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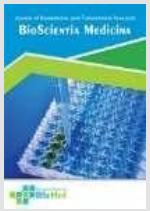

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Opioid-Free Anesthesia (OFA) as a Safe Anesthetic Choice for Epilepsy Patient

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A B S T R A C T

Background: The opioid-free anesthesia (OFA) approach, although not widely employed in anesthesia, offers distinct benefits for some populations, such as epilepsy patients, due to the propensity of opioids to trigger seizures. Hence, the objective of this study was to conduct an opioid-free anesthesia (OFA) procedure on the left lateral rhinotomy in a patient with concurrent epilepsy. **Case presentation:** Our patient is a 59-year-old woman suffering from epilepsy with a left nasal cavity tumor, scheduled for a left midfacial degloving rhinotomy. Given the patient's epilepsy comorbid, we have opted for an opioid-free anesthesia (OFA) procedure. OFA procedures are not yet widely employed in anesthesia; however, they offer advantages for specific patient populations, including epilepsy patients, as opioids have the potential to induce seizures. **Conclusion:** The various OFA protocols being conducted worldwide require refinement, and the potential interactions of each component should be explored further.

1. Introduction

Opioids have a long history in medicine and are often used as anesthetic and analgesic agents. Opioids are highly potent analgetic agents and are the main analgetic agents in surgery and post-surgery.[1,2] However, this highly versatile drug has some side effects such as exacerbation of hypotension, respiratory depression, bradycardia, somnolence, urinary retention, dependence, and also increases the seizure threshold. The opioid-free anesthesia (OFA) procedure is a procedure that is not yet commonly used in anesthesia; however, this procedure has advantages for certain populations, one of which is epilepsy patients, since opioids have the potential to induce seizure onset. Therefore, this study aimed to perform an OFA procedure on left lateral rhinotomy in patients with epilepsy comorbidity.

2. Case Presentation

A 59-year-old female diagnosed with a left nasal cavity tumor was planned for a lateral rhinotomy with a midfacial degloving sinistra approach. The patient had a history of epilepsy with phenytoin treatment of 100 mg every 6 hours orally. The last episode of seizure was eight months ago, which was triggered by stress/anxiety. Seizures generally improve with administration of diazepam 10 mg per rectal.

Opioid-free anesthesia was performed in this patient, starting with premedication administration of dexamethasone 10 mg IV and midazolam 1.5 mg IV. Induction began with a dexmedetomidine loading dose 1 mcg / kgBW in 10 minutes, followed by magnesium sulfate 2.4 grams of intravenous drip and thiopental 180 mg IV. Before incision, the patient was given ketorolac 30 mg IV and paracetamol 900 mg IV injections as an analgetic preventive measure. Anesthesia maintenance was conducted using thiopental 3 mg/kg/hour, lidocaine 1mg/kg/hour, dexmedetomidine 0.2-0.7 mcg/kg/hour, and $MgSO_4$ 2.5 mcg/kg/hour. Stable anesthesia conditions were achieved with a systolic blood pressure of 90-110 mmHg, diastolic 65-85 mmHg, heart rate of 60-70 x/minute, respiratory rate 16-18 x/minute, SpO_2 98-100% and $EtCO_2$ 35-40 cm H_2O. During anesthesia, the qCON and qNOX were within the range of 40-65.

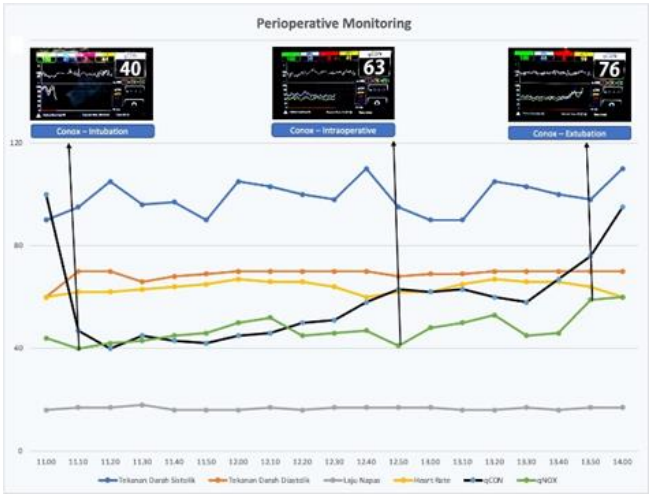

Figure 1. Intraoperative hemodynamic graph of the patient.

Table 1. Perioperative opioid-free anesthesia medications in this case.

Medication	**Dosage**	**Total dosage**	**Purpose**
Premedication			
Midazolam	0.025 mg/kg	1,5 mg	Anxiolytic
Induction			
Dexmedetomidine	1 mcg/kg	60 mcg	Anesthetic adjuvant
$MgSO_4$	40 mg/kg	2400 mg	Muscle relaxant
Thiopental	3 mg/kg	180 mg	Sedative
Lidocaine	1.5 mg/kg	90 mg	Analgetic
Maintenance			
Ketorolac	30 mg	30 mg	Analgetic
Paracetamol	15 mg/kg	900 mg	Analgetic
Dexmedetomidine	0.2 – 0.7 mcg/kg/h	70 mcg	Anesthetic adjuvant
$MgSO_4$	2.5 mcg/kg/h	450 mcg	Muscle relaxant
Thiopental	3 mg/kg/h	540 mg	Sedative
Lidocaine	1 mg/kg/h	180 mg	Analgetic

After the surgery was completed, the patient was awakened in full consciousness. The postoperative pain was controlled with a numeric pain rating scale in the recovery room of 1/10 and 24 hours postoperative 0/10, using postoperative analgesia of ketorolac 30 mg every 8 hours IV and Paracetamol 500 mg every 6 hours orally.

3. Discussion

Epilepsy is a chronic neurological condition that requires special attention in the anesthesia process, even for non-neurosurgery operations.[2] Status epilepticus is a serious condition that can cause permanent brain damage. The use of opioid drugs is one of the risk factors that can cause seizures because of their action on mu and kappa opioid receptors.[1-3] These opioid drugs work by lowering a person's seizure threshold.[3-5] Meperidine exhibits the most pronounced links to myoclonus seizures and tonic-clonic seizure events among opioids. Furthermore, fentanyl, alfentanil, sufentanil, and morphine have been associated with inducing generalized seizures in patients, even at low to moderate doses, particularly when administered intrathecally.[6,7] Opioid anesthetic agents have also been demonstrated to elevate EEG activity in individuals with focal epilepsy. Studies have indicated that remifentanil and alfentanil can stimulate electrical activity when identifying epileptogenic zones during epilepsy surgery.[5-7] Based on the effect of increased risk of seizures, OFA can be an alternative as an anesthesia treatment for these patients.

Opioid-free anesthesia (OFA) involves the administration of anesthesia during surgery without the use of opioids, making it a rather extreme approach to minimizing opioid use.[8,9] The OFA technique also applies opioid-free analgetic therapy for postoperative therapy in patients, with the principle of multimodal analgesia.[10,11] However, in its application, OFA requires more accurate nociception monitoring.

In this case, we used CONOX as an intraoperative pain and awareness monitoring device. CONOX, used as a monitoring tool, has two parameters, qCON and qNOX. Both indices operate in conjunction with recorded EEG signals from the brain. qCON measures the depth of anesthesia, while qNOX predicts the likelihood of a pain-related arousal response. qCON analyzes EEG data from the frontal lobe, providing an estimation of the anesthesia level on a scale from 99 (fully awake) to 0 (isoelectric EEG). A qCON index ≥ 80 indicates a state of consciousness or mild sedation, while an index within the range of 60 to 40 corresponds to an appropriate level of anesthesia for surgical procedures. In ENT surgery, it is said that OFA can be applied as an alternative to anesthesia. A study on tonsillectomy and adenotonsillectomy surgery in children with ASA I and II physical status stated that opioid-free anesthesia techniques can provide safe and efficient perioperative conditions.[12]

Table 2. Interpretation of CONOX.[12]

Score	qCON	qNOX
80-99	Full awareness	The patient is fully responsive to pain stimulus
75	Sedation	
40-60	General anesthesia	The patient is less responsive to pain stimulus
20	Deep anesthesia	The patient is more likely to show no response to pain stimulus
0	Isoelectric EEG	

For magnesium, magnesium has an analgesic effect that regulates calcium influx into cells and acts as an antagonist of NMDA receptors. Magnesium acts by lowering postoperative scores. The dose that can be used is 30-50 mg/kg, followed by an intravenous infusion of 10 mg/kg/hour.[13,14] In addition, magnesium is chosen as a muscle paralyzer because the effects of non-depolarizing NMBD are reduced in chronic phenytoin users. Intravenous lidocaine is also used to achieve the desired analgetic effect with a loading dose of 1-2 mg/kg followed by an infusion of 1-2 mg/kg/hour. Lidocaine works by suppressing impulses formed from injured nerve tissues and proximal dorsal ganglion roots by inhibiting sodium

channels, N-methyl-d-aspartate receptors, and G-protein paired receptors. As an anti-inflammatory agent, lidocaine works to inhibit the release of inflammatory cytokines such as leukotriene β4, interleukin-1α, and histamine, as well as inhibit adhesion, migration, neutrophil accumulation, macrophage activity, and enzyme liberation so that it can inhibit the transduction process.[14] Because there are contraindications to the use of ketamine in these patients, we chose to use dexmedetomidine as an additional analgetic agent; the agonist effect on specific alpha-2 receptors also makes this drug less hypotensive and has the effect of keeping the heart rate from increasing during the intubation process. Intraoperatively, it can assist operators by maintaining the operating field from bleeding.

Ketorolac 30 mg IV as an NSAID is also given, where this drug functions in inhibiting the transduction process in the pain system. Paracetamol 1 gram IV is also given as an additional analgetic, where paracetamol inhibits cyclooxygenase pathways, especially in the brain, and activates the descending serotoninergic pathway. We also used thiopental as a sedative agent in this patient because thiopental has anti-seizure effects and lowers $CMRO_2$, making it safer in patients with a history of epilepsy. Thiopental shows isoelectric EEG images, which can be useful in patients with a history of epilepsy. Thiopental works by potentiating GABAA channel activity. Thiopental binds to Cl-ionophore at GABAA receptors and increases the duration of Cl-ionophore opening time so that hyperpolarization in neurons occurs and there is a decrease in excitation. Therefore, the post-synaptic inhibitory effect of GABA in the thalamus will be extended.[15] Thiopental also acts on glutamate, adenosine, and nicotinic acetylcholine receptors.[15,16] Anesthesia in this patient was stable, while the patient's hemodynamics were also stable during anesthesia. Furthermore, the patient's CONOX score was stable, with qCON in the range of 40-65 and qNOX in the range of 40-60. Although the used drugs have lower analgetic potential compared to opioids, when used multimodally, they can have a potent effect and may substitute perioperative opioids.

4. Conclusion

The use of opioids in the anesthesia process is indeed a very routine procedure; however, OFA has recently emerged as a safe alternative to general anesthesia in certain groups of patients. The risk and benefit ratio of OFA should be considered individually. The various OFA protocols being conducted worldwide require refinement, and the potential interactions of each component should be explored further.

5. References

1. Bohringer C, Astorga C, Liu H. The benefits of opioid-free anesthesia and the precautions necessary when employing it. Translational Perioperative and Pain Medicine, 2020; 7(1): 152–7.
2. Perks A, Cheema S, Mohanraj R. Anaesthesia and epilepsy. British Journal of Anaesthesia, 2012; 108(4): 562–71.
3. An G, Wang G, Zhao B, Zhang X, Li Z, Fu J, et al. Opioid free anesthesia compared for laparoscopic radical colectomy with pain threshold index monitoring: a randomized controlled study. BMC Anesthesiol. 2022; 22(1): 241.
4. Chowdhury L, Laha A, Chaudhuri T, Chatterjee S. Chronic phenytoin therapy-induced vecuronium resistance. Indian Journal of Pharmacology. 2011; 43(2): 214–5.
5. De Cassai A, Geraldini F, Tulgar S, Ahiskalioglu A, Mariano ER. Opioid-free anesthesia in oncologic surgery: the rules of the game. Journal of Anesthesia, Analgesia and Critical Care. 2022; 2(1): 8.
6. Larkin CM, O'Brien DF, Maheshwari D. Anaesthesia for epilepsy surgery. BJA Educ. 2019; 19(12): 383-9.
7. Chui J, Manninen P, Valiante T, Venkatraghavan L. The anesthetic considerations of intraoperative

electrocorticography during epilepsy surgery. Anesth Analg. 2013; 117: 479–86.

8. Butterworth JF. Morgan & Mikhail's clinical anesthesiology. 6th ed. McGraw-Hill. 2018.
9. Daykin H. The efficacy and safety of intravenous lidocaine for analgesia in the older adult: a literature review. British Journal of Pain. 2017; 11(1): 23–31.
10. European Monitoring Centre for Drugs and Drug Addiction. New psychoactive substances: 25 years of early warning and response in Europe: an update from the EU Early Warning System. Publications Office. 2022.
11. Lavand'homme P, Estebe J-P. Opioid-free anesthesia: a different regard to anesthesia practice. Current Opinion in Anaesthesiology. 2018; 31(5): 556–61.
12. Mann GE, Flamer SZ, Nair S, Maher JN, Cowan B. Opioid-free anesthesia for adenotonsillectomy in children. International Journal of Pediatric Otorhinolaryngology. 2021; 140: 110501.
13. Saboory E, Derchansky M, Ismaili M, Jahromi SS, Brull R. Mechanisms of morphine enhancement of spontaneous seizure activity. Anesthesia & Analgesia. 2007; 105(6): 1729–35.
14. Shafer SL, Rathmell JP, Flood P. Stoelting's pharmacology and physiology in anesthetic practice (Fifth edition). Wolters Kluwer Health. 2015.
15. Tochie JN, Bengono RS, Metogo JM, Ndikontar R, Ngouatna S. The efficacy and safety of an adapted opioid-free anesthesia regimen versus conventional general anesthesia in gynecological surgery for low-resource settings: A randomized pilot study. BMC Anesthesiology. 2022; 22(1): 325.
16. Uribe A, Zuleta-Alarcon A, Kassem M, Sandhu GS, Bergese SD. Intraoperative seizures: anesthetic and antiepileptic drugs. Curr Pharm Des. 2017; 23: 6524-32.