similarly attempts at using derivatives of the EEG such power analysis; median frequency and spectral edge frequency have not proved to be clinically useful.

More recently a number of potentially better EEG derivatives have been developed including:

- Bispectral index (BIS), Aspect Medical.
- Patient State Index (PSI), Physiometrix.
- State and Response Entropy, GE Healthcare.
- Narkotrend, MonitorTechnik.
- SNAP Index, Everest.
- Cerebral State Monitor, Dannemeter.

The bispectral index (BIS) is the most extensively investigated with the largest body of published literature. It uses a proprietary algorithm which uses power spectral analysis, bispectral analysis, and a time-based analysis for suppression. The resulting index is then presented on a scale from 100 (awake) to zero (isoelectric EEG). The anesthetic range is typically 40-60. The empirical and statistical nature of the index requires ongoing improvement and supplementation as more cases are added to the database and as new drugs or drug combinations are evaluated. While this is in general desirable progress, it also means that the outcome of clinical trials of the device are linked to specific iterations of the software.
BIS has been found to be quite closely correlated to changes in brain metabolic rate, to the degree of hypnosis, and the absence of (explicit) recall. It is not a useful independent indicator of analgesia other than in the potentiation of the hypnotic state produced by analgesics. EMG activity from the facial muscles has also been found to confound the accuracy of the BIS number as a predictor of hypnotic state. Thus the elimination of the EMG by a muscle relaxant may result in a profound lowering of the BIS number. Another unexpected drug-related interaction is the lowering of the BIS value by esmolol.

The BIS has been shown in a number of trials to closely track the progression from awake to deepening levels of anesthesia. Unfortunately, there are overlapping standard deviations at each level of sedation or anesthesia. This means that while on average most patients will be anesthetized and unresponsive at BIS < 60, a small number of patients will be awake even below 50, while others will be asleep at values greater than 60. However, very recent clinical trials indicate that the use of this monitoring does produce a statistically significant reduction in the incidence of awareness. For example, in the Australian B-aware trial the incidence of awareness was reduced from 12 in 1,200 patients to 2 in 1,200 patients.

Entropy describes the randomness or complexity of a signal. The algorithm used in the GE/Datex-Ohmeda monitor is in the public domain. The monitor provides 2 indices, State and Response Entropy. The State Entropy encompasses EEG frequencies of 0.8 – 32Hz i.e. the cortical EEG while the Response Entropy uses the range 0.8 – 47 Hz. The latter includes the EMG which is thought (hoped) by some to be an index of the need for analgesia. There has not yet been much clinical literature about the device but it is hoped that these 2 indices which are also scaled from 0 – 100 will indicate both the need for hypnotics and analgesics.

Patient State Index includes spatial changes in the EEG power distribution while the Narcotrend, SNAP and Cerebral State Monitor use their own modifications of the EEG analysis. All of these and the Entropy are still in need of substantial clinical evaluation.

Middle Latency Auditory evoked potentials (MLAEP)

The EEG is derived from the electrical activity of brain cells scattered throughout the cortex and sub-cortical areas and therefore is not anatomically specific. The (auditory) evoked potentials are a response to a specific (auditory) stimulus and the anatomical pathways involved are better defined. The
Middle latency auditory evoked potential is thought to reflect the conduction of the impulse along thalamo-cortical pathways. The response is exceedingly small in relation to the random EEG activity and so multiple repetitive auditory stimuli (clicks) are required and the resulting surface detected response is summated. Typically more than 256 clicks are required to obtain an interpretable tracing.

Until recently the time required to obtain interpretable tracings substantially limited the utility of MLAEP despite the fact that they seem to have many of the other characteristics of the ideal monitor. Jensen and colleagues has utilized an algorithm that incorporates autoregressive modeling and this has resulted in a very rapid and dynamic response. Prototypes of other algorithms are also available.

Clinical trials and experience with MLAEP is substantially less than with BIS. However, the response rate does appear to be a little faster than BIS but once the individual is unconscious the response does not indicate varying depths of anesthesia as well. Like BIS, there is also quite a wide standard deviation around the threshold values and it has been found to have an accuracy that is similar to BIS. There is currently no active distributor for the device in the USA although it is still marketed in Europe.

**Conclusion**

Much progress has been made in establishing suitable outcome parameters and in developing user friendly monitors based on algorithms that show an increasing degree of clinical utility and dependability. No monitor used currently in the operating room including the electrocardiogram and non invasive blood pressure have such a degree of accuracy and precision that they are 100% sensitive and specific. Current depth of anesthesia monitors are now approximating our other standard monitors in terms of predictive accuracy. I would anticipate that within the decade such monitors will become part of routine intraoperative care but at present the paucity of randomized outcome studies of the prevention of intraoperative awareness makes it inappropriate to deem them a requirement in every patient.

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