أجهزة قياس عمق التخدير المعتمدة على رسم المخ

رسالــــــة

توطئة للحصول على درجة الماجستير **فى التخدير**

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ELECTROENCEPHALOGRAM-BASED DEPTH OF ANESTHESIA MONITORS

Essay

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List of Abbreviations and Acronyms

5-HT2A	:	5-hydroxytryptamine 2A (Serotonin type 2).
AAI	:	ALine ARX index.
ABR	:	Auditory Brainstem Response.
AC	:	Alternating current.
AEP	:	Auditory evoked potential.
AMLR	:	Auditory Middle Latency Response.
AMPA	:	α-amino-3-hydroxy-5-methyl-4-isoxa-zole propionic acid.
ASA	:	American Society of Anesthesiologists
ASSR	:	Auditory steady-state response.
ASYM	:	Asymmetry Indicator.
BIS	:	Bispectral Index.
CEA	:	Carotid endarterectomy.
CNS	:	Central Nervous System.
DC	:	Direct current.
DSA	:	Density Spectral Array.
DSA	:	Density spectral array.
EEG	:	Electroencephalogram.
EMG	:	Electromyographic.
EP	:	Evoked Potential.
FDA	:	Food and Drug Administration.
FFT	:	Fast Fourier transformation.
GABA	:	γ-aminobutyric acid.
GABAergic	:	γ-aminobutyric acid–mediated.
IFT	:	Isolated Forearm Technique.
IV	:	Intravenous.
L	:	Left.
MAC	:	Minimal alveolar concentration.
MAC-BAR	:	MAC-Blockade of Autonomic Reflexes.
MLAER	:	Midlatency auditory evoked response.

List of Abbreviations and Acronyms (Cont.)

N2O	:	Nitrous oxid
NMBAs	:	Neuromuscular blocking agents.
NMDA	:	N-methyl-d-aspartate.
OR	:	Operating room.
Pb	:	Positive component.
Pk	:	Prediction probability.
PSA	:	Patient State Analyzer.
PSI	:	Patient state index.
PTSD	:	Post-traumatic stress disorder.
R	:	Right.
RE	:	Response entropy.
SD	:	Standard deviations.
SE	:	State entropy.
SEF	:	Spectral edge frequency.
SQI	:	Signal quality indicator.
SR	:	Suppression ratio.
Xe	:	Xenon.

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الملخص العربى

تؤثر أدوية التخدير الكلي على الجهاز العصبي المركزي، وعلي هذا فالوصول لدرجة عمق تخديرية مناسبة أثناء العمليات الجراحية ضروري دون أن يكون هذا العمق زائد، فيؤثر على وظائف القلب والدورة الدموية. أو أقل من الحد المطلوب فيصحبها الإدراك والوعي أثناء العملية الجراحية.

تقليدياً يتم تحديد درجة عمق التخدير أثناء العملية الجراحية من خلال فقدان الاستجابة الحركية والتغيرات التي تحدث فى الجهاز العصبي اللاإرادي كالتغيرات فى وظائف القلب والدورة الدموية.

وقد استحدثت طرق حديثة لقياس درجة العمق التخديري أثناء العمليات الجراحية وذلك لتفادي حدوث إدراك أثناء العمليات الجراحية عن طريق أجهزة قياس عمق التخدير المعتمدة على رسم المخ.

وتعتمد هذه الأجهزة على قياس النشاط الكهربائى للمخ والتغيرات التى تطرء عليه نتيجة التخدير الكلى, حيث أن رسم المخ يقوم برصد هذه التغيرات التى تتأثر بدرجة عمق التخدير مما يعكس درجة عمق التخدير.

تقوم هذه الأجهزة بتحليل تلك الأشارات عن طريق عمليات حسابية معقدة وتحويلها الى مدلولات وارقام يسهل فهمها وتعكس درجة عمق التخدير, مما يساعد على اعطاء المريض الجرعات المناسبة من أدوية التخدير بدون حدوث ادراك أثناء العملية أو يكون عمق التخدير زائد فيؤثر على وظائف الجسم, و ايضا تساعد على سرعة أفاقة المريض بعد العملية الجراحية وتوفير جرعات التخدير الغير ضرورية, كما تعكس هذه الأجهزة درجة تدفق الدم للمخ التى لها أهمية فى عمليات جراحة المخ.

الأجهزة المتاحه حاليا تشمل جهاز الطيف الثنائى, جهاز مؤشر حالة المريض, جهازالناركوترند, جهازالأنتروبى و جهاز قياس الموجات السمعية المستحسة و تقوم هذة الأجهزة بأعطاء رقم يدل على درجة الوعى وعمق التخدير.

Introduction

General anesthetic agents are central nervous system (CNS) poisons. Achieving adequate depth of general anesthesia during surgical procedures is desirable. While too deep an anesthetic may result in cardiovascular depression and prolonged awakening times, a rather harmless complication of minor clinical interest, the opposite-too light anesthesia- is more difficult to detect and frightening from the patient's point of view, and may be associated with intra-operative awareness **(Ropcke, 2004)**.

Traditionally, depth of anesthesia has been assessed from autonomic and movement responses, with efforts concentrated on maintaining cardiovascular stability along with immobility. However, movement in a non-paralyzed subject during anesthesia has been shown to represent a spinal response. Immobility is easily achieved with neuromuscular blocking agents (NMBAs). When NMBAs are used, neither immobility nor cardiovascular stability can be considered to represent depression or presence of cortical functions such as consciousness and recall. Previously, the hypnotic component in balanced anesthesia has been beyond the scope of monitoring **(Rampil et al., 1993)**.

Currently it is possible to quantitate the depth of hypnosis using one of the commercially available EEG-based depth of anesthesia monitors.

A primary reason for the use of EEG-based monitoring in general anesthesia is to detect and warn the anesthesiologist that retrievable memories are being formed by the patient, i.e. awareness **(Voss and Sleigh, 2007).**

Intra-operative awareness

Intra-operative awareness is defined as a recalled event in which a patient becomes conscious during a procedure performed under general anesthesia. The term "awareness" is limited to 'explicit memory' during anesthesia and does not include the time before general anesthesia is fully induced or the time of emergence from general anesthesia **(Ghoneim, 2000).**

Recall is the ability to retrieve stored memories. 'Explicit memory' is assessed by the patient's ability to recall specific events that took place during general anesthesia. 'Implicit memory', which is not addressed in the American Society of Anesthesiologists (ASA) Practice Advisory, is assessed by changes in performance or behavior without the ability to recall specific events that took place during general anesthesia that led to those changes. A report of recall may be spontaneous or elicited only after several interviews. Dreaming, although it is possibly associated with awareness **(Sebel et al., 2004),** is not considered Intra-operative awareness

Scope of the problem

Intra-operative awareness has been brought to our attention and even sensationalized often by the media over the past few years, as a major problem during anesthesia. The true incidence and the actual incidence have been questioned. Others have even questioned if the complication has been reported in order to garner sympathy at the least and financial gain at the most **(Varinee et al., 2008).**

Certainly the incidence of Intra-operative awareness under general anesthesia is rare (0.1-0.2%) but given that some 21 million anesthetics are administered annually in the United States alone, this figure translates to an occurrence of 20,000 to 40,000 cases. Worldwide the number of cases would easily reach into the millions, especially in countries that lack the resources to administer the newer inhalational anesthetics through state-of the art anesthetic machines. To those who have experienced anesthesia awareness, it is considered a distressing complication which can cause significant psychological sequelae including post-traumatic stress disorder (PTSD) **(Osterman et al., 2001).** The syndrome and its sequelae have been discussed on television talk shows, and have been the topic of many articles and panels at national and international meetings.

Risk factors for inta-operative awareness

In 2006 the Task Force on Intra-operative Awareness, established by the ASA, released a “Practice Advisory for Intra-operative Awareness and Brain Function Monitoring.” The advisory identified certain patient characteristics and surgical factors that increase the risk of intra-operative awareness. Patient-related factors include age, limited cardiac reserves, drug resistance or substance abuse (including the long-term use of benzodiazepines, cocaine or alcohol) and a history of difficult intubation or previous episodes of Intra-operative awareness. Certain procedures are associated with increased risk, including cesarean section, cardiac surgery, trauma surgery and procedures for which muscle relaxants are used. Preoperative consultation may be helpful in identifying patients who will be at risk for intra-operative awareness **(Beverley et al., 2008).**

The causes of intra-operative awareness are as yet unknown, and the problem may be multifactorial. At least 4 broad categories of causes are plausible. First, unexpected patient-specific variability in dose requirements of anesthetic drugs may be a result of altered expression or function of target receptors. Second, patients may be unable to tolerate a sufficient dose of anesthetic because of low physiologic reserves related to factors such as poor cardiac function or severe hypovolemia. Third, physiologic characteristics that would indicate the need for a dose change may be masked by factors such as use of β-adrenergic receptor blockers or presence of a pacemaker. Fourth, intended drug delivery systems may be compromised by events such as equipment malfunction or misuse. Of these, the first category would be especially distressing because the patient would be exposed to a seemingly adequate dose of an anesthetic, but the resulting depth of anesthesia would be inadequate **(Beverley et al., 2008),** these patients are in need for monitoring the level of hypnosis, which have been an issue of major concern in anesthetic practice.

The fundamental neurophysiological basis of loss of consciousness is commonly (but not always) a depowering of cortical activity, which is the scientific principle of most of the available EEG-based depth of anesthesia monitors, understanding the mechanism of action of general anesthetics and their sites of action is necessary for understanding the scientific principles of depth of anesthesia monitors.

This review will describe the mechanism of action of general anesthetics, the processing of the raw EEG and the currently available EEG-based depth of anesthesia monitors and their scientific principles, advantages, disadvantages and clinical applications.

Aim of the work

The aim of this work is to review the current medical literature addressing the subject of electroencephalography (EEG)-based depth of anesthesia monitors to help in understanding its scientific principles, advantages, disadvantages and the possible clinical application of each.

Mechanism of Action of General Anesthetics

What is General Anesthesia?

Oliver Wendell Holmes in 1846 introduced the word "anesthesia" to signify insensibility to surgical pain. However, there is still no consensus on a more objective definition of general anesthesia **(Drury, 2000).** At different concentrations inhaled anesthetics induce a variety of reversible, clinically important effects. Low concentrations can induce amnesia, euphoria, analgesia, hypnosis, excitation, and hyperreflexia. Higher concentrations cause deep sedation, muscle relaxation, and diminished motor and autonomic responses to noxious stimuli, effects that progress to "surgical" anesthesia. Some volatile anesthetics also protect the myocardium against the effects of ischemia, an important component of anesthetic action for many patients (**Jason et al., 2003**).

Rigorous definitions have been introduced for investigations of the underlying mechanisms of anesthetic effects in humans and animals and for the clinical assessment of the depth of anesthesia. These effects must be reversible and produced without the need for supplemental muscle relaxants, benzodiazepines, narcotics, or autonomic modulators. Loss of appropriate response to specific spoken commands is used to identify hypnosis (the impairment of perceptive awareness) in anesthetized subjects. In addition, patients may have perceptive awareness without recall because memory is more sensitive to anesthetics than awareness. Laboratory animals are assessed for loss of righting reflexes-the inability to return to an upright position in response to non-painful stimuli —