Extended Monitoring of the Sedated Patient: Bispectral Index, Narcotrend® and Automated Responsiveness Monitor

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Key Words

Sedation • Endoscopy • Monitoring • Bispectral index • Narcotrend® • Automated responsiveness

Abstract

It has been demonstrated that a processed EEG derivative may reflect the patient's level of consciousness during endoscopic sedation. However, to date a clinical benefit of EEG monitoring with respect to relevant safety parameters in routine gastrointestinal endoscopy has not been demonstrated. During long-lasting procedures (e.g. ERCP, ESD) a propofol-sparing effect has been shown, but a benefit regarding patient safety could not be documented. The use of an automated responsiveness monitor may help to achieve and to maintain the level of conscious sedation with propofol, but its precise role in endoscopic sedation is undefined.

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Introduction

During endoscopic sedation, changes of the patient's level of consciousness occur along a continuum ranging from minimal (anxiolysis) or moderate (conscious sedation) to deep sedation and general anesthesia. In addition

to adequate monitoring of cardiorespiratory parameters for detection of early signs of patient distress, clinical monitoring of the patient's level of consciousness is mandatory. However, the observation of the patient's awareness, compliance with the procedure, pain reactions and reflex status is difficult to assess in a darkened procedure room with the endoscopist and assisting nurse placed near the head of the patient, which is routinely the case during upper GI endoscopy.

In this context, it may be helpful that alterations of cerebral function caused by anesthetic agents are reflected in the electroencephalogram (EEG) rhythm [1]. Increasing hypnotic effect is associated with a slowing of the EEG. Thus, evaluation of the EEG provides some objective information about the hypnotic state of the patient. For general anesthesia, it has been shown that EEG guidance avoids both under- and overdosing of hypnotic agents and is valuable for detecting potentially harmful situations for the brain (e.g. cerebral hypoxemia). The complex visual interpretation of an EEG recording (which is time-consuming and requires special knowledge) is, however, not practical during endoscopic procedures and, therefore, several automated EEG analysis systems have been developed. These systems are based on a complex, computer-generated, mathematical multiparametric analysis of the EEG. The EEG electrodes (which were

then connected to a computer device) were placed on the forehead of the patient, so that this technique can be practical during upper as well as lower GI endoscopy (fig. 1 and 2). So far three different devices have been investigated for so-called 'neuromonitoring' during sedated endoscopic procedures.

EEG Monitoring Using the Spectral Edge Frequency

Spectral parameters as the median or the spectral edge frequency (a processed EEG derivative which converts EEG waveforms from the time to the frequency domain by using fast Fourier transformation) has been used most often to quantitatively characterize EEG activity in anesthesia. In a study from Israel [2], a total of 32 patients underwent ERCP and were randomized to receive intravenous midazolam ($n = 17$) or propofol ($n = 15$) for endoscopic sedation. They adjusted the administration of the sedative agents with a bolus and subsequent incremental doses until the patients reached a target spectral edge frequency (about 12 Hz) and thereafter maintained the hypnotic state (by administration of repeated doses) as close as possible to the target spectral edge frequency. The study was not designed to evaluate the clinical usefulness of EEG monitoring, but demonstrated that by using this approach, a better patient tolerance, shorter recovery and lesser hemodynamic side effects were obtained with the use of propofol than with midazolam during ERCP.

EEG Monitoring with Bispectral Index Monitoring

Bispectral monitoring is used to evaluate sedation depth in intensive care medicine and for surgical patients, and has now been also thoroughly evaluated for its use in endoscopy [1]. The computer-generated bispectral index (BIS) [ranging from 0 (coma) to 100 (fully awake)] reflects the level of sedation regardless of the patient's demographics and the type of hypnotic drugs used. For obtaining general anesthesia routinely, BIS levels between 40 and 60 were necessary. In a preliminary study of 50 patients who underwent several endoscopic procedures under sedation with diazepam and meperidine, a significant temporal correlation of the BIS level and the clinical assessment of patient consciousness was described [3]. Another pilot study described bispectral monitoring as part of a closed monitoring cycle for the continuous infusion of propofol in 16 patients sedated

Fig. 1. For EEG monitoring, only three commercially available EEG electrodes are placed on the patient's forehead, thus enabling upper as well as lower GI endoscopy and additional monitoring by capnography.

Fig. 2. The EEG analysis is displayed on a PC monitor (here using the Narcotrend® device) which can be observed together with the results from different monitoring devices (in this example from pulse oximetry and capnography).

for colonoscopy [4]. However, in more recent studies, BIS monitoring was not found useful to titrate propofol sedation for colonoscopy [5, 6]. In both trials, neither propofol dose reduction nor corresponding shorter recovery times were attained by using BIS monitoring. There was a substantial time lag between the decrease of the BIS level below 70 and the respective clinical findings, in-

Table 1. Randomized controlled trials evaluating different neuromonitoring techniques in sedated patients undergoing ERCP

Author	Patients n	Sedative drugs used	Targeted sedation level	Total drug dose without and with neuromonitoring, mg
Wehrmann et al., 2002 [13]	80	propofol	deep sedation (clinically evaluated) Narcotrend® D0–2	374 ± 166 290 ± 158*
Al-Sammak et al., 2005 [11]	40	midazolam plus fentanyl	MOAA/S 2–3 BIS 70–80	19 ± 3 16 ± 3*
Paspatis et al., 2009 [10]	90	propofol	MOAA/S 0 BIS 40–60	554 ± 182 477 ± 187*

* p < 0.01. MOAA/S = Modified observer assessment of alertness and sedation score; BIS = bispectral index monitoring.

dicative of a deeper sedation state. These observations were confirmed when using BIS monitoring during nurse-administered propofol sedation for endoscopic ultrasound examinations [7]. An insufficient sensitivity of the BIS to predict the clinically determined patient's consciousness was also observed in another study using sedation with midazolam and meperidine for colonoscopy [8]. However, during longer-lasting interventional endoscopic procedures, like endoscopic submucosal dissection (ESD) of early gastric cancers [9], or interventional ERCP [10], two recent randomized controlled studies (conventional sedation with propofol vs. BIS-guided sedation with propofol) demonstrated a significant reduction of the used total propofol dose and a corresponding shorter recovery time when using BIS monitoring. These results were also confirmed by a former and smaller trial on 40 patients using sedation with midazolam and meperidine for ERCP [11].

EEG Monitoring Using the Narcotrend® Device

The Narcotrend® device also uses a multiparametric mathematical algorithm for analyzing the EEG rhythm. It is based on a suggested visual EEG analysis put forward by the German neurophysiologist Joachim Kugler in 1981 [12]. There is one randomized controlled study showing that the use of this device during propofol-sedated ERCP in 80 patients enables a more effective titration of propofol (significantly lower total dose of propofol in the EEG-monitoring study arm) and is correspondingly associated with faster patient recovery [13].

In summary, different EEG-monitoring techniques have been proven to be technically feasible for their use

in the endoscopy suite. During routine endoscopic procedures, most data showed no relevant clinical benefit of EEG monitoring over clinical assessment and conventional cardiorespiratory monitoring. During longer-lasting interventional endoscopic procedures (table 1), a significant propofol-sparing effect of EEG monitoring could be documented in three randomized trials associated with a more rapid recovery of the patients.

Monitoring of the Patient's Responsiveness with Automated Devices

For most diagnostic endoscopic examinations, the level of moderate sedation was held to be sufficient to induce adequate patient tolerability. Therefore, the early detection of any loss of consciousness of the sedated patient is mandatory.

For these purposes, an automated responsiveness testing system may be useful. In an automated responsiveness monitor (ARM), a computer-generated voice instructs the patient to press a button and the ability of the patient to react within a dedicated time period is considered presumptive evidence of consciousness. Such a device consisted of a button incorporated into a hand piece that was linked to a computer-generated voice that instructed subjects via an earphone to press the button. This request was repeated up to 5 times over a 10-second interval. With each repetition, the voice became louder and more insistent. Furthermore, the instructions may be accompanied by progressively more vigorous vibration of the hand piece in some devices. The voice and the vibration both stopped immediately when the button was pressed. Failure to activate the ARM button within 10 s

after the request was considered to be a nonresponse and was displayed by the system as an alert.

In anesthesiological studies, it has been shown in healthy volunteers that the use of an ARM device can guide individual titration of propofol because failure to respond precedes the clinically monitored loss of consciousness and was not susceptible to any false-normal responses [14]. In another trial of the same group evaluating BIS monitoring and the ARM in 18 healthy volunteers under intravenous infusion of propofol, the ARM appears to be useful as an automated measure of sedation and may provide the basis for automated monitoring and titration of sedation for a propofol delivery system [15]. Therefore, such an ARM device was also incorporated in the computer-assisted personalized sedation propofol delivery system which automatically delivered propofol via a perfusion pump [16]. To date, no further reports on the use of an ARM for endoscopic sedation exist.

A more sophisticated technique in this respect is the analysis of auditory-evoked potentials (AEP) for the as-

essment of the depth of sedation. AEP are changes of the EEG activity produced by auditory stimuli applied via earphones. From the EEG activity, the mid-latency AEP are extracted by a computer-generated online analysis, with the result expressed as a composite index. In a small pilot trial on 30 patients who underwent upper and lower GI endoscopy under sedation with midazolam and alfentanil, a good correlation between the clinical assessment and the AEP composite index was reported [17]. In a more recent and larger trial on 115 patients [18] receiving low-dose midazolam plus propofol for colonoscopy, however, the correlation coefficient between the clinical findings and the AEP index was markedly lower ($r = 0.47$) than the correlation with BIS ($r = 0.77$). Furthermore, the authors noted recurrent artifacts during analysis of AEP and concluded that BIS monitoring was superior to AEP monitoring for titrating the chosen sedation regime.

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