Case Report

Entropy as an indicator of cerebral perfusion in patients with increased intracranial pressure

James Khan, Ramamani Mariappan, Lashmi Venkatraghavan

Department of Anesthesia and Pain, Toronto Western Hospital, University Health Network, University of Toronto, Toronto ON, Canada

Abstract

Changes in electroencephalogram (EEG) patterns correlate well with changes in cerebral perfusion pressure (CPP) and hence entropy and bispectral index values may also correlate with CPP. To highlight the potential application of entropy, an EEG-based anesthetic depth monitor, on indicating cerebral perfusion in patients with increased intracranial pressure (ICP), we report two cases of emergency neurosurgical procedure in patients with raised ICP where anesthesia was titrated to entropy values and the entropy values suddenly increased after cranial decompression, reflecting the increase in CPP. Maintaining systemic blood pressure in order to maintain the CPP is the anesthetic goal while managing patients with raised ICP. EEG-based anesthetic depth monitors may hold valuable information on guiding anesthetic management in patients with decreased CPP for better neurological outcome.

Key words: Cerebral perfusion pressure, electroencephaogram, increased intracranial pressure, response entropy, state entropy

Introduction

Patients with an acute increase in intracranial pressure (ICP) often present with a decreased level of consciousness secondary to reduced cerebral perfusion pressure (CPP). In these patients, CPP is maintained by increased systemic blood pressure as a result of Cushing's reflex. Hence, peri-operative management goals in these patients primarily focus on maintaining the systemic blood pressure (BP).

Entropy and bispectral index (BIS) are commonly used electroencephalographic (EEG) based depth of anesthesia monitors. It has been shown that changes in EEG patterns correlate well with changes in CPP[1,2] and hence entropy and BIS values may also correlate with CPP. Previous reports have shown that sudden decrease in cerebral perfusion was associated with lower BIS value.[3-6]

We report two cases where entropy values suddenly increased after cranial decompression in patients with elevated ICP. We obtained verbal and written consent from the patient's family.

Address for correspondence: Dr. Lashmi Venkatraghavan, Department of Anesthesia and Pain, Toronto Western Hospital, University of Toronto, 399 Bathurst Street, McL 2-405, Toronto, ON, M5T 2S8, Canada.
E-mail: lashmi.venkatraghavan@uhn.ca

Access this article online	
Quick Response Code:	Website: www.joacp.org
	DOI: 10.4103/0970-9185.137280

Case Reports

Patient 1

A 25-year-old male ASA I, weighing 70 kg, presented for left parietotemporal craniotomy and resection of temporal lobe tumor. He underwent a successful tumor resection and was admitted in the neuro-intensive care unit (NICU) post-operatively. On post-operative day 2, the patient's level of consciousness deteriorated and he became unresponsive (Glasgow coma scale [GCS] 5/15). Computed tomography showed a large intracranial hematoma in the left temporal lobe with the midline shift. Patient was intubated in NICU and positive pressure ventilation was instituted at a higher rate and then transferred to the operating room for emergency decompression and hematoma evacuation.

Endotracheal tube (ETT) was connected to the anesthetic machine (Aisys Care station (GE Health Care, Madison, WI. USA) ventilator and hyperventilated to keep end-tidal carbon dioxide ($EtCO_2$) at 30-33 mmHg. Entropy electrodes were attached on the forehead opposite to the side of surgical

incision and were connected to transducer and the module. His baseline entropy (response entropy (RE)/state entropy (SE) values were 37/33 without any sedation. Since his GCS and baseline entropy value were low, received only 100 mcg of fentanyl and 50 mg rocuronium. 2% xylocaine with adrenaline infiltration for head pin fixation followed by scalp flap infiltration with 0.5% bupivacaine + adrenaline (1 in 200,000) was done to reduce the pain thereby the anesthetic requirement. No other anesthetic agents were given for craniectomy because of the low entropy values. Entropy values remained low until the cranial decompression. Immediately following the removal of the bone flap, entropy value suddenly increased to (RE/SE) 94/83. Patient then received 50 mg bolus of propofol and sevoflurane was started. Entropy temporarily decreased to below (RE/SE) 40/40 but rebounded to 90/80 within 30 s. Sevoflurane concentration was then increased and additional doses of propofol were given. Entropy decreased to (RE/SE) 37/32 and remained low for the remainder of the procedure [Figure 1].

Following the procedure, patient was transferred to NICU. He was on mechanical ventilation for 8 days and transferred to rehabilitation center.

Patient 2

A 65-year-old female weighing 50 kg, presented to the emergency department with acute hydrocephalus secondary to subarachnoid hemorrhage (World federation of Neurologic Surgeon Grade 5, Fischer Grade 4). Her admission GCS was 5/15. Her past medical history included hypertension on oral anti-hypertensive medications. She was intubated and arterial line was started and shifted to the operating room for insertion of an external ventricular drain (EVD).

Upon arrival to the operating room, her initial blood pressure was 190/85 with heart rate of 90 beats/min. Initial entropy readings (RE/SE) were 56/50. Patient was connected to the ventilator and hyperventilated to achieve an $EtCO_2$ level of 30 mmHg. Patient received 25 mcg of fentanyl, 30 mg of rocuronium and a propofol infusion was started at 20-30 mcg/kg/min was started. Scalp infiltration was done with 2% xylocaine with adrenaline. Anesthesia was titrated to keep the entropy of 40-60. Blood pressure remained elevated and entropy readings were consistent during initial stages of surgical exposure.

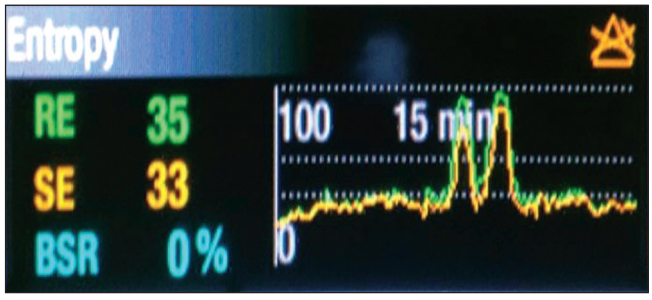

Figure 1: Entropy values during cranial decompression in patient 1 *BSR = Burst suppression ratio, RE = Response entropy, SE = State entropy

Immediately following the insertion of the EVD, both RE and SE values increased by 20 points (58-80 for RE and 51-72 for SE) and there was a mild reduction in blood pressure (205/99-176/80) [Table 1]. Propofol infusion rate was increased to 50 mcg/kg/min and this subsequently decreased the entropy values to 40-60. Post-operatively patient was transferred to NICU and then discharged to a rehabilitation center in her local town.

Discussion

Our cases suggest that entropy can be used as a surrogate marker for changes in CPP during cranial decompression in patients with increased ICP. Advances in anesthesia have led to the development of monitors such as entropy and BIS for assessing the depth of anesthesia. These monitors rely on the EEG information gathered from three electrodes from the patient's forehead.[7]

Entropy consists of two parameters: SE and RE. SE is computed over the frequency range from 0.8 to 32 Hz, which represents the EEG part of the frequency spectrum. Therefore, SE reflects the cortical state of the patient. RE is computed over the frequency range from 0.8 to 47 Hz, covering both the EEG and the EMG-dominant areas of the spectrum. Consequently, RE−SE difference serves at least partly as an indicator of upper facial EMG activation. RE−SE difference may increase transiently during strong nociceptive stimuli.[8]

It is well-known that EEG patterns correlate with cerebral blood flow (CBF).[1,2] When CBF decreases to 25-35 mL/100 g/min, EEG first loses its faster frequencies (8-14 Hz). With further

Table 1: Patients hemodynamics and entropy values during cranial decompression in patient 2

Time	Heart rate	Blood pressure	RE/SE
0:00	84	204/94	59/51
0:01	87	208/89	58/51
0:02	88	220/105	46/36
0:03	84	205/99	58/51
0:04	83	182/83	65/53 ↑ cranial decompression
0:05	80	176/80	80/72
0:06	79	168/81	75/66
0:07	79	160/78	71/65

**RE = Response entropy, SE = State entropy*

reductions in CBF (18-25 mL/100 g/min) EEG becomes increasingly slower (4-7 Hz). When the CBF reduces further to 12-18 mL/100 g/min and 10-12 mL/100 g/min, EEG becomes increasingly slower (1-4 Hz) to complete EEG suppression respectively, indicating hypoxic brain cell death.[1,2] The reduced irregularity and complexity of an EEG waveform in response to reduced CBF is analogous to increasing depth of anesthesia. Thus, theoretically, the effect from reduced CBF would cause a similar dose-dependent reduction in entropy values.

In our cases, entropy values were very low at the time of electrode placement with very little or no anesthetics given. This is possibly due to slow EEG activity due to decreased baseline CPP. After cranial decompression, ICP was relieved leading to a sudden increase in CPP. We believe that this increase in perfusion was reflected as an increase in entropy values.

In patients with acutely elevated ICP, minimal anesthetic agents are needed because of low GCS. Administration of un-titrated doses of anesthetic may lead to decrease in BP and further reduction of CPP. After cranial decompression, there is an increased cerebral perfusion, which can lead to an improved level of consciousness. Patients often need more anesthetics during this stage to produce amnesia. Hence, depth of anesthesia monitors may be helpful in these cases for a better peri-operative care and better titration of anesthetics. The absolute values from the depth of anesthesia monitors can provide information on the level of consciousness and the relative changes may provide valuable information about changes in cerebral perfusion.

Although entropy or BIS have not been validated for monitoring cerebral perfusion, previous case reports suggest their potential application. In a study by Morimoto *et al.*[3] describes a case where BIS values dropped to around 0-20 after the induction of general anesthesia. BIS levels improved with the management of blood pressure suggesting that lower BIS values were probably due to cerebral hypoperfusion. In another report, Welsby *et al.*[4] describes a case where a patient suffered an intra-operative cerebral embolus and BIS levels precipitously dropped from 50-60 to below 15-10, again reflecting the influence of decreased perfusion on EEG-based anesthetic monitors. There are other case reports describing decreased BIS levels in response to cerebral hypoperfusion secondary to ischemic brain injury.[6,7] In addition, there is a recent increase in interest in NICUs for the use of EEG-based monitors to detect ischemia or cerebral hypoperfusion.[2]

One of the limitations of our case report is the lack of quantitative measurement of CBF. Transcranial Doppler is often used to measure velocity and can give an indirect measure of CBF. Unfortunately, the urgency of these cases and the lack of access to middle cerebral artery during the case limited its use before and during cranial decompression. Furthermore, another important cause for increased intra-operative entropy values in acute neurosurgical conditions is seizure activity. Seizures cause an increase in EEG and EMG activity and thus increase entropy values. In addition, administration of propofol and sevoflurane could have abolished the seizure activity, causing the decrease in the entropy values. Though this is a possibility in our cases but it is highly unlikely given the temporal association with cranial decompression and the accompanying decrease in BP. (i.e., restoration of cerebral perfusion). Furthermore, there were no other hemodynamic changes (e.g., tachycardia, rise in $EtCO_2$) indicating possible seizure activity.

Conclusion

EEG-based anesthetic monitors may not only provide information on level of anesthesia but may have a pivotal role into guiding anesthetic management in patients with decreased CPP. Further investigations are needed to assess the utility of these EEG-based monitors as an indicator for detecting changes in cerebral perfusion.

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How to cite this article: Khan J, Mariappan R, Venkatraghavan L. Entropy as an indicator of cerebral perfusion in patients with increased intracranial pressure. J Anaesthesiol Clin Pharmacol 2014;30:409-11.
Source of Support: Nil, **Conflict of Interest:** None declared.