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Case Report

Case report: Large increases in entropy during general anesthesia to awake values antagonized with additional administration of rocuronium

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Abstract. We present the case of a 47-year-old female patient (ASA II) with acute cholecystitis, type 2 diabetes and grade 2 obesity (Body Mass Index 36 kg/m²) undergoing laparoscopic cholecystectomy under general anesthesia in our institution (SCJU Oradea). Depth of anesthesia was monitored with a General Electric Healthcare (GE) Entropy Module and muscle relaxation was monitored with a neuromuscular transmission module (NMT). During the procedure we noted a sudden large increase in RE and SE to awake values. An additional dose of rocuronium was administered and both RE and SE values decreased immediately. This exact scenario was repeated two times during the case. The patient reported no awareness postoperatively.

Key Words: state entropy, response entropy, rocuronium, general anesthesia.

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Introduction

Entropy is a device which helps in analyzing electroencephalogram (EEG) and contains state entropy (SE) and response entropy (RE). SE is computed from the electroencephalogram in the 0.8-Hz to 32-Hz range and should encompass mainly the hypnotic elements of the electroencephalogram, whereas response entropy is computed from 0.8 to 47 Hz, which includes a significant amount of the facial electromyography (EMG). Thus, when EMG activity is low, state entropy and response entropy should be the same, but with arousal and an increase in facial EMG, response entropy should increase. The initial clinical studies with this device showed that it produced results comparable to those of the Bispectral Index (BIS) when tested with intravenous and inhaled hypnotic anesthetics (Vakkuri et al 2004; Călin et al 2021).

The ability to monitor the levels of patient consciousness while undergoing general anesthesia is clinically important because an inadequate level of anesthesia can result in patient intraoperative awareness, an overdose of anesthesia can result in a prolonged recovery and an increased risk of postoperative complications (Kerssens et al 2005; Andrade et al 2007). The use of depth of anesthesia monitors is claimed to provide a more accurate assessment of the level of anesthesia and aid the tailoring of the anesthetic dose to the individual patient. Tailored dosing potentially reduces drug consumption and the number of adverse effects, with possibly faster emergence from anesthesia with an earlier patient discharge from the recovery room (Călin et al 2021).

M-Entropy (GE Healthcare) indicates depth of anesthesia through two parameters, State Entropy (SE) and Response Entropy (RE). SE is computed over the EEG dominant part of the frequency spectrum (0.8–32 Hz) reflecting the hypnotic component. RE covers both the EEG and electromyogram (EMG) component of the spectrum (0.8–47 Hz). (Viertio-Oja et al 2004) and is the faster reacting of the two parameters. Increased RE values from EMG interference are not uncommon, but theoretically SE values should not increase with EMG interference as the frequency spectrum reflects solely the EEG component. RE-SE difference has been variably reported to be a useful indicator of facial EMG activation or antinociception (Mathews et al 2007; Liu et al 2005; Hans et al 2006; Călin et al 2021).

We report our observation of large increases in both RE and SE to awake values under sevoflurane and rocuronium anesthesia, with complete return to deep anesthesia values with administration of an incremental rocuronium dose.

Case report

A 47-year-old female patient (ASA II) with acute lithiasis cholecystitis, type 2 diabetes and grade 2 obesity (Height=165 cm, Weight=98 kg, BMI=36 kg/m²) underwent a laparoscopic cholecystectomy procedure in our institution (SCJU ORADEA). Intraoperatory we measured the following variables, such as:

Table 1. General patient measurements consumption). A 47-year-old female patient (ASA II) with acute lithiasis cholecystitis, type 2 diabetes and grade 2 obesity (Height=165 cm, Weight=98 kg, BMI=36 kg/m²) underwent a laparoscopic cholecystectomy procedure in our institution.

Gender/Age (years)	BMI/ DM	HR before intubation	SBP(Systolic blood pressure) this is the abbreviation in Romanian language before intubation	Entropy RE/ SE before IOT	OR time (min)	Total Sevofluran (mL)	Total Rocuroniu (mg)	Total Fentanyl (mg)	Total Propofol (induction) (mg)
F/47	36/ DM	75	125 most ofetn BP is given as systolic over dyastolic or as mean.	98/91	95	30	90	0.6	200

Table 2. Entropy response to muscle relaxation with rocuronium

Time	Entropy RE/SE	TOF%	Hr(Bpm)	SBP(mmHg)	SpO_2	Sevoflurane%	Flow(L/min)	FiO_2	Rocuronium(mg)
Before IOT(3min)	98/91	100%	75	125	99%	2.2%	2l/min	50%	60 mg
15min	47/44	10%	80	92	100%	2.2%	2l/min	50%	-
30 min	50/48	20%	70	105	100%	2.2%	2l/min	50%	-
45 min	96/88	70%	75	122	100%	2.4%	2l/min	50%	20 mg
60 min	46/42	15%	77	113	100%	2.2%	2l/min	50%	-
75 min	90/80	65%	74	115	100%	2%	2l/min	50%	10 mg
95 min	47/45	10%	80	130	100%	1.5%	2l/min	50%	-
Before extubation	96/90	90%	85	140	99%	0	2l/min	50%	-

anesthetic duration (in minutes), change of heart rate baseline at 10 min, change of systolic blood pressure baseline at 15 minutes, total use of sevoflurane (mL), fentanyl (mg) rocuronium (mg) and propofol (induction) (mg) and a flow of fresh gases amounting to 2 L/min (50% oxygen and 50% air). (Table 1)

Anesthesia was induced with midazolam, fentanyl and propofol. Tracheal intubation was facilitated with rocuronium. Anesthesia was maintained with sevoflurane, fentanyl, rocuronium, with target end-tidal sevoflurane of 2.2%. Continuous ECG, plethysmography, non-invasive blood-pressure, end-tidal carbon dioxide and agent concentrations were monitored. Depth of anesthesia was monitored with an Entropy module General Electric Healthcare (GE) and muscle relaxation was monitored with a neuromuscular transmission (NMT module GE Health Care). During the procedure we noted a sudden large increase in RE and SE to awake values (96 and 88 respectively). There were no autonomic signs of inadequate depth of anesthesia or analgesia with heart rate and blood-pressure remaining stable. Pupils were small and central and no tears or sweating. The NMT monitor showed a train-of-four (TOF) count of four (TOF 70%). A dose of rocuronium was administered and both RE and SE values decreased immediately to <47. This exact scenario was repeated two times during the case. The patient reported no awareness postoperatively (Table 2).

While an increase in RE can be as a result of EMG interference, an increase in SE is universally considered to be because of an increase in level of consciousness. Certainly, a sudden increase in both SE and RE indicates an increase in consciousness towards the awake state until proved otherwise (Xing et al 2019; Oh et al 2019). Our case illustrates that this increase can in fact be because of EMG interference in the case of both the RE and SE parameters and titration of anesthetic agents should not be based solely using these indices. This observed artifact in the SE reading is probably because of the fact that EMG activity contains some frequencies below 32 Hz (Kawaguchi et al 2009; Aho et al 2011).

Discussions

The General Electric (GE) entropy module uses the unilateral self-adhesive fronto-temporal sensor, specifically made for the GE product. The module works only with GE monitoring systems with the appropriate software loaded. The SE, RE, and a single channel of the raw electroencephalogram are displayed on the same screen as the other monitored variables. The displayed state entropy range is 0 (isoelectric EEG) to 91 (fully awake), and the response entropy range is 0 to 100. The anaesthetic range is 40 to 60 (Newton et al 1992; Ellerkmann et al 2004; Călin et al 2021).

The GE Entropy™ Module is indicated for adult and pediatric patients older than 2 years within a hospital for monitoring the state of the brain by data acquisition of electroencephalograph (EEG) and frontal electromyograph (FEMG) signals. The spectral entropies, response entropy (RE) and state entropy (SE), are processed EEG and FEMG variables. In adult patients, response entropy and state entropy may be used as an aid in monitoring the effects of certain anaesthetic agents, which may help the user to titrate anaesthetic drugs according to the individual needs of adult patients. Furthermore, in adults the use of entropy parameters may be associated with a reduction of anaesthetic use and faster emergence from anaesthesia. The entropy measurement is to be used as an adjunct to other physiological parameters. Entropy is a measure of irregularity in a signal (EMG. EEG) (Vakkuri et al 2005; Klockars et al 2006; Călin et al 2021). With Entropy used together with other monitored parameters, such as the hemodynamic measurements and NMT, you can get a complete picture of the patient status combined on one screen. The presented case provides a perfect example of the limitations of devices that monitor the hypnotic component of anesthesia. One of the main sources of distortion in EEG records obtained via scalp electrodes is muscle activity recorded as EMG. Although, EMG and EEG seem to mainly interfere at frequencies corresponding to the EEG beta and gamma band, i.e., frequencies above 30 Hz, EMG influence on lower frequencies cannot be neglected. Hence, in case of the Entropy module, both indices

-SE and RE- will be influenced by EMG. In this case, muscle activity may have led to paradoxically increasing SE and RE values, since delivery of rocuronium resulted in decreasing indices. A similar phenomenon has also been described for the BIS monitor (Panousis et al 2007; Hans et al 2006; Călin et al 2021). Still, the clinical interpretation of this EMG influence requires caution. On BIS- monitoring, the EMG is displayed separately so information on EMG may be seen.. High index values have been previously judged to be "spurious", and BIS values from a signal containing EMG have been interpreted as an "overestimate" of index values (Baldesi et al 2004). It is important to mention that the use of muscle relaxants can also cause paradoxically low index values, as observed for the BIS monitor in a volunteer study (Schuller et al 2015; Călin et al 2021).

The SE and RE indices evaluate the shape of the filtered EEG amplitude spectrum. The SE/RE algorithm that is based on the Shannon entropy, produces higher index values for a more uniform shape of the spectrum, while a typical anesthesia EEG spectrum with pronounced low frequencies leads to low index values (Viertio-Oja et al 2004). The high cut-off frequencies are 32 Hz for SE and 47 Hz for RE. RE includes higher frequencies that may be more prone to influence by muscle activity, but also contain information from the EEG gamma band, that can be reflective of activation of cortical neurons during consciousness (Schneider et al 2014; Călin et al 2021).

Conclusion

We conclude that no decisions regarding the patient's hypnotic state should be solely based on indices calculated from EEG as available in monitoring devices. EEG-based parameters are not a substitute of standard monitoring parameters, but add useful information to these parameters. Consequently, a combination of EEG and standard parameters provide a better estimate of the level of anaesthesia than each of the components alone

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