Case Reports/Case Series

Case report: Alterations in bispectral index following absolute alcohol embolization in a patient with intracranial arteriovenous malformation

[Modification de l'index bispectral suite à une embolisation avec alcool absolu chez un patient souffrant de malformation artérioveineuse intracrânienne]

Koniparambil P. Unnikrishnan MD, Prabhat Kumar Sinha MD, Kamath Sriganesh MD DM, Puthuvassery R. Suneel MD

Purpose: We report a case of bispectral index (BIS) falling to zero during absolute alcohol embolization of an intracranial arteriovenous malformation (AVM) under anesthesia. This case highlights the unusual effect of a therapeutic dose of parenteral alcohol on the central nervous system using BIS monitoring.

Clinical features: A 29-yr-old male with a left parieto-occipital arteriovenous malformation underwent neuroendovascular embolization under general anesthesia. During injection of absolute alcohol injection into the AVM nidus, the patient developed hypertension and tachycardia coincident with a profound and sustained reduction of BIS values to zero, despite a stable level of anesthesia. Immediate angiography revealed no evidence of hemorrhage or new changes in the patient's cerebral vasculature. Post-procedure, the patient remained drowsy for several hours with signs of alcohol intoxication. He had full neurological recovery.

Conclusions: In the presence of normal cerebral angiographic findings, suppression of BIS values may serve as an early indicator of CNS responses to intracranial injection of absolute alcohol for embolization of an arteriovenous malformation.

CAN J ANESTH 2007 / 54: 11 / pp 908–911

Objectif *: Nous rapportons un cas d'index bispectral (BIS) tombant à zéro durant l'embolisation avec alcool absolu d'une malformation artérioveineuse intracrânienne (AVM) sous anesthésie. Ce cas souligne l'effet inhabituel d'une dose thérapeutique d'alcool parentéral sur le système nerveux central à l'aide d'un monitorage par BIS.*

Eléments cliniques *: Un homme de 29 ans avec une malformation artérioveineuse pariéto-occipitale gauche a subi une embolisation neuro-endovasculaire sous anesthésie générale. Durant l'injection d'alcool absolu dans le nid AVM, le patient a développé de l'hypertension et de la tachycardie, coïncidant avec une réduction profonde et soutenue des valeurs BIS jusqu'à zéro, malgré un niveau d'anesthésie stable. Une angiographie immédiate n'a révélé aucun signe d'hémorragie ou de nouveaux changements dans le système vasculaire cérébral du patient. Après l'intervention, le patient est demeuré somnolent durant plusieurs heures et montrait des signes d'ivresse alcoolique. Il a eu une récupération complète sur le plan neurologique.*

Conclusion *: En présence de résultats angiographiques cérébraux normaux, la suppression des valeurs BIS peut servir d'indicateur précoce des réactions du système nerveux central à une injection intracrânienne d'alcool absolu à des fins d'embolisation d'une malformation artérioveineuse.*

From the Department of Anaesthesiology, Sree Chitra Tirunal Institute for Medical Sciences & Technology, Trivandrum, Kerala, India.
Address correspondence to: Dr. K. P. Unnikrishnan, Department of Anaesthesiology, Sree Chitra Tirunal Institute for Medical Sciences & Technology, Trivandrum-695011, Kerala, India. E-mail: unnikp@sctimst.ac.in
Accepted for publication May 3, 2007.
Revision accepted August 16, 2007.

INTRACRANIAL arteriovenous malformations (AVMs) are relatively uncommon but increasingly recognized lesions that can cause serious neurological events including intracranial hemorrhage, seizure, or neurological deficits. Multiple surgical and interventional radiological procedures have been used to treat AVMs with varying degrees of success. Cerebral embolotherapy is one of the established techniques in the treatment of AVMs, which often necessitates the use of general anesthesia.[1] It is reported that embolization using absolute alcohol rapidly obliterates and shrinks the arteriovenous malformation providing better long-term success than with other sclerosants.[2] The bispectral index (BIS) monitor may serve a special role for cerebral embolization performed under general anesthesia. It is well known that apart from anesthetic agents, that BIS can be affected by factors including temperature changes or cerebral insults. We report an unusual case of an intracranial AVM embolization procedure wherein BIS values of zero were observed during absolute alcohol embolization under general anesthesia. Consent for publication of this report was obtained from the patient's family, in accordance with the patient health information guidelines of the Sree Chitra Tirunal Institute for Medical Sciences & Technology.

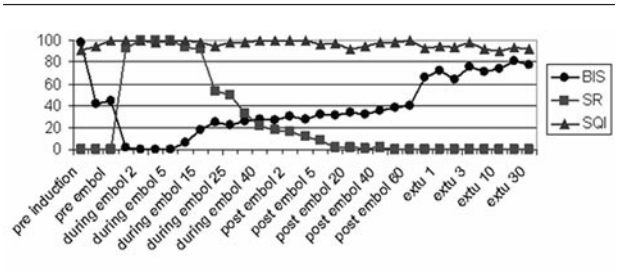

FIGURE Trends of bispectral index (BIS) data including suppression ratio (SR) and signal quality index (SQI) at different time points for intracranial arteriovenous malformation embolization by ethanol. For details see text.

Case report

A 29-yr-old, 52 kg male of ASA physical status I presented with recurrent seizures of five months' duration. He was diagnosed with a left parieto-occipital arteriovenous malformation and was scheduled for neuroendovascular embolization under general anesthesia. The remainder of his medical history was unremarkable and his physical examination was normal.

The patient received oral diazepam 5 mg and glycopyrrolate 0.2 mg *im* as premedication 45 min before the procedure. In the neuroradiology suite, prior to anesthetic induction, the following monitors were applied: BIS over the left frontal region, electrocardiography, pulse-oximetry and invasive blood pressure as recorded from the left radial artery. His baseline heart rate was 70 beats·min^{-1}, blood pressure 110/80 mmHg, SpO_2 99% and BIS value = 98.

Anesthesia was induced with propofol 100 mg *iv*, morphine 6 mg *iv* and pancuronium 8 mg *iv* to facilitate tracheal intubation. Anesthesia was maintained with 1-1.5% isoflurane in N_2O and oxygen with BIS values between 45–50, and ventilation was controlled to maintain end-tidal carbon dioxide values between 32–36 mmHg. A central venous line was inserted through the right subclavian vein following induction of anesthesia. The parieto-occipital AVM was catheterized successfully through the right femoral artery following which a total of volume of 32 mL of anhydrous absolute alcohol (100%) was injected intermittently over 45 min. The alcohol solution was prepared by the hospital pharmacy immediately prior to injection. During the alcohol injections, arterial blood pressure increased gradually from 100/74 mmHg to a maximum of 145/85 mmHg, and the patient's heart rate increased from 70 to 95 beats·min^{-1}. Quite suddenly, the patient's BIS values decreased precipitously to zero over a one-minute time frame. The suppression ratio was > 90% for 15 min while BIS values remained between 2–25 over the next 40 min (Figure). During this event, the end-tidal concentration of isoflurane was maintained between 0.8–1% and the signal quality index (SQI) consistently remained > 90. The interventional radiologist was informed about the BIS changes and subsequent angiography was undertaken, which revealed no evidence of hemorrhage or further changes in the patient's cerebral vasculature. A decision was made to continue with the procedure while using deliberate hypotension to maintain a mean arterial pressure of 60 mmHg with sodium nitroprusside (SNP) infused at 1–2 μg·kg^{-1}·min^{-1} to reduce the flow within the AVM during each subsequent alcohol embolization. Intravenous fluid hydration with lactated Ringer's solution supplemented with 7.5% sodium bicarbonate 2 mEq·kg^{-1} was administered to increase urinary output and pH.

At the end of the procedure, isoflurane was discontinued and residual neuromuscular blockade was reversed. However, the patient was slow to recover, with BIS values remaining around 60–70 over the next 30 min. Upon awakening, the patient's trachea was extubated in the neuroradiology suite. However, the patient appeared to be alcohol-intoxicated and his breath smelled of alcohol. In the intensive care

unit, urinalysis revealed the presence of hemoglobin and red blood cells. Arterial blood gas analysis demonstrated a base deficit of -7, which was corrected with a repeat dose of 7.5% sodium bicarbonate. Other routine biochemical variables were within normal limits. During his intensive care unit stay, the sodium nitroprusside infusion was continued to normalize systolic pressure around 110 mmHg to minimize normal perfusion pressure breakthrough. The rest of his post-procedural course was uneventful, and the patient was discharged from the hospital three days later without any neurological deficits.

Discussion

Management strategies for intracranial AVMs include embolization, radio surgery and/ or surgical excision. Patients with large complex AVMs consisting of several discrete fistulae with multiple feeding arteries are amenable for endovascular embolization. The aim of embolization is to obliterate as many fistulae and the respective feeding arteries as possible using various embolic materials, such as coils, balloons, polyvinyl alcohol particles and liquid agents including absolute alcohol. Injection of absolute alcohol into the feeding arteries and fistulae induces thrombosis and occlusion of the AVMs. However, the use of alcohol as a sclerosing agent is not without untoward complications.

Joffe and Bank[3] reported profound hypoglycemia, metabolic acidosis and intravascular hemolysis in a pediatric patient following a 1 $mL \cdot kg^{-1}$ alcohol injection for AVM ablation.

Stefanutto and Halbach[4] observed severe bronchospasm precipitated by alcohol injection during embolization of a dural fistula. They postulated that the non-target bolus of alcohol reached the bronchiolar vasculature and induced severe bronchospasm. Behnia[5] used 80 mL of absolute alcohol intermittently, for embolization of a lower extremity AVM in a young patient under general anesthesia. At the end of the procedure, the patient was awake but appeared alcohol intoxicated despite a blood alcohol level of only 36 $mg \cdot dl^{-1}$. In the same patient who underwent two further embolizations, similar complications, including hyperthermia, acidosis, cherry red urine, hypertension, tachycardia and increased airway pressures were observed. It was postulated that these changes were due to alcohol-induced intravascular hemolysis and its secondary effects on regulatory centres.[5] Although we have not confirmed or excluded intravascular hemolysis by measuring free plasma hemoglobin, urinary hemoglobin was positive in our reported case, suggesting the presence of intravascular hemolysis.

Sharma *et al.*[6] reported the occurrence of asystole and apnea following injection of 10 mL of absolute alcohol into a D_{11} hemangioma and attributed the same to a direct depressant effect of alcohol on the sinus node. Mitchell *et al.*[7] analyzed 92 alcohol embolizations in 56 patients to study the effect of alcohol on pulmonary artery (PA) pressures. They noted slight increases in PA blood pressure during alcohol embolization that correlated with elevated systemic blood pressure, suggesting that noxious stimulation from the alcohol injection causes sympathetic stimulation, even when patients are under general anesthesia. In our patient, we also observed tachycardia and hypertension during alcohol injection and cherry red urine with acidosis towards the end of procedure. However, our patient did not experience increased airway pressure or any dysrhythmias during the procedure. While we did not measure PA pressures and alcohol levels in our patient, post-procedure day one, the patient's biochemistry investigations including blood urea nitrogen and serum creatinine, complete blood count and electrolytes were within normal limits.

A BIS value of zero has not been reported previously in association with absolute alcohol embolization of intracranial AVMs. This event occurred despite the cumulative dose of injected alcohol remaining well within the recommended therapeutic range of 1 $mL \cdot kg^{-1}$.[8] The temporal relationship between alcohol injection and a sudden marked fall in BIS value during a period of stable anesthetic concentrations makes alcohol a plausible cause of this critical event. We postulate that this could have been due to the synergistic action of absolute alcohol and general anesthetic agents on central nervous system (CNS) centers both at the cortical and reticular activating system level. We hypothesized that since the total ethanol used was less than the recommended dose, this event could have been due to direct regional CNS effects rather than systemic alcohol toxicity causing CNS depression. Our patient did not suffer any prolonged adverse neurological sequelae despite this intraoperative finding. Welsbey *et al.*[9] noted a precipitous fall in BIS index from 55–60 to < 10 after separation from cardiopulmonary bypass in a patient undergoing left ventricular assist device removal who later succumbed to an extensive cerebral infarct. The authors of that report concluded that a sudden change in intraoperative BIS values might be the first indication of a serious cerebral event. However, in our reported case, we had the opportunity to perform immediate cerebral angiography which showed no acute change in the intracranial angio-architecture following the sudden change in BIS scores.

Normally, electrocardiographic and electromyographic artifacts are filtered by the BIS monitor's proprietary algorithm. In our patient, the SQI was 90–100% during the procedure and there was no muscle activity detected by electromyography and no external interference. Moreover, the ECG electrodes were placed without affecting the BIS. The raw electroencephalogram (EEG) trace during the event was unusual, mostly isoelectric or burst suppression pattern at that time. Furthermore, the burst suppression ratio was > 90% during the sudden depression of BIS indicating the fall in BIS value was genuine.

Cohen *et al.*[10] examined the effects of placebo and low and high doses of alcohol on EEG activity in 21 healthy males and found that alcohol had significant effects on EEG activity at frontal and central montages. These authors suggested that differential responsiveness of both cortical regions and EEG frequency band exists related to the effects of alcohol. In our case, it is possible that the BIS sensor placed in the frontal region on the ipsilateral side might have been more sensitive in detecting EEG changes attributable to regional alcohol injection.

Hayashida *et al.*[11] observed acute EEG slowing and BIS reduction in a patient at the start of cardiopulmonary bypass. They attributed the observation to cerebral hypoperfusion due to reduced arterial pressure and hemodilution. In our patient, deliberate mild hypotension using SNP infusion during alcohol injection could have been another contributing factor. This, along with local hemodilution caused by alcohol could have contributed to the sudden reduction in BIS. Moreover, alcohol flushed through cerebral vasculature might also have resulted in decreased electrical activity because of its inherent CNS depression. Furthermore, it is possible that the abrupt change in cerebral hemodynamics prior to and immediately following alcohol injection can lead to altered regional cerebral autoregulation which may require a certain period of time to restore the normal cerebral hemodynamics.

To conclude, in a susceptible individual, even a "therapeutic" dose of absolute alcohol for cerebral embolization can result in sudden depression of the CNS during the conduct of general anesthesia. Bispectral index monitoring provides a potentially valuable tool in the early detection of altered CNS function with a potential to avert intracranial catastrophe in such a setting. This experience suggests a potential additional role for monitoring BIS values during interventional neuroradiological procedures performed under general anesthesia.

Acknowledgements

We thank Dr. Krishnamoorthy Thamburaj, MD, DM, Assistant Professor, Imaging Sciences and Interventional Radiology, Sree Chitra Tirunal Institute for Medical Sciences & Technology, Trivandrum, Kerala, India for his helpful comments on the manuscript.

References

1 *Yakes WF, Krauth L, Ecklund J, et al.*. Ethanol endovascular management of brain arteriovenous malformations: initial results. Neurosurgery 1997; 40: 1145–52; discussion 1152–4.

2 *Chapot R, Laurent A, Enjolras O.* Fatal cardiovascular collapse during ethanol sclerotherapy of venous malformation. Intervent Neuroradiol 2002; 8: 321–4.

3 *Joffe D, Bank WO.* Morbidity in a pediatric patient having alcohol ablation of an arteriovenous malformation. Can J Anesth 2006; 53: 527–8.

4 *Stefanutto TB, Halbach V.* Bronchospasm precipitated by ethanol injection in arteriovenous malformation. AJNR Am J Neuroradiol 2003; 24: 2050–1.

5 *Behnia R.* Systemic effects of absolute alcohol embolization in a patient with a congenital arteriovenous malformation of the lower extremity. Anesth Analg 1995; 80: 415–7.

6 *Sharma D, Jain V, Rath GP.* Asystole during percutaneous ethanol injection of symptomatic vertebral haemangioma. Anaesth Intensive Care 2006; 34: 656–8.

7 *Mitchell SE, Shah AM, Schwengel D.* Pulmonary artery pressure changes during ethanol embolization procedures to treat vascular malformations: can cardiovascular collapse be predicted? J Vasc Interv Radiol 2006; 17: 253–62.

8 *Mason KP, Michna E, zurakowski D, Koka BV, Burrows PE.* Serum ethanol levels in children and adults after ethanol embolization or sclerotherapy for vascular anomalies Radiology 2000; 217: 127–32.

9 *Welsbey IJ, Ryan JM, Booth JV, Flanagan E, Messier RH, Borel CO.* The bispectral index in the diagnosis of perioperative stroke: a case report and discussion. Anesth Analg 2003; 96: 435–7.

10 *Cohen HL, Porjesz B, Begleiter H.* Ethanol-induced alterations in electroencephalographic activity in adult males. Neuropsychopharmacology 1993; 8: 365–70.

11 *Hayashida M, Chinzei M, Komatsu K, et al.* Detection of cerebral hypoperfusion with bispectral index during paediatric cardiac surgery. Br J Anaesth 2003; 90: 694–8.