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Editorial

Light or deep general anaesthesia: does it matter and how to assess it?

In a recent issue of Eur J Anaesth, Rehberg and colleagues compared two delivery techniques for intravenous anaesthesia, manual infusion vs. target-controlled infusion (TCI), both handled by inexperienced anaesthesiologists [1]. They found that the only benefit from TCI was to reduce the time spent at 'light' anaesthesia levels, as defined by a bispectral index (BIS™) over 60. They also observed that BIS™ with both techniques was usually around 30, which is usually considered an unnecessary overdosage. These results prompt us to discuss which level of anaesthesia is really desirable in clinical practice and how it should be assessed.

For centuries, anaesthesia was simply defined as sufficient 'privation of the senses' to make surgery possible. Since the middle of the 19th century, practitioners realized that several levels of anaesthesia could be achieved [2]. More recently, it has been demonstrated that this depth of anaesthesia correlated with the hypnotic drug concentration in the central nervous system. This led to the development of TCI algorithms in order to control and adjust the depth of anaesthesia through the control of concentration [3]. However, the concentration required for the same drug effect differs among individuals and depends on age, physiological status, co-administered drugs, intensity of stimulation, etc. The same drug concentration may result in an insufficient depth of anaesthesia in one patient, and an excessive depth in another. Consequently, it was recognized that the process of anaesthesia should start by delivering an *a priori* initial dosage based on statistical considerations (i.e. a dosage that has a high probability of being adequate), but should always be followed by individual depth of anaesthesia assessment to adjust drug delivery.

Light anaesthesia is theoretically easy to diagnose: the patient is awake, moves spontaneously or responds to commands and often (but not always) has explicit memory of this period. But in clinical practice, light anaesthesia may not be recognized when the patients are paralysed, when they are too weak to move, when the anaesthetist does not pay attention fast enough to the clinical signs or when the time to deepen anaesthesia is delayed by safety concerns as bleeding, by technical problems (empty syringe or vaporizer), or by insufficient pharmacological knowledge and inappropriate dosing adjustment [4]. In the absence of specific risk factors, the incidence of awareness is estimated at around 0.2%, which means that, e.g. in France where about 6 million general anaesthetics are administered every year, 12 000 patients have a statistical risk of intraoperative awareness. This risk is even higher in situations such as general anaesthesia for Caesarean section, cardiac surgery or trauma! Unanticipated awareness is always frightening for the patient and may induce post-traumatic stress disorders [5] and/or legal claims [6]. TCI, which allows rapid step-by-step increases in target concentration without overdosage, may improve the control over depth of anaesthesia, especially when anaesthesiologists are inexperienced as clinically verified by Rehberg and colleagues [1].

To increase sensitivity and decrease delay in detecting light anaesthesia, monitoring techniques based on on-line analysis of cortical EEG have been developed and released for clinical practice over the last decade [2]. The first was the BIS™ developed by Aspect Medical Systems [7], followed more recently by competitors based on different EEG analysis algorithms such as entropy, spectral, topographical or visual analyses [8]. Despite different signal analysis algorithms, these techniques are based on a common rationale: anaesthetic depth modifies spontaneous cortical EEG changes towards slowing, synchronization and loss of randomness. Both BIS and entropy showed a good statistical correlation with loss or return of consciousness [9–12], supporting their use to detect intraoperative awareness, whereas the performances of other measures have been less substantiated [13–17]. However, a statistical correlation is not a true measure of

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clinical effects but only a surrogate [2], and it may sometimes fail to predict accurately [18]. Several case reports have described clinically asleep patients having high BIS, often because of the muscular activity in non-paralysed patients [19]. Conversely, in the 'B-aware' study, comparing BIS to standard practice in high risk of awareness patients, BIS monitoring reduced the incidence of awareness, but two cases of awareness among 1225 patients were nevertheless observed in the BIS™-monitored group [20].

In summary, EEG measures provide additional information to clinical and pharmacological assessments of anaesthetic depth, which may help in detecting awareness but they do not replace clinical assessment and should always be interpreted within the clinical context, e.g. use of muscle relaxant, electrical artefacts, etc.

Monitoring depth of anaesthesia may be useful to detect not only a too light level of anaesthesia but also excessively deep anaesthesia. Excessive depth of anaesthesia is difficult to diagnose clinically since, like adequate anaesthesia, it is characterized by the absence of consciousness and response to command. Excessive depth of anaesthesia is usually recognized when unwanted drug side-effects such as hypotension, bradycardia, prolonged apnoea, delayed recovery, etc. are achieved, which occur at concentrations far above the minimal concentration that would likely have been sufficient. Between drug-induced deleterious effects and adequate anaesthesia is a wide window of overdosage with unnecessary drug administration. This is illustrated by the study of Rehberg and colleagues [1] where anaesthetist subjective assessment of anaesthesia was consistently and repeatedly estimated around 5 on a scale from 0 to 10, i.e. not too deep and not too light, whereas BIS™ values were around 30, indicating deep anaesthesia! Maintaining BIS™ values around 50 in this study would probably have reduced hypnotic drug consumption by 20–30%. A similar benefit has been demonstrated many times for all EEG monitoring devices [21–24].

Apart from excessive drug consumption, is it dangerous to give a patient a hypnotic overdose?

From the pharmacokinetic point of view, it may delay recovery, especially after long-term infusions of drugs that accumulate in the body. This concern may be relevant after using midazolam or isoflurane when used for intensive care sedation or long anaesthetic cases. However, for drugs with better pharmacokinetic profiles such as propofol, sevoflurane or desflurane, the reduction in extubation or discharge time from the recovery unit is only of a few minutes, which is hardly clinically relevant [21] despite statistically significant differences. One recent study and a few conference abstracts suggest that hypnotic overdosage during surgery might be associated with an increased long-term mortality [25]. However, it must be noted that the 1-year mortality rate in this study was quite high (>5%) and that half of the patients died from the continuing course of their cancer. There is not yet enough evidence to be sure that anaesthesia overdosage is a contributing cause to long-term adverse outcomes and the apparent anaesthesia overdosage, despite anaesthetic doses within the usual range, might as well have been a symptom of severe comorbidity, which was the marker of poor prognosis.

Nevertheless, the patients in the control group of the study by Monk and colleagues [25], as well as the patients in Rehberg and colleagues's study [1] received excessive hypnotic drug without any apparent clinical benefit and the EEG-guided depth of anaesthesia monitoring would have helped to avoid it.

In conclusion, it matters to avoid both light and excessively deep anaesthesia, and electrophysiological monitoring techniques can help titrate drug delivery to individual requirements because they provide quantitative estimates that are much more sensitive than clinical assessment to diagnose both underdosage and overdosage. This has been demonstrated in many studies with BIS™, the first device released, and new data from other EEG analysis techniques show similar results. Such a monitoring is usefully complemented but not replaced by sophisticated drug delivery systems such as TCIs, which allow titration to a desired level of anaesthesia, especially when anaesthesia is delivered by inexperienced anaesthesiologists.

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