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CASE REPORT

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Use of inhaled sevoflurane to treat post-operative intractable cerebral edema in neurosurgical intensive care unit

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ABSTRACT:

Background: Burst suppression are widely used in case of refractory increased intracranial pressure for deep state of brain inactivation. Inhaled sevoflurane via the anesthetic conserving device could be useful for the sedation of patients in the intensive care unit (ICU), but prospective studies have been small study.

Case report: A 53-year-old male patient with confusion, not follow to command and status epilepticus had been hospitalized and diagnosed glioblastoma multiforme at left temporal lobe. By the time initial therapy had begun with dexamethasone and anti-epileptic drug, the symptoms had improved. The patient was performed craniotomy with tumor removal during intra-operative found intractable cerebral edema and changed operation to decompressive craniectomy, in post-operative period after increased dosage of propofol and midazolam to control intracranial pressure, patient developed hypotension, then norepinephrine was titrated to maintain mean arterial pressure more than 65 mmHg and used inhaled sevoflurane to decrease dose propofol for maintain hemodynamics then during 5 day usage inhaled sevoflurane, norepinephrine could wean off and Glasgow coma scale was improve. Follow up brain EEG at 1st week showed no epileptiform discharge, antiepileptic drug could de-escalated and CT scan showed no refractory cerebral edema or hemorrhage. Ventilator was weaned off and the patient was transfer to step down ward.

Conclusion: When managing intractable cerebral edema patient with inhaled sevoflurane showed that lower opioid dose intensity, promote resolving from seizures or status epilepticus, decrease dose of vasopressor to maintain hemodynamics and no adverse events supported the use of inhaled sevoflurane via the anesthetic conserving device in this patient who have clinical need for burst suppression.

Keywords: Intractable cerebral edema, Decompressive craniectomy, Barbiturates coma, Inhaled sevoflurane, Anesthetic conserving device

INTRODUCTION

Burst suppression are widely used to suppress cerebral metabolic rate in case of refractory increase intracranial pressure. Potential mechanism of action has been mainly attributed to suppression of cerebral oxygen metabolism up to 40% to 50%. [1-4] However, high doses cause prolong hypotension, cardiovascular instability, and delayed neurological examination in the postoperative period.[5,6] Recently, the bispectral index (BIS) monitor, a processed EEG, has emerged as an alternative to standard EEG to document the cerebral effect of CMR-reducing effects. [7-8]
Sevoflurane, similar to barbiturate, produces a dose-dependent decrease in cerebral metabolism to end point of EEG show burst suppression. Inducing EEG isoelectricity by increasing the inhaled concentration of sevoflurane beyond 2.0 to 2.5 minimum alveolar concentration for cerebral protection in refractory intracranial hypertension.[9] .In this case report, we assessed EEG burst suppression measured with BIS monitor score 0-10 and RASS measurements range –1 to –4 as an alternative to standard EEG because in this case report, we could not perform continuous EEG.

Inhalational conserving systems have been used for sedation in the Neurocritical Care Unit.[10-12] Sevoflurane had shown some benefits compared with intravenous sedation. This give better hemodynamic stability
and expired end-tidal concentration provides the real time method that can monitor cerebral concentration, which aids dose titration and minimizes risk of drug overdosing. [13]

This is a case report of a single patient admitted to the neurosurgical ICU who had post-operative refractory intracranial hypertension and status epilepticus, and were treated by inhaled sevoflurane combination with propofol and midazolam aimed to induced burst-suppression on bispectral index monitor.

Case presentation

A 53-year-old man diagnosis glioblastoma multiforme at left temporal lobe presented with confusion, not follow to command 4 day ago after admission he developed status epilepticus and computer tomography (CT) brain and MRI brain showed intra-axial mass at left parieto-temporal lobe and left basal ganglion with cortex-sparing with vasogenic edema involved left internal capsule (anterior, posterior limb and genu) and left superior cerebral peduncle with sulcal effacement of left cerebral hemisphere, left lateral ventricular effacement, left sided midbrain displacement, rightward midline shift (1.3 cm) and left subfalcine and left uncal herniation likely progressive disease. He was planned to performed craniotomy with tumor removal during intra-operative found intractable cerebral edema and decompressive craniectomy and 20% mannitol administration were done then post-operative he developed status epilepticus. He was admitted in the neuro-ICU after procedure for post-operative care and intracranial hypertension management with 30 degree head elevation, intravenous fentanyl, 2% propofol, cis-atracurium and midazolam administration according to table 1. concomitant treatments for brain edema and status epilepticus that the patient received after increased dosage of propofol and midazolam, this patient was hypotension so we give norepinephrine titration to maintain mean arterial pressure more than 65 mmHg and give sevoflurane administration (Fig. 1) to decrease dose of propofol for maintain hemodynamics.

KEY MESSAGES:

- Larger doses of intravenous burst suppression associated with cardiovascular instability. Inhale sevoflurane has shown benefits and autoregulation remained intact at MAC 1.0.

Informed consent was obtained from either the patient himself or his family. Patient admitted in Neurosurgical department and neurosurgical Intensive Care Unit, Phramongkutklao Hospital. The primary endpoint was efficacy of strategy defined as opioid dose sparing effects and time to improve GCS. Secondary endpoints were opioid requirements, spontaneous breathing, time to control status epilepticus, time to wake-up and extubation, percentage of time in Bispectral index (BIS) range 0 to 10, RASS measurements range –1 to –4, and no major adverse effects of violations and adverse events.

Figure 1. Example of anesthetic conserving device used in the neurosurgical intensive care unit

Figure 2. Monitor bispectral index (BIS) after anesthetic conserving device in the neurosurgical intensive care unit.

Ethics approval and consent to participate

Institutional Review Board Royal Thai Army Medical Department Ethics Committee approved this study research no.S069h/64 followed Council for International Organization of Medical Science (CIOMS) Guidelines 2012 and Good Clinical Practice of International Conference on Harmonization statement no.IRBRTA 1818/2564 and informed consent was done before the operation and patient was full consciousness and from either the patient himself or his family and patient decided by himself (informed consent was done after dexamethasone administration and his confusion improved at first admission about surgical planning and medication for refractory intracranial hypertension management).

Post-operative intractable cerebral edema and status epilepticus was successfully treated using prolonged inhaled sevoflurane sedation for 5 days in the ICU by repeated EEG showed no epileptiform discharge and follow up CT scan show no progression of cerebral edema and during the 5 day, surgical flap from decompressive craniectomy showed no tension or wound dehiscence. Follow up CT Brain showed no intra-cerebral hemorrhage, we concluded that inhaled sevoflurane sedation can be used in refractory intracranial hypertension. After 5 day of inhaled sevoflurane sedation norepinephrine could wean off and when stop inhaled sevoflurane sedation Glasgow coma scale was improve to E3VtM5 pupil 3 mm in diameter react to light both eyes. Follow up brain EEG at 1st week showed no epileptiform discharge, antiepileptic drug could de-escalated and CT brain non-contrast showed no complication or refractory cerebral edema. Ventilator was weaned off and the patient was transfer to step down ward.

RESULTS

Opioid and propofol dose intensity was 30% lower than before apply the device for the overall burst suppression period according to table 1. concomitant treatments for brain edema and status epilepticus that the patient received and spontaneous breathing occurred after disconnect the device 1 hour on day 6. Times to improve of Glasgow coma scale were short and wake-up after disconnect the device on day 8. No common adverse events such as prolong hypotension, delirium, oliguria and atrial fibrillation and inhaled sevoflurane via the anesthetic conserving device provides safe due to this patient could maintain stable hemodynamics,

Table 1. Concomitant treatments for brain edema and status epilepticus that the patient received and BIS during 120 hours showed 5-10 and RASS range -1 to -4.

Day/Drug (dosage)	Sevoflurane (MAC) average/ max dose(MAC)	Propofol (mg/kg/min) average/max dose	Midazolam (mg/hr)	Fentanyl (µg/hr)	Cisatracurium (mg/hr)	Norepinephrine (µg/kg/min)
Immediate post operative – 8 hr	-	0.15/0.2	14	120	10	1.1
1	0.8/1	0.12/0.17	10	120	10	0.7
2	0.9/1	0.1/0.15	10	100	10	0.53
3	0.9/1	0.07/0.13	10	100	10	0.36
4	0.9/1	0.05/0.12	8	80	8	0.22
5	1/1	0.03/0.12	5	80	8	0.15
6	-	0.01/0.05	-	50	-	0.07
7	-	-	-	50	-	0.04
8	-	-.	-	30	-	0.02
9	-	-	-	30	-	0.013

Value present as average dose/max dose.

decreased dose of intravenous sedation such as propofol or midazolam that cause worse hemodynamics and good quality sedation to this patients due to maintain stable bispectral index (BIS) 0-10. Long-term inhaled sevoflurane sedation in this case 120 hours was associated with no delirium. After 5 days of inhaled sevoflurane sedation, norepinephrine could wean off .

DISCUSSION

Sevoflurane inhalation showed safe and good quality sedation. Long-term inhaled sevoflurane sedation more than 120 hours would be associated to less vasopressor dosage. Purrucker et al. also used sevoflurane sedation via the AnaCoDa in 25 patients with acute stroke or subarachnoid hemorrhage, showed that sevoflurane led to sufficient sedation, but decreased MAP and CPP in a selected cerebrovascular neurocritical care population and about a third of these patients had severe adverse reactions including intolerable ICP increases but in this case report, we performed decompressive craniectomy and avoid hypoventilation by adjusted ventilator and end-tidal CO_2 monitoring and used NIRS monitoring intracranial hypertension as alternative modality combined with scalp flap tension and follow up CT brain that showed no progression of cerebral edema and hemorrhagic transformation. For Advantages and Disadvantages in inhaled sevoflurane sedation discussed in table 2.

Our experience mainly concerned intractable cerebral edema and we monitored end-tidal CO_2 to avoid hypoventilation and this patients was underwent decompressive craniectomy and manage intracranial hypertension as 3rd tier and used of near-infrared spectroscopy alternative to intracranial pressure monitoring. ACD enables the delivery of volatile agents by any standard ICU ventilator [14] and inhaled sedation using volatile agents such as sevoflurane can be used in brain lesion intensive care patients, provided a full multimodal neuro-monitoring is required[15].

For cerebral injury, cerebral vasodilation may lead to increased ICP, but at the same time volatile anesthetics are known to stabilise the endothelial barrier. There was experiment demonstrates that low-dose short-term sevoflurane sedation did not affect ICP and MAP and attenuate early brain edema formation, potentially by preserving adherens junctions. The inflammatory cascade is initiated, which leads to further brain damage[16]. In addition, endothelial cell injury leading to blood–brain barrier dysfunction is an important component of the reactive inflammation[17]. Reducing early brain injury is still the main emphasis of intracranial hypertension therapies. The reduction of brain edema, an independent predictor for unfavourable outcome. Tight and adherens junction proteins, such as zonula occludens protein-1 (ZO-1) and beta-catenin (β-catenin) are key components of blood–brain barrier function. Following neurosurgical procedure, junction proteins are affected, which leads to increased permeability of the blood–brain barrier. Disruption may be protected by volatile anesthetics. which results in a lower brain water content [18]. Sevoflurane is known to either dilate large vessels or constrict arterioles, but impact on ICP are contradictory. ICP was increased at concentration 1MAC in one study [19]. Whereas ICP was reported to remain unaffected between 0.7 and 1.3 MAC [20] and between 0.5 and 1.5 MAC [21]. We were interested in not only safety aspects, in particular ICP and MAP, but also exploring potential protective effects on the blood–brain barrier. Use of sevoflurane as a sedative would not further increase ICP, protective effect resulting from stabilization of the blood–brain barrier may be feasible and provides hemodynamic stability. The decrease in brain water might be because of a sevoflurane-induced membrane stability [22] and enhancement of the inhibition of neurotransmitter-controlled ion channels, such as gamma-amino butyric acid, glycine, and glutamate in the central nervous system, is discussed as a possible antiseizure effect [23-27] and association with reductions in cerebral oxygen extraction and without increases ICP. However, the observation of substantial MAP/CPP reductions and other adverse effects are concerning and warrant caution in this off-label treatment.

Table 2. Advantages and Disadvantages in inhaled sevoflurane sedation [12]

Advantages	Disadvantages
Rapid onset	Increased dead space
Short times to extubation and wake up	Reflection of CO_2
Stable in maintain quality of awakening /Agitation score (RASS) to -1 to -4	Need of a scavenging system
Analgesic effect and Pain Score monitoring with sympathetics response	
Effective bronchodilator	
Hepatic and renal safety due to clearance with respiratory system	
Short times to resolved in status epilepticus and antiepileptics drug de-escalation	
Good choice for burst suppression to management in intracranial hypertension but carefully in ventilation management and used in 3rd tier after decompressive craniectomy	
Adjunct in case of hemodynamic unstable due to heavy intravenous sedation such as propofol or midazolam	
Lower agitation and improved pain control	
Reduced post-operative delirium	
Good choice for postoperative sedation after neurosurgery procedure but carefully in ventilation management	

CONCLUSION

Lower opioid dose intensity, promote resolving from seizures or status epilepticus, decreased dose of vasopressor to maintain hemodynamics and no adverse events supported use of inhaled sevoflurane.

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AUTHORS' CONTRIBUTIONS

(I) Conceptualization: P. Boontoterm, Kiangkitiwan, Feungfoo. (II) Data curation: P. Boontoterm, Sakoolnamarka. (III) Formal analysis: P. Boontoterm, Sakoolnamarka, Feungfoo. (IV) Funding acquisition: Feungfoo.Methodology: P. Boontoterm, Sakoolnamarka, Feungfoo. (V) Project administration: P. Boontoterm, Feungfoo. (VI) Visualization: P. Boontoterm, Sakoolnamarka. (VII) Writing - original draft: P. Boontoterm, Sakoolnamarka. (VIII) Writing – review & editing: P. Boontoterm, Sakoolnamarka, Feungfoo.

SUPPLEMENTARY MATERIALS

none

ABBREVIATIONS

ACD, Anesthetic conserving device; AF, Atrial fibrillation; BBB, blood–brain barrier; BIS, Bispectral index; BMI, Body mass index, BP, Blood pressure; CIOMS, Council for International Organization of Medical Science; cm, centimeter; CMR, Cerebral metabolic rate; CPP, Cerebral perfusion pressure; CT, Computer Tomography; DC, Decompressive craniectomy; ECG, Electrocardiogram; EEG, Electroencephalography; GCS, Glasgow Coma Scale; IRBRTA, Institutional Review Board Royal Thai Army; ICP, Intracranial pressure; ICU, Intensive care unit; IV, Intravenous; kg, Kilogram; MAC, minimum alveolar concentration; MAP, mean arterial pressure; mg, miligram; MRI, Magnetic resonance imaging; mmHg, millimeters of mercury; NIRS, Near-infrared spectroscopy; $PaCO_2$, Partial pressure of carbondioxide; RASS, Richmond Agitation and Sedation Scale; SpO_2, Peripheral O2 saturation; ZO-1, zonula occludens protein-1; µg, microgram

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