Thai J Neurol Surg 2023;1(1):12-20.

Research Article

Burst Suppression by Using Combined Inhaled Sevoflurane and Propofol in Postoperative Period in Patient with Refractory Intracranial Hypertension: A Case Report

Panu Boontoterm, MD[1]

[1]*Department of Neurosurgery, Phramongkutklao Hospital*

Abstract

Background: Barbiturate coma are widely used in postoperative period in patient with refractory intracranial hypertension 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, but few evidence support to this procedure.

Main Content: A 53-year-old man had glioblastoma multiforme at left temporal lobe presented with confusion 4 days ago and developed epilepsy. He was planned to performed craniotomy with tumor removal during Intra-operative found intractable cerebral edema then his clinical progressed to uncontrolled intracranial hypertension and refractory status epilepticus. inhaled sevoflurane administration was performed to decrease dose of propofol for maintain hemodynamics. Intractable cerebral edema and status epilepticus was successfully treated in this patients.

Conclusion: The use of inhaled sevoflurane reduced opioid dose intensity , promote resolving from status epilepticus, decrease dose of vasopressor to maintain hemodynamics and no adverse events.

Keywords: refractory intracranial hypertension, barbiturates coma, inhaled sevoflurane, anesthetic conserving device

บทคัดย่อ

กรณีศึกษารายงานผู้ป่วย การหยุดกระบวนการเมแทบอลิซึมของสมองโดยใช้ยาซีโวฟลูเรนผ่านทางระบบการหายใจร่วมกับการให้ยาโปรโพฟอลในผู้ป่วยหลังผ่าตัดสมองที่มีภาวะความดันในกะโหลกศีรษะสูงที่ไม่สามารถควบคุมได้

ภาณุ บุญต่อเติม พ.บ.,ว.ว.ประสาทศัลยศาสตร์, ว.ว.เวชบำบัดวิกฤต
หน่วยศัลยกรรมประสาท กองศัลยกรรม โรงพยาบาลพระมงกุฎเกล้า

ที่มาและความสำคัญ: การหยุดกระบวนการเมแทบอลิซึมของสมองมีการใช้อย่างแพร่หลายในกรณีที่มีภาวะความดันในกะโหลกศีรษะสูงที่ไม่สามารถควบคุมได้ มีการใช้ยาซีโวฟลูเรนผ่านทางระบบการหายใจเพื่อช่วยให้ผู้ป่วยในหอผู้ป่วยวิกฤติอยู่ในภาวะสงบแต่มีการศึกษาแบบไปข้างหน้าสำหรับการใช้ค่อนข้างน้อย

กรณีศึกษา: ผู้ป่วยชายอายุ 53 ปีได้รับการวินิจฉัยเป็น glioblastoma multiforme ที่สมองส่วน temporal lobe ด้านซ้ายมาด้วยอาการสับสน 4 วันก่อนมาโรงพยาบาลและมีภาวะชักต่อเนื่องผู้ป่วยได้รับการผ่าตัดเปิดกะโหลกเพื่อเอาเนื้องอกในสมองออกในระหว่างการผ่าตัดพบภาวะความดันในกะโหลกศีรษะสูงที่ควบคุมไม่ได้และหลังผ่าตัดเกิดภาวะชักต่อเนื่อง เมื่อปรับขนาดยาลดความดันในกะโหลกศีรษะและยาควบคุมอาการชักพบว่ามีระดับการไหลเวียนโลหิตต่ำจึงได้นำยาซีโวฟลูเรนผ่านทางระบบการหายใจเพื่อช่วยควบคุมอาการชักและลดภาวะความดันในกะโหลกศีรษะสูงในผู้ป่วยรายนี้ได้อย่างประสบผลสำเร็จ

สรุป: การใช้ยาซีโวฟลูเรนผ่านทางระบบการหายใจช่วยลดขนาดของยากลุ่มโอปิออยด์ ช่วยให้ภาวะชักต่อเนื่องดีขึ้น ลดขนาดของยาเพื่อเพิ่มความดันเลือด และมีระบบการไหลเวียนโลหิตที่คงที่ และ เมื่อใช้ในขนาดที่เหมาะสมไม่พบเหตุการณ์ไม่พึงประสงจากการใช้ยา ในผู้ป่วยที่ทำการศึกษา

คำสำคัญ: ภาวะความดันในกะโหลกศีรษะสูงที่ไม่สามารถควบคุมได้, การหยุดกระบวนการเมแทบอลิซึมของสมอง, การใช้ยาซีโวฟลูเรนผ่านทางระบบการหายใจ

Introduction

Barbiturate coma are widely used to suppress cerebral metabolic rate in case of post operative refractory intracranial hypertension. Potential mechanism of action has been mainly attributed to suppression of cerebral metabolic rate (CMR) of oxygen 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. Sevoflurane induces isoelectricity by increasing the inhaled concentration of sevoflurane beyond 2.0 to 2.5 minimum alveolar concentration for cerebral protection in refractory intracranial hypertension9 .In this case report, we assessed EEG burst suppression measured with BIS monitor score 0-10 as an alternative to standard EEG. We did not performed multichannel EEG due to marked scalp flap swelling.

Inhalation anesthetic agents have sometimes used for sedation in the Neurosurgical critical Care Unit[10-12]. Sevoflurane had shown some benefits compared with intravenous sedation. It provides 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 was presented with confusion, not followed 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 remove. Intra-operative period was found intractable intraoperative brain swelling then 20% mannitol administration and repeated dose and decompressive craniectomy were done then post-operative he developed status epilepticus. He was admitted in the neurosurgical ICU after procedure for post-operative care and intracranial hypertension management with 30 degree head elevation, intravenous fentanyl, 2% propofol, cisatracurium 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 (Figure 1) to decrease dose of propofol for maintain hemodynamics. Informed consent was obtained from both patient himself or his family. Patient admitted in Neurosurgical department and neurosurgical Intensive Care Unit,

Phramongkutklao Hospital. The primary endpoint was efficacy of sevoflurane defined as opioid dose sparing effects and time to improve GCS. Secondary endpoints were spontaneous breathing, time to control status epilepticus, time to wake-up and extubation, percentage of time in Bispectral index (BIS) range 0 to 10 and no major violations and adeverse events. Ethics approval and consent to participate by 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

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

Figure 1 Example of Anesthetic Conserving Device used in the respiratory circuit of mechanical ventilation.

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.

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.

Result

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 inhaled sevoflurane via the anesthetic conserving device provides safe due to this patient could maintain stable hemodynamics, 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. Previous studies10 showed that used sevoflurane sedation in 25 patients with acute stroke or subarachnoid hemorrhage, showed that sevoflurane led to sufficient sedation, but decreased mean arterial pressure (MAP) and cerebral perfusion pressure (CPP) in a selected cerebrovascular neuro-critical care population and

about a third of these patients had severe adverse reactions including intolerable intracranial pressure (ICP) increases but in this case report, we performed decompressive craniectomy and avoid hypoventilation by adjusted ventilator and end-tidal CO2 monitoring and used NIRS monitoring region frontal cerebral blood flow 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. For cerebral injury, cerebral vasodilation may lead to increased ICP, but at the same time volatile anesthetics are known to stabilize the endothelial barrier. There was experiment[16] 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[14-16]. 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 (beta-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

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	

Figure 2 Monitor bispectral index (BIS) after Anesthetic Conserving Device in the neurosurgical intensive care unit.

by volatile anesthetics. which results in a lower brain water content[18]. Sevoflurane is known to dilate large vessels and 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 anti-seizure 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.

Limitation

The case report had some limitations. First, we did not performed intracranial pressure monitoring due to unplannable intraoperative uncontrolled cerebral edema and hemodynamic unstable so we could not titrate sevoflurane and propofol according to ICP parameter. Finally, we did not performed full multimodal neuro-monitoring such as autoregulation monitoring by pressure reactivity index to find optimum mean arterial pressure.

Future direction

Our experience mainly concerned intractable cerebral edema. Used of near-infrared spectroscopy alternative to autoregulation monitoring as cerebral oximetry index.

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.

Conflict of interests

No potential conflict of interest relevant to this article was reported.

References

1. McDermott MW, Durity FA, Borozny M. Temporary vessel occlusion and barbiturate protection in cerebral aneurysm surgery. Neurosurgery 1989;25:54–61.
2. Shapiro HM. Barbiturates in brain ischaemia. Br J Anaesth 1985;57:82–95.
3. Spetzler RF, Hadley MN. Protection against cerebral ischemia: the role of barbiturates. Cerebrovasc Brain Metab Rev 1989;1:212–29.
4. Drummond JC, Patel PM. Neurosurgical anesthesia. In: Miller RA, Eriksson LI, Fleisher LA, et al, eds. Miller's Anesthesia Philadelphia: Elsevier; 2009:2045–87.
5. Bendo AA, Kass IS, Hartung J. Anesthesia for neurosurgery. In: Barash PG, Cullen BF, Stoelting RK, eds. Clinical Anesthesia Philadelphia: LWW; 2006:746–89.
6. Winer JW, Rosenwasser RH, Jimenez F. Electroencephalographic activity and serum and cerebrospinal fluid pentobarbital levels in determining the therapeutic end point during barbiturate coma. Neurosurgery 1991;29:739–41.
7. Riker RR, Fraser GL, Wilkins ML. Comparing the bispectral index and suppression ratio with burst suppression of the electroencephalogram during pentobarbital infusions in adult intensive care patients. Pharmacotherapy 2003;23:1087–93.
8. Eveson L, Vizcaychipi M, Patil S. Role of bispectral index monitoring and burst suppression in prognostication following out-of-hospital cardiac arrest: a systematic review protocol. Syst Rev. 2017 Sep 25;6(1):191.
9. Niu B, Xiao JY, Fang Y. Sevoflurane-induced isoelectric EEG and burst suppression: differential and antagonistic effect of added nitrous oxide. Anaesthesia 2017;72(5):570–9.
10. Purrucker JC, Renzland J, Uhlmann L, Bruckner T, Hacke W, Steiner T. Volatile sedation with sevoflurane in intensive care patients with acute stroke or subarachnoid haemorrhage using AnaConDa®: An observational study. Br J Anaesth 2015;114:934–43.
11. Misra S, Koshy T. A review of the practice of sedation with inhalational anaesthetics in the intensive care unit with the AnaConDa(®) device. Indian J Anaesth 2012;56:518–23.
12. Meiser A, Laubenthal H. Inhalational anaesthetics in the ICU: Theory and practice of inhalational sedation in the ICU, economics, risk–benefit. Best Pract Res Clin Anaesthesiol 2005;19:523–38.
13. Bösel J, Purrucker JC, Nowak F, Renzland J, Schiller P, Pérez EB, et al. Volatile isoflurane sedation in cerebrovascular intensive care patients using AnaConDa(®): Effects on cerebral oxygenation, circulation, and pressure. Intensive Care Med 2012;38:1955–64.
14. Soukup J, Scharff K, Kubosch K, Pohl C, Bomplitz M, Kompardt J.State of the art: sedation concepts with volatile anesthetics in critically Ill patients. J Crit Care 2009;24:535–44.
15. Ruszkai Z., Bokrétas G.P. and Bartha P.T. 2014. Sevoflurane therapy for life-threatening acute severe asthma : a case report. Can. J. Anesth 61: 943–50.
16. Beck-Schimmer B, Restin T, Muroi C, Roth Z'Graggen B, Keller E, Schläpfer M. Sevoflurane sedation attenuates early cerebral oedema formation through stabilisation of the adherens junction protein beta catenin in a model of subarachnoid haemorrhage: A randomised animal study. Eur J Anaesthesiol 2020 May;37(5):402–12.
17. Suzuki H, Fujimoto M, Kawakita F. Tenascin-C in brain injuries and edema after subarachnoid hemorrhage: findings from basic and clinical studies. J Neurosci Res 2018; 98:42–56.
18. Altay O, Suzuki H, Hasegawa Y, et al. Isoflurane attenuates blood–brain barrier disruption in ipsilateral hemisphere after subarachnoid hemorrhage in mice.

Stroke 2012; 43:2513–6.

19. Petersen KD, Landsfeldt U, Cold GE, et al. Intracranial pressure and cerebral hemodynamic in patients with cerebral tumors: a randomized prospective study of patients subjected to craniotomy in propofol–fentanyl, isoflurane–fentanyl, or sevoflurane–fentanyl anesthesia. Anesthesiology 2003; 98:329–36.
20. Bundgaard H, von Oettingen G, Larsen KM, et al. Effects of sevoflurane on intracranial pressure, cerebral blood flow and cerebral metabolism. A doseresponse study in patients subjected to craniotomy for cerebral tumours. Acta Anaesthesiol Scand 1998; 42:621–7.
21. Artru AA, Lam AM, Johnson JO, et al. Intracranial pressure, middle cerebral artery flow velocity, and plasma inorganic fluoride concentrations in neurosurgical patients receiving sevoflurane or isoflurane. Anesth Analg 1997; 85:587–92.
22. Bedirli N, Bagriacik EU, Yilmaz G, et al. Sevoflurane exerts brain-protective effects against sepsis-associated encephalopathy and memory impairment through caspase 3/9 and Bax/Bcl signaling pathway in a rat model of sepsis. Journal of International Medical Research. July 2018:2828-42.
23. Stetefeld HR, Schaal A, Scheibe F, Nichtweiß J, Lehmann F, Müller M, Gerner ST, Huttner HB, Luger S, Fuhrer H, Bösel J, Schönenberger S, Dimitriadis K, Neumann B, Fuchs K, Fink GR, Malter MP; IGNITE Study Group, with support from the German Neurocritical Care Society (DGNI). Isoflurane in (Super-) Refractory Status Epilepticus: A Multicenter Evaluation. Neurocrit Care 2021 Dec;35(3):631-9.
24. Madžar D, Reindl C, Giede-Jeppe A, et al. Impact of timing of continuous intravenous anesthetic drug treatment on outcome in refractory status epilepticus. Crit Care 2018;22(1):317.
25. Caronna E, Vilaseca A, Maria Gràcia Gozalo R, et al. Long-term prognosis related to deep sedation in refractory status epilepticus. Acta Neurol Scand 2020;142(6):555–62.
26. Li H, Lang XE. Protein kinase C signaling pathway involvement in cardioprotection during isoflurane pretreatment. Mol Med Rep. 2015;11:2683–8.
27. Bösel J, Purrucker JC, Nowak F, Renzland J, Schiller P, Pérez EB, Poli S, Brunn B, Hacke W, Steiner T. Volatile isoflurane sedation in cerebrovascular intensive care patients using AnaConDa(®): effects on cerebral oxygenation, circulation, and pressure. Intensive Care Med 2012 Dec;38(12):1955-64.