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Review paper

Asleep or awake? That is the question… A review of techniques available for monitoring the depth of anaesthesia

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ABSTRACT

Introduction: The problem of intraoperative awareness concerns about 0.1%–0.2% of patients .The perfect method to evaluate the depth of sleep should be objective, so that the response is quick and precise – to increase or decrease the depth of anaesthesia. More scales originated in order to detect cases of intraoperative awareness. Also, new equipment was built so that anaesthesiologists could properly monitor the depth of anaesthesia.

Aim: The aim is to describe methods and devices monitoring the depth of anaesthesia.

Material and methods: This work was based on the available literature and the experience of the authors.

Results and discussion: Recently a few devices were constructed, all of which can be divided into passive and active systems. Passive systems assess the collected data, while active ones first stimulate and then receive and process data. Passive systems use computer analysis of electroencephalographic signal, and some of them additionally evaluate alterations of frontal electromyogram. According to some, monitors currently available on the market show around 80% effectiveness in preventing intraoperative awareness. Other researchers showed that evidence of their effect on intraoperative awareness is limited.

Conclusions: It seems that when it comes to the effect of anaesthetic agents on such a precise organ as the brain, there is still much to discover. As long as we do not fully know what awareness is and what mechanisms influence the state of staying awake and of anaesthetic sleep, and on which levels it happens, we will not be able to prevent intraoperative awareness effectively.

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1. INTRODUCTION

Surgical procedures have been performed since time immemorial. Initially, people who underwent invasive treatment had to suffer tremendous physical and mental pain because then anaesthetics were not known yet. In the course of time, a number of substances which alleviated pain as well as obliterating consciousness were invented, yet their application was not always successful.

The first documented general anaesthesia took place on 30 September 1846. It was administered by William Morton, who used ether during tooth removal.[1] Since then, a great number of new anaesthetics have been introduced for general anaesthesia, intravenous and inhaled agents, different methods and techniques of inducing anaesthesia have developed. More and more efficient equipment to induce anaesthesia and monitor patients as well as standards of anaesthesiologic workshop have been introduced, which has consequently improved patients' safety.

As a dynamically developing field of medicine, anaesthesiology follows challenges of modern surgery. In order to meet them, research is done into methods of monitoring the depth of anaesthesia, so that the patient is provided with maximum comfort, at the same time reducing the risk of anaesthesia-related complications.

Initially, monitoring patients' condition concerned only observation and clinical examination. In 1847, Plomley divided anaesthetic sleep into stages: analgesia; excitement, with or without consciousness; and the stage of deep anaesthesia.[2]

The first scale of the depth of anaesthesia induced with ether was introduced by John Snow on the basis of such physical signs as eyelash reflex, eyeball movements, depth and frequency of breaths, activity of intercostal muscles. He described five stages of anaesthesia and recommended that the procedure be performed after the eyelash reflex was lost, that is in the fourth stage. When breathing disturbance appeared in the form of 'rattling breath,' it was a signal to reduce the depth of anaesthesia.[3]

In the distant past patients were quite often conscious during surgical procedures, because too deep anaesthesia was related to a higher percentage of morbidity and mortality. In 1920, Guedel proposed a four-stage scale of the depth of anaesthesia, which was widely accepted for many years. The division into particular stages was based on the tension of muscles, the depth and frequency of breaths and eyeball movements.[4]

In the course of time, new agents were invented – intravenous anaesthetics and skeletal muscle relaxants – which led to reducing doses needed for general anaesthesia. At the same time, attempt were made to ensure good operative conditions. In 1950, Winterbottom documented the first case of intraoperative awareness. The patient heard and remembered conversations which took place during the procedure and felt intraoperative pain.[5] This encouraged practitioners and researchers to investigate the problem and look for new methods of monitoring the depth of anaesthesia, which resulted in a number of postulates that were to help delineate standards in anaesthesiology. In 1957, Woodbridge enumerated four elements which contribute to general anaesthesia: sensory blockade, motor blockade, blockade of autonomous responses, and unconscious sleep.[6] In 1987, Prys-Roberts indicated that unconscious sleep with loss of memory was one of the main assumptions of a properly performed anaesthesia, while other elements were just 'additions.' These views evolved further.[7] Stanski and Shafer believed that not only hypnotic agents but also analgesics should be administered in proper doses, and only a combined effect of both could ensure the right comfort and safety of the patient.[8]

More scales originated in order to detect cases of intraoperative awareness. Also, new equipment was built so that anaesthesiologists could properly monitor the depth of anaesthesia. In the 2012 recommendations of the Committee on Quality and Safety in Anaesthesia of the Polish Society of Anaesthesiology and Intensive Therapy concerning intraoperative awareness it was stated that 'the quality of anaesthesia is determined by its depth. It is a result of stifling the activity of the central and peripheral nervous system. Assessment of the depth of anaesthesia, resulting from a subjective analysis of clinical parameters, is currently more and more based on objective data retrieved with the use of state-of the-art devices monitoring particular elements of anaesthesia, including the level of obliterating awareness (pharmacological sleep).'[9]

The problem of intraoperative awareness concerns about 0.1%–0.2% of patients under anaesthesia.[10–13] The risk group includes people with genetic (mutation of melanocortin 1 receptor) or acquired resistance to anaesthetics. Additionally, there are patients who abuse alcohol, drug addicts, patients chronically on opioids, metabolism-enhancing medications, antiretroviral medications, or high doses of betablockers. Awakenings occur also in patients who do not tolerate high doses of anaesthetics due to low heart reserve, patients who undergo procedures which require lowering doses of anaesthetics. The risk group encompasses also patients with prolonged intubation and those who undergo total intravenous anaesthesia (TIVA). In the case of Caesarean section, the risk increases to 0.4%; in cardiosurgery in extracorporeal circulation – to 9%, while in obese patients – to 10%. In the case of multiorgan injuries and emergency procedures, the risk of awareness is higher than 10%.[14–15]

Analyses of monitoring the depth of anaesthesia should take into consideration methods which were used before the era of monitoring. During each anaesthesia this should include: assessment of patient's movements, depth and pattern of breathing, eyeball movements, pupil dilation and its reaction to light, possible lacrimation, moistness and colour of the skin, capillary refill time, pulse tension. Assessment of the cardiac cycle and blood pressure measurement can suggest what steps to take during anaesthesia, yet one needs to remember that 33% of intraoperative awareness cases occur when life parameters are stable.[16]

2. AIM

The aim of this paper is to describe methods and devices monitoring the depth of anaesthesia.

3. MATERIAL AND METHODS

This work was based on the available literature and the experience of the authors.

4. RESULTS AND DISCUSSION

The perfect method to evaluate the depth of sleep should be objective, so that the response is quick and precise – to increase or decrease the depth of anaesthesia. For that purpose, recently a few devices were constructed, all of which can be divided into passive and active systems. Passive systems assess the collected data, while active ones first stimulate and then receive and process data. Passive systems available on the market include: BIS, SNAP monitor, IoC monitor, Narcotrend monitor, SedLine monitor, Entropy, Conox (Table 1).

All of them use computer analysis of electroencephalographic (EEG) signal, and some of them additionally evaluate alterations of frontal electromyogram (EMG). Monitors based on EEG analysis can provide inadequate records if there is a device generating the electromagnetic field nearby, e.g. an electrocoagulation device, when during administering anaesthesia ketamine or nitrous oxide are applied. The displayed value can also be influenced by the activity of skeletal muscles. Both of the above agents do not suppress gamma waves in EEG, which can be received by the device as a state of insufficient anaesthesia when the patient is in fact under sufficiently deep anaesthesia.[17–19]

Biscpectral index (BIS), index of consciousness (IoC), and SNAP index are EEG signal processed in real time from the frontotemporal electrode, presented in the form of a number between 0 and 100. The recommended values for

Table 1. Summarizes pros and cons of each of the methods described above.

Methods monitoring the depth of anesthesia	Limitations	Advantages
BIS	Neurosurgery Electrocoagulation Use of ketamine / nitrous oxide during anesthesia Impact of glass muscle activity Passive method	Ease to use A large number of references using this method
SNAP monitor IoC monitor Narcotrend (EEG analysis)	Neurosurgery Electrocoagulation Use of ketamine / nitrous oxide during anesthesia Impact of glass muscle activity Passive method Limited references	Ease to use
SedLine monitor (EEG analysis)	Neurosurgery Electrocoagulation Use of ketamine / nitrous oxide during anesthesia Impact of glass muscle activity Passive method Limited references	EEG spectrum density analysis both hemispheres Ease to use High precision
Cerebral State Monitor , Entropia , Conox (EEG and EMG analysis)	Neurosurgery Electrocoagulation Use of ketamine / nitrous oxide during anesthesia Passive method Limited references	EMG analysis Ease to use
aepEX	Neurosurgery ENT – ear procedures Damage to the auditory pathway at any level More absorbing method in use Limited references	Active method
VERS	Neurosurgery Ophthalmology Visual damage at any level More absorbing method in use Limited references	Active method
Pupillometry	Neurosurgery Visual damage at any level Ophthalmology/ENT/maxillofacial surgery (limited access to the patient) Use of nitrous oxide / thiopental during anesthesia Limited references Using the device during anesthesia requires a lot of practice	Active method Small size of the device

general anaesthesia for BIS and IoC are between 40 and 60. In turn, SNAP values should remain between 54 and 74.

Narcotrend monitor, similarly to BIS, automatically analyses EEG records, looking for patterns, and the result which undergoes processing is presented in the form of visual parameters from A (conscious) to F (deeply unconscious), while D/E is the state proper for general anaesthesia. The letter scale was improved with Narcotrend index, whose values are between 0 (no EEG activity) to 100 (conscious). The D level of anaesthesia corresponds to values 37–64, while the E level to 13–36.[9,20] Weber et al. showed lower consumption of anaesthetic agents and faster awakening after the procedure in randomized controlled trial with Narcotrend in children's anaesthesia for endoscopic procedures.[21]

Another device worth applying is SedLine monitor, which is based on 4-channel EEG, separately monitoring both hemispheres. Apart from the global patient state index (PSI), whose reference value during administering general anaesthesia should be between 25 and 50, the analysis encompasses also the spectral density of EEG wave from over both hemispheres. The result is displayed as a colourful spectrogram separately for each hemisphere. This makes it possible to locate areas with enhanced bioelectric activity more precisely.

The limitation of BIS, that is the effect of skeletal muscles activity, made researchers look for a method that would separate the activity of the brain cortex from the activity of muscles. Their work resulted in Cerebral State Monitor, Entropy and Conox.[22–23]

On the basis of the analysis of frontotemporal EEG records, cerebral state monitor shows a numerical value (cerebral state index – CSI) between 0 and 100, correspondent to the depth of anaesthesia. Recommended reference values are identical as for BIS. Cerebral state monitor also indicates the value of frontotemporal EMG. High EMG values can interfere with the CSI records. This might be related to a strong pain stimulation, muscle stiffness, too low a level of muscle relaxation or presence of a source of strong electromagnetic field (e.g. electric coagulation). If after eliminating factors which can increase the value of EMG and a decrease in its value the CSI is still high, the depth of anaesthesia is insufficient. At the moment, there are no studies that would prove that employing CSM has an impact on the number of cases intraoperative awareness.[24]

Entropy is comprised of two parameters, that is the state entropy (SE) and the response entropy (RE). SE is based on the analysis of EEG waves and corresponds to the activity of the cortex, while RE is based on the analysis of EEG and EMG waves, which depicts subcortical activity. When an external stimulus (e.g. pain) appears, RE first and then SE will start increasing. SE values range between 0 and 91, while RE values between 0 and 100, and the 40–60 margin is believed to be proper for general anaesthesia. One needs to mention that a difference between RE and SE larger than 5–10 may indicate that intraoperative analgesia is insufficient.[24] Singh et al. proved that entropy is a useful index of the depth of anaesthesia in procedures with a laryngeal mask airway, propofol and sevoflurane.[25]

Conox monitor informs the user about two parameters: qCON and qNOX. On the basis of EEG analysis, qCON is assessed as it corresponds to the depth of anaesthesia. In turn, qNOX can provide an insight into whether a patient responds to external stimuli. One should not identify this with monitoring pain. Both values should remain within the margin of 40–60.[26] Conox is one of the most state-of-the-art medical devices, that is why so far there has been no data about its effectiveness. The first trials applying this method are encouraging; it seems that Conox monitoring makes it possible to considerably save anaesthetic agents and wake the patient up faster, still maintaining the right depth of anaesthesia (initial reports, our own data).

Among the working systems available on the market, it is worth mentioning devices which monitor evoked action potentials (auditory, visual, somatosensory) and pupillometry with the possibility of stimulation (light, electrical), that is aepEX and AlgiScan.

The aepEX system records auditory evoked potentials (AEPs), that is an electrophysiological brain response to auditory stimulation. The aepEX monitor displays an averaged electrophysiological response of the nervous system to generated sounds (the so called click) and calculates the aepEX index, that is an index of deviations of a curve showing information about the amplitude and latency of response. The aepEX index determines a correlation between the depth of anaesthesia and the state of patient's awareness. The system generates loud clicks in the patient's ears through headphones. Then, it monitors subsequent AEPs, transforming them into a numerical index in the range between 1 and 100. The system monitors activity of the brain stem, unlike most of the systems based on passive EEG analysis, which assess activity from the cortex. The AAI combines the value of passive assessment (EEG from the frontal region) with active assessment – the response of the brain stem to an auditory stimulus. After processing, the result of the measurement is displayed in the form of a number. The result between 30 and 40 indicates that the depth of anaesthesia is sufficient and the organism does not respond to an external stimulus at any level of the auditory pathway. A few studies have shown that applying this method lowers the amount of necessary anaesthetics and makes it possible to wake the patient up faster after the surgery.[22,24,27]

Somatosensory evoked potentials are obtained through stimulation of sensory fibres of peripheral nerves (most often of the limbs), at the same time registering the presence, quality and strength/power of the evoked response depending on the applied stimulus. This method did not find a wider application in monitoring the depth of anaesthesia. It is used mainly to monitor the intraoperative function of the spinal cord, peripheral nerves or the brain stem.

VERS – that is visual evoked response potentials – are generated by a series of flashes from special goggles, lenses. This method did not enjoy a wider application in monitoring the depth of anaesthesia. Its application is limited to monitoring the function of the visual pathway during procedures in the anterior cranial fossa, the base of skull (the pituitary gland).[23,24]

Among the currently available active methods, it is worth considering pupillometry. It is based on assessing the size of the pupil and its reactivity depending on the stimulus (visual, electric, measurement of pupil's size in response to surgical stimulation).

The key in assessing and measuring the pupil is investigating the response of the sympathetic system to an automatic electric stimulation (10–60 mA) and its assessment on the basis of observations of changes in pupillary response. This way a pupillometer measures and calculates the pain pupillary index (PPI), whose value in the scale between 1 and 10 corresponds to the reactivity to external factors, that is to the depth of anaesthesia. The values which should be aimed at during anaesthesia are between 4 and 6.[28]

Despite easy availability of devices monitoring the depth of anaesthesia, their applicability in practice requires further studies. The results of undertaken analyses are not unanimous. According to some, monitors currently available on the market show around 80% effectiveness in preventing intraoperative awareness.[29] Extensive analyses of Cochrane from 2007 and 2014 showed that BIS-anaesthesia reduces the risk of awareness in groups of greatest risk to a considerable extent.[30,31] According to Myles and Avidan, the application of BIS does not exclude, however, a possibility of intraoperative awareness.[16] Continuous development of anaesthesiologists' knowledge and improvement of anaesthetic techniques can help reduce the risk of intraoperative awareness by 50%.[16,31]

There have been attempts to assess applications of BIS monitoring with reference to the depth of patients' sedation in ICUs. The latest metanalysis by Cochrane from 2018 (4245 studies) did not find enough evidence to show that BIS is more useful in clinical assessment of patients.[32]

Another metanalysis comparing clinical effectiveness and costs of anaesthesia with the use of Entropy, BIS and Narcotrend showed that evidence of their effect on intraoperative awareness is limited. Yet reduced use of anaesthetic agents and shortened time of sleep after anaesthesia were proved.[33]

5. CONCLUSIONS

Undoubtedly, employing additional methods of monitoring the depth of anaesthesia makes it possible to increase the depth more safely when it is necessary (e.g. during a repeated attempt at intubation).

It seems that when it comes to the effect of anaesthetic agents on such a precise organ as the brain, there is still much to discover. As long as we do not fully know what awareness is and what mechanisms influence the state of staying awake and of anaesthetic sleep, and on which levels it happens, we will not be able to prevent intraoperative awareness effectively.

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