Case Study

Opioid free anesthesia for posterior fossa tumors undergoing craniotomy tumor removal: A case series

Tengku Addi Saputra[1*], Iwan Fuadi[1], Iwan Abdul[1]

[1]Departement of Neuroanesthesiology and Critical Care, Medical Faculty Universitas Padjajaran/Dr. Hasan Sadikin Hospital, Bandung, Indonesia.

Correspondence: Tengku Addi Saputra, Departement of Neuroanesthesiology and Critical Care, Medical Faculty Universitas Padjajaran/Dr. Hasan Sadikin Hospital, Bandung, Indonesia. addisaputra1980@gmail.com

ABSTRACT

The posterior fossa contains the cerebellum, midbrain, pons, medulla, and cranial nerves. The Cerebello Pontine Angle (CPA) brain tumor accounts for 5-10%. There is interest in the use of Opioid Free Anesthesia (OFA) and opioid-free analgesics are used to be part of Enhanced Recovery After Surgery (ERAS) in the posterior fossa tumor craniotomy. The case series describes opioid-free craniotomies for CPA and cerebellar meningioma infratentorial tumors. All patient induction using, dexmedetomidine, propofol, lidocaine, rocuronium, and xylocaine 10% oropharyng spray and maintained using dexmedetomidine (0.2–0.8 mcg/kgbb/hour), propofol (25–150 mcg/kgbb/minute), intermittent rocuronium, and 50% oxygen: 50% air. The ICU patient received mechanical ventilation following surgery. OFA with dexmedetomidine eliminates opioid reliance in most conventional anesthetics, extubates ICU patients less than 24 hours of surgery, lowers the length of stay (LOS), and minimizes opioid side effects and rapid recovery. Anesthetic management using OFA can be carried out in fossa posterior tumor craniotomy, so the ERAS protocol can be implemented in this case series.

Keywords: Anesthesia management, Opioid Free Anesthesia (OFA), Perioperative, Posterior fossa tumor

Introduction

Anesthesia without systemic, neuraxial, or intra-cavitary opioids is called opioid-free anesthesia (OFA) [1, 2]. Opioid Free Anesthesia in brain tumor surgery is new, however, several cases have been reported in supratentorial surgery, which is rare in infratentorial surgery [3]. OFA and opioid-free analgesics are part of the Enhanced Recovery After Surgery (ERAS) procedure. OFA reduces opioid side effects, rapid recovery, and gastrointestinal function [4, 5]. OFA with multimodal analgesia (MMA), or balanced opioid-sparing analgesia, aims to improve nonopioid adjuncts, regional methods, and neuraxial anesthesia [6, 7].

Access this article online	
Website: www.japer.in	**E-ISSN:** 2249-3379

How to cite this article: Saputra TA, Fuadi I, Abdul I. Opioid free anesthesia for posterior fossa tumors undergoing craniotomy tumor removal: A case series. J Adv Pharm Educ Res. 2024;14(3):94-101. https://doi.org/10.51847/9PCyXicaFv

Conventional high-dose opioid anesthesia reduces neurosurgical hemodynamic instability [8]. Opioids reduce anesthetic stress but prolong extubation and impair neuronal function [9, 10]. Due to these contradictory reasons and the desire to avoid opioids, opioid-free anesthesia, and perioperative analgesia are becoming more popular [10].

The posterior fossa contains the cerebellum, midbrain, pons, medulla, and several cranial nerves [11]. Cerebellopontine angle (CPA) tumors are part of the posterior fossa, the CPA is a triangular space in the posterior cranial fossa bounded by the tentorium superiorly, the brainstem posteromedially, and the petrous part of the temporal bone posterolaterally. Between 5-10% of all intracranial tumors are located in the CPA. The most common tumors in the CPA are vestibular schwannoma, meningioma, and epidermoid tumors. Vestibular schwannoma accounts for 75-85% of all CPA tumors [11, 12]. The current incidence of vestibular schwannoma among all ages ranges from 3.0 to 5.2 per 100,000 people per year. The highest incidence occurs in those aged ≥ 70 years [13].

Anesthetic techniques for craniotomy must be able to reduce the stress response to pain during intubation and surgical manipulation because they are related to postoperative morbidity

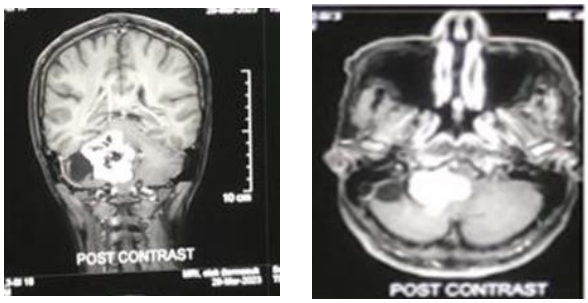
and mortality [14]. Surgical procedures for posterior fossa tumors are very complicated due to the narrow space, requiring long duration of surgery, complex handling, and the risk of cranial nerve injury [15]. The risk of complications is Venous Air Embolism (VAE) [16, 17].

A peripheral nerve blockade technique has been found, which blocks the nerves in the head area, called the scalp block technique. This technique is an alternative to the use of high-dose opioids [18-20]. The combination of OFA using TIVA with propofol and dexmedetomidine and scalp block is a multimodal analgesia (MMA) that can be done, in line with the ERAS protocol in posterior fossa craniotomy in this case.

Case

Case 1

A 56-year-old woman, 45 kg and 154 cm (BMI 19kg/m2) ASA 2 with chief complaints of worsening headaches since 2 months before admission, blurred vision, hearing loss, and weakness in the right leg. The patient has a history of hypertension controlled by consuming amlodipine 1x10 mg po and candesartan 1x80 mg po. The patient is always allowed to walk because of Lightheadedness. The previous operations VP shunt 3 months ago. History of seizures and vomiting was denied. Neurological examination found dysfunction of nerves III and VIII. The hemodynamic examination was within normal limits, preoperative laboratory examination was within normal limits with Hb 9.9 g / dl. Chest X-ray and ECG were normal. MRI examination in **Figure 1** showed a mixed extra-axial mass (solid cystic, cystic, and peritumoral arachnoid cyst components) in the right CPA mass measuring 5.7x3.9x4.8 cm which pressed on the cerebral peduncle, pons, right ventricle IV ec which was suspected to be a vestibular schwannoma.



a) b)

Figure 1. Head MRI Contrast

Anesthesia management

Preemptive analgesic paracetamol 1 gr iv was given before induction. Monitoring was installed in the form of ECG, saturation, arterial blood pressure, and BIS. Induction was performed with dexmedetomidine 1mcg/kgbb (45 mcg) iv for 15 minutes, propofol 2-2.5mg/kgbb (110 mg) iv, lidocaine 1.5mg/kgbb (60 mg) iv, rocuronium 0.8-1mg/kgbb (40 mg) iv, xylocaine spray 10% was given to the oropharynx, intubation was performed and control ventilation. After the patient was intubated, a scalp block was performed with 0.25% bupivacaine. CVC and arterial line for intraoperative hemodynamic monitoring were performed. Anesthesia maintenance with dexmedetomidine 0.2 - 0.8 mcg/kg/hour, propofol 25-150 mcg/kg/minute, rocuronium 0.15 mg/kg (7 mg) iv intermittently every 45 minutes, BIS maintained 40 - 60. The patient was positioned in the park bench position.

The operation lasted about 6 hours and a brain relaxation score of 1. Hemodynamic status during the procedure was stable with bleeding about 1,100cc and urine output 1,350cc. Fluid intake during surgery was 2000 cc of crystalloid, 500cc of colloid, 40 grams of mannitol iv, 10 mg of dexamethasone iv, and 745cc of Packed Red Cell (PRC). Hemodynamic status can be seen in **Figure 2**.

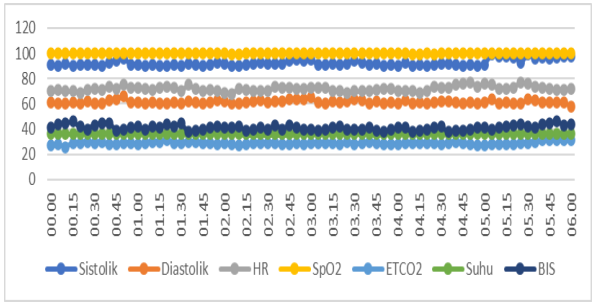


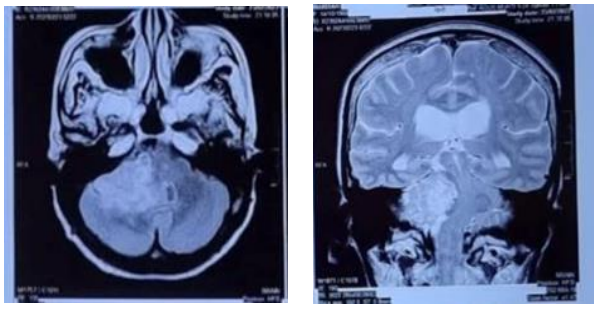
Figure 2. Intraoperative Heamodynamic Monitoring

Post-surgical management

Postoperatively, the patient was treated in the ICU (Intensive Care Unit) for 2 days. The patient was given a ventilator with tidal volume 8mL/kgBW, respiratory rate 12 times per minute, and PEEP 5, and gradual weaning was performed. The patient was extubated 18 hours after surgery with compos mentis consciousness. Haemoglobin after surgery was 11,0 g/dL. While in the ICU, the patient was given dexmedetomidine 0.2 - 0.4 mcg/kgBW/hour, paracetamol 4x1 gram iv. Mannitol was still given 4x125cc tapering off. The postoperative pain score was a Visual Analogue Scale (VAS) score 1-2. The patient was moved to the high care unit (HCU) on day two after surgery.

Case 2

A woman, 54 years old, 50 kg and 160 cm (BMI 19,5 kg/m^2) ASA 2 with frequent lightheadedness and impaired hearing function followed by a decrease in appetite but no weight loss. This had been experienced for 1 year. Seizures and extremity paralysis were denied. There were no comorbid or any allergies. Neurological examination found the dysfunction of the vestibulocochlear nerve (VIII), and laboratory, ECG, and thorax x-ray were found to be within normal limits. Haemoglobin was 14.3 g/dl. Contrast head MRI in **Figure 3** showed a heterogeneous solid mass in the dextra CPA measuring 2.2 x 1.7 x 2.6 cm with perifocal edema up to the cerebellum and emphasis on the pons.



a) b)

Figure 3. Head MRI Contrast

Anesthesia management

Preemptive analgesia paracetamol 1 g iv was given. ECG, saturation, arterial blood pressure, and BIS were monitored. Induction was performed with dexmedetomidine 1 mcg/kg bw (50 mcg) iv for 15 minutes, propofol 2 mg/kgBW (100 mg), lidocaine 1.5 mg/kgBW (75 mg) iv, rocuronium 0.8 mg/kgBW (40 mg) iv, xylocaine spray 10% on the oropharynx. Intubation was then performed and control ventilation. After the patient was intubated, a scalp block with 0.25% bupivacaine was performed. CVC and arterial lines were installed for intraoperative hemodynamic monitoring. The patient was then positioned on the Park bench, left lateral. The maintenance anesthesia with dexmedetomidine 0.2 - 0.8 mcg / kgbb / hour, propofol 25 - 150 mcg /kgBW/minute, rocuronium 0.15 mg / kgbb (7.5 mg) intermittently and given mannitol 40 grams. Intraoperative hemodynamics was relatively stable and BIS maintained 40-60. The operation was completed within 5 hours. Total fluid intake was 2525 ml crystalloid, 205 ml packed red cells, 900 ml bleeding, and 1000 ml urine production. ETT was retained for ICU admission. Hemodynamics intraoperative see in **Figure 4**.

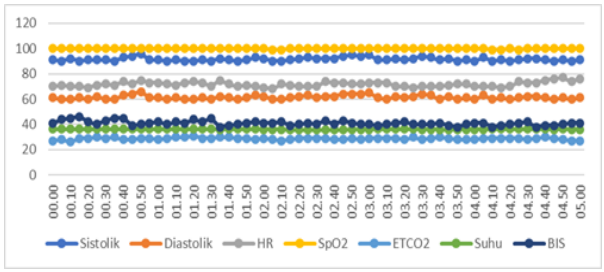


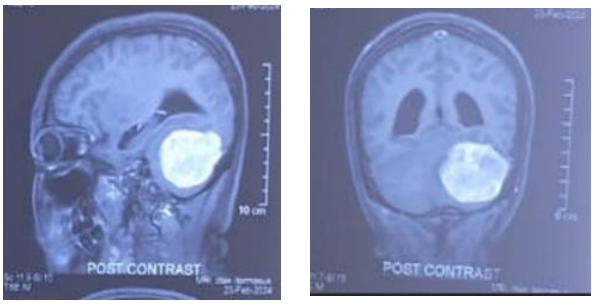
Figure 4. Intraoperative Haemodynamic Monitoring

Post-surgical management

The patient was treated in the ICU. The patient was given a ventilator with tidal volume 8mL/kgBW, respiratory rate 14 times per minute, and PEEP 5, and gradual weaning was performed. The patient was still sedated using propofol 25 - 50 mcg/kgBW/minute, dexmedetomidine 0.2 - 0.4 mcg/kg/hour, and paracetamol 3x1gram per day, mannitol was given 4x125 cc tapering off. On day 2 in the intensive care unit, sedation was stopped, and extubation was performed 12 hours postoperatively after ensuring adequate breathing. Hemoglobin after surgery was 10,8 g/dL Hemodynamics were stable, analgesics were continued. The patient was transferred to HCU two days postoperative.

Case 3

A woman, 46 years old, 45 kg and 150 cm (BMI 20 kg/m^2) ASA 2 came with complaints of headache 3 days before being admitted to the hospital. Currently, the patient also complains of staggering and often falls when walking, and often experiences vomiting. The patient had previously performed a VP shunt 3 months ago. The patient has a history of hypertension controlled with amlodipine 1x 5 mg. History of drug/food allergy was denied. Impairment of the vestibulocochlear nerve (VIII). Preoperative laboratory examination was within normal limits with Hb 12.6 g/dl. The results of physical examination and, ECG and thorax X-ray were found within normal limits. The results of contrast in **Figure 5** shows that MRI examination obtained Space Occupying Lession extra-axial Infratentorial on the convexity of the posterior fossa sinistra size 5.3x5.2x4.1 cm with suspected meningioma.



a) b)

Figure 5. Head MRI Contrast

Anesthesia management

The patient was planned for craniotomy tumor removal under general anesthesia and monitoring with oxygen saturation, ECG, EtCO2, arterial blood pressure, and BIS. Preemptive analgesic paracetamol 1 g iv was given. Induction was performed with dexmedetomidone 1 mcg/kg bw (45 mcg) for 15 minutes, lidocaine 1.5 mcg/kg bw (70 mg) iv, xylocaine spray 10% was given to the oropharynx. Rocuronium 0.8 - 1mcg / kgb (40 mg) was given followed by intubation using ETT and control ventilation. After the patient was intubated, a scalp block was performed with 0.25% bupivacaine. CVC and the arterial line were placed for intraoperative hemodynamic monitoring. The patient was then positioned prone. The anesthesia formula used dexmedetomidine 0.2 - 0.8 mcg/kgbb/hour, propofol 25-150 mcg/kgbb/min, and rocuronium 0.15mg/kgbb (7mg) iv intermittently. Intraoperatively found brain relaxation score 1. Intraoperative hemodynamics was relatively stable, and BIS was around 40-60. The operation was completed within 4 hours. Total fluid intake was 2600 ml crystalloid, Mannitol 30 grams, packed red cells 487 ml, bleeding 1000 ml, and urine production 800 ml. After surgery, an ETT was retained until the ICU. Haemodynamics intraoperatively can be seen in **Figure 6**.

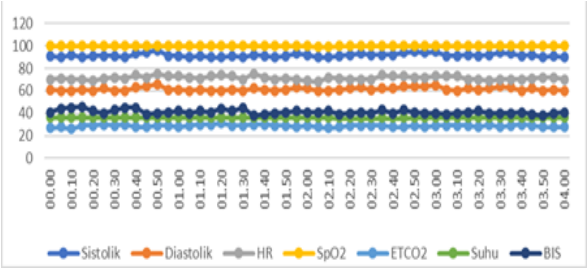


Figure 6. Intraoperative Haemodynamic Monitoring

Post-surgical management

The patient was admitted to th89559e ICU sedated, breathing was controlled using a Volume Control 8mL/kgBW, respiratory rate 14 times per minute, and PEEP 5 and gradual weaning was performed. The patient was sedated using propofol 25 - 50 mcg/kgBW/minute, dexmedetomidine 0.2 - 0.4 mcg/kgBW/hour, mannitol 4x125 cc tapering off, and paracetamol 4x1gram per day. After 16 hours propofol was stopped and extubated after ensuring adequate breathing. Haemoglobin after surgery was 11,8 g/dL. Hemodynamically stable, analgesics were continued in this patient. The patient was transferred to the HCU on the second day after surgery.

Table 1. Finding on Fossa Posterior Mass

Complication	Case 1	Case 2	Case 3
Deficite of neurologic	Yes N. III dan N. VIII	Yes N. VIII	Yes N. VIII
Increased ICP	No	No	No
Position during Operation	*Park Bench*	*Park Bench*	*Prone*
Risk of VAE	-	-	-
Blood Loss Intraoperative	1.100 cc	900 cc	1000 cc
Duration Operation	6 hour	5 hour	4 hour
Brain Relaxation Score	1	1	1
VAS Score	0-1	0-1	0-1
PONV	-	-	-
Length Of Stay In ICU	2 days	2 days	2 days

Results and Discussion

Conventional anesthesia usage opioids are often used in the operative period for intraoperative analgesics and postoperative pain management. Intraoperative opioids are used for anesthetic lodging and blunting sympathetic response [21, 22]. Perioperative opioid use is associated with respiratory depression, gastrointestinal dysfunction, postoperative nausea and vomiting (PONV), pruritus, urinary retention, delirium, and potential opioid addiction [23]. Not only that, opioid side effects can also cause longer hospital stays and develop into chronic pain [21]. Therefore, to avoid these undesirable side effects, opioid-free anesthesia and opioid-free perioperative analgesia are used [10].

Opioid Free Anesthesia (OFA) is a technique where there is no systemic, neuroaxial, or intra-cavitary opioid administration during anesthesia [3, 24, 25]. Opioid Free Anesthesia provides the advantage of rapid recovery and prevents acute post-surgical side effects of opioids [26]. The ERAS protocol has been shown to benefit patients, including shorter length of stay (LOS), better postoperative functional status, lower perioperative complications, higher patient satisfaction, and lower healthcare costs [27-29]. ERAS in craniotomy surgery can certainly be implemented [30, 31]. The finding on fossa posterior mass can be see in **Table 1**. The pathophysiology and mechanisms of post-craniotomy PONV are multifactorial in etiology and are related to factors associated with anatomical mechanisms of physiologist, patient population, type of surgery, and anesthetic technique [23, 32]. Strategies to increase nonopioid adjuncts, regional techniques, and neuraxial anesthesia are the goals of using OFA with multimodal analgesia (MMA), or balanced analgesia with an opioid-sparing approach [21].

In these 3 cases, patients were given the same treatment, patients fasted 6 hours preoperatively, patients were given preemptive paracetamol 1 gram, 30 minutes before induction which aims to prevent sensitization of central pain pathways in accordance with ERAS protocols in neurosurgical surgery such as acetaminophen, gabapentin/pregabalin, tramadol, Non-Steroid Anti-Inflammatory Drugs (NSAIDs) [6, 7].

Induction was performed in all three cases of posterior fossa tumors by administering dexmedetomidine, propofol, rocuronium, injectable lidocaine, and topical lidocaine to the oropharynx and supraglottic before intubation. The administration of intravenous lidocaine aims to suppress the secondary hemodynamic response after intubation and topical lidocaine to suppress the cough reflex, suppress sympathetic response, prevent Mean Arterial pressure (MAP) fluctuation, and more stable hemodynamics. After induction and intubation, there was no hemodynamic spike. The patient was also given scalp block anesthesia (bupivacaine 0.25%) to reduce the pain threshold without the risk of hemodynamic disturbances. Scalp block can reduce the need for opioids and reduce the incidence of hypertension, tachycardia, and neuroendocrine stress [18]. This is consistent with the case above, where intraoperatively there was no tachycardia and hypertension even though it did not use analgesic formulations with opioids.

Anesthesia maintenance is performed with Total Intravenous Anesthesia (TIVA) using propofol and dexemedetomidine via a syringe pump without the use of inhaled anesthetic agents [33]. Total Intravenous Anesthesia (TIVA) with propofol for maintenance of general anesthesia reduces the risk of PONV. The drug combination in TIVA is expected to achieve complete, balanced anesthesia and reduce the dose of each drug, thereby reducing the side effects of all drugs in the mixture. Avoidance of volatile anesthetics and opioids intraoperatively leads to a high reduction in PONV [31, 32].

Dexmedetomidine is a selective α-2 agonist that can effectively attenuate the sympathetic response during endotracheal intubation. Side effects of dexmedetomidine include hypotension, hypertension, nausea, bradycardia, atrial fibrillation, and hypoxia [34, 35]. Dexmedetomidine has the

effect of reducing cerebral blood flow (CBF), and cerebral oxygen consumption (CRMO2), and decreasing intracranial pressure [36-38]. This effect is strengthened by the use of a combination with propofol. It also has neuroprotective effects because it can reduce nerve cell inflammation and nerve cell degeneration [34, 39, 40].

The administration of dexmedetomidine in tumor craniotomy surgery can suppress hemodynamic responses during laryngoscopy and intubation. In addition, to monitor the depth of anesthesia we can use bispectral index (BIS) scores [41]. BIS monitoring in all 3 cases found 40 to 60. There was no significant difference in stress response to surgery between opioids (fentanyl) and non-opioids (dexmedetomidine) used as intraoperative analgesics during elective craniotomy [37, 42]. Dexmedetomidine was associated with reduced incidence of PONV, reduced pain, and postoperative analgesic consumption [31, 43].

Propofol is an intravenous anesthetic agent that has properties such as decreased CMRO2, decreased CBF, maintenance of flow-metabolism coupling, decreased intracranial pressure (ICP), inhibition of glutamate release, activation of GABA-A receptors, cerebral autoregulation, CO2 response, and neuroprotection [38]. Propofol has a rapid onset of action and shorter duration of action to facilitate rapid recovery, reduce the incidence of PONV, and is anticonvulsant [44]. When propofol is given at high doses for a long duration (> 5 mg/kg/hour for more than 48 hours) it can cause metabolic acidosis, rhabdomyolysis, liver failure, and myocardial failure referred to as propofol infusion syndrome [45, 46]. Until now, TIVA with propofol is still an option for anesthesia in neurosurgical cases either through continuous infusion or TCI. Postoperative pain management helps prevent an increase in intracranial pressure thus reducing the risk of intracerebral hemorrhage. The combination of intravena analgesics and local anesthetics can reduce the need for opioids [47, 48].

The posterior fossa is a very narrow space consisting of the Pons, medulla, cerebellum, and 4th ventricle. Facilitating safe exposure and reducing tissue damage and edema are the main goals of anesthesiologists [49]. The CPA is a triangular space in the posterior cranial fossa bounded by the tentorium superiorly, the brainstem posteromedially, and the petrous portion of the temporal bone posterolaterally [12], which houses cranial nerves V, VI, VII, and VIII along with the anterior inferior cerebellar artery [11]. The most common symptoms of lesions involving the CPA include hearing loss, tinnitus, dizziness, vertigo, headache, and gait dysfunction [12]. CPA tumors are benign, slow-growing tumors with low malignancy potential (1%). Between 5-10% of all intracranial tumors are located in the CPA. The most common tumors in the CPA are vestibular schwannoma, meningioma, and epidermoid tumors. Treatment options include observation, radiosurgery, and microsurgery [12, 50]. Vestibular schwannomas account for 75-85% of all CPA tumors [50, 51]. Surgical procedures in these cases are complicated due to the narrow space, long duration of surgery, complex handling, and risk of cranial nerve injury [15]. In neuroanesthesia practice, brain relaxation status is very important. It relates to surgical conditions, retraction injuries, and patient outcomes [49, 52, 53]. Venous air embolism in posterior fossa surgery may occur if there is subatmospheric pressure on the exposed blood vessels. Some data shows the risk of VAE in the sitting position is between 40%-45%, while in the lateral, face-down, park bench position it is lower at between 10%-15% [16, 54, 55]. Complications after surgery include headache, bleeding, stroke, vascular injury, infection, cranial nerve injury, tumor recurrence, CSF leak, and death. Conventional surgical complications involving cranial nerve dysfunction are caused by lesions to the facial, trigeminal, and vestibulocochlear nerves [12].

Postoperatively the patient was given analgesic paracetamol 4x1gram and dexmedetomidine 0.2 - 0.4 mcg/kg/hour without opioid administration and obtained a VAS pain score of 1-2. Length Of Stay while in the ICU 48 hours postoperatively and extubated less than 18 hours, after being extubated there was no coughing, bucking, or pain. Patients do not complain of postoperative nausea and vomiting, fluid diet nutrition can be given early, and on the 3rd postoperative day, the patient can move to an HCU. The use of the OFA technique in this craniotomy tumor removal procedure was found to be hemodynamically stable intraoperatively and postoperatively the patient did not complain of postoperative nausea and vomiting. In these 3 patients, good outcomes were obtained, with rapid recovery without any surgical complications. Opioid Free Anesthesia (OFA) technique can be performed with excellent perioperative management and the selection of anesthetic drugs with TIVA is a combination that can be considered for future studies according to the ERAS protocol in patients with posterior fossa tumors.

Conclusion

Opioid Free Anesthesia can be performed in posterior fossa tumor patients undergoing craniotomy tumor removal procedure. The OFA not only minimizes opioid side effects but allows rapid recovery. ERAS protocol in infratentorial tumors can be implemented with the use of opioid replacement drugs such as dexmedetomidine so that patient outcomes are even better after brain tumor surgery.

Acknowledgments: We would like to express our sincere gratitude to Neuronesthesia and critical care of Padjadjaran University for their invaluable support and contributions to this study.

Conflict of interest: None

Financial support: This study supported by Padjajaran University Bandung, Indonesia.

Ethics statement: This study was conducted in accordance with the ethical standards. This study has obtained informed consent from the patient. The confidentiality and privacy of the participants were rigorously maintained throughout the study.

References

1. Rane BR, Gaikwad DS, Jain AS, Pingale PL, Gujarathi NA. Enhancement of pioglitazone hydrochloride solubility through liquisolid compact formulation using novel carrier neusilin Us2. Pharmacophore. 2022;13(3-2022):64-71.
2. Patel P, Patel P, Mahajan A, Koradia S, Saluja A, Shah K. Formulation, evaluation, and optimization of diacerein loaded transferosomal gel for arthritis. Pharmacophore. 2022;13(2-2022):7-16.
3. Sultana A, Torres D, Schumann R. Special indications for Opioid Free Anaesthesia and Analgesia, patient, and procedure-related: Including obesity, sleep apnoea, chronic obstructive pulmonary disease, complex regional pain syndromes, opioid addiction, and cancer surgery. Best Pract Res Clin Anaesthesiol. 2017;31(4):547-60. doi:10.1016/j.bpa.2017.11.002
4. Hassan F, Hatah E. A thematic analysis of non-pharmacological intervention strategies in the management of diabetic patients in Malaysia. Arch Pharm Pract. 2022;13(3-2022):62-9.
5. Al Shidhani A, Al Salmani A, Al Saidi Y, Al Shehhi M, Al Khanjari H, Al Aamri M, et al. Polypharmacy and medication compliance among patients with type 2 diabetes in Oman: A cross-sectional study. Arch Pharm Pract. 2022;13(3-2022):48-53.
6. Khozenko A, Lamperti M, Velly L, Simeone P, Tufegdzic B. Role of anaesthesia in neurosurgical enhanced recovery programs. Best Pract Res Clin Anaesthesiol. 2021;35(2):241-53. doi:10.1016/j.bpa.2020.11.001
7. Hagan KB, Bhavsar S, Raza SM, Arnold B, Arunkumar R, Dang A, et al. Enhanced recovery after surgery for oncological craniotomies. J Clin Neurosci. 2016;24:10-6. doi:10.1016/j.jocn.2015.08.013
8. Madani B, Burzangi A, Alkreathy H, Karim S, Shaik RA, Khan L. Thymoquinone prevents doxorubicin-induced hepatic-injury by mitigating the impairment of mitochondrial respiration and electron transport. Int J Pharm Res Allied Sci. 2022;11(3-2022):89-97.
9. Tonkovic D, Stambolija V, Lozic M, Martinovic P, Pavlovic D, Sekulić A, et al. Scalp block for hemodynamic stability during neurosurgery. Period Biol. 2015;117(2):247-50.
10. Darmawikarta D, Sourour M, Couban R, Kamath S, Reddy KK, Shanthanna H. Opioid-free analgesia for supratentorial craniotomies: A systematic review. Can J Neurol Sci. 2019;46(4):415-22.
11. Cottrell JE, Patel P. Cottrell and patel's neuroanesthesia 7th edition. Elsevier Health Sciences; 2022.
12. Lak AM, Khan YS. Cerebellopontine angle cancer. [Updated 2023 May 20]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK559116/
13. Marinelli JP, Beeler CJ, Carlson ML, Caye-Thomasen P, Spear SA, Erbele ID. Global incidence of sporadic vestibular schwannoma: A systematic review. Otolaryngol Head Neck Surg. 2022;167(2):209-14.
14. Markovic BJ, Karpe B, Potocnik I, Jerin A, Vranic A, Novak-Jankovic V. Effect of propofol and sevoflurane on the inflammatory response of patients undergoing craniotomy. BMC Anesthesiol. 2016;16(18):1-8.
15. Chand MB, Thapa P, Shrestha S, Chand P. Peri-operative anesthetic events in posterior fossa tumor surgery. Postgrad Med J NAMS. 2012;12(2).
16. Mirski MA, Lele AV, Fitzsimmons L, Toung TJ. Diagnosis and treatment of vascular air embolism. Anesthesiology. 2007;106(1):164-77.
17. Rozet I, Vavilala MS. Risks and benefits of patient positioning during neurosurgical care. Anesthesiol Clin. 2007;25(3):631-53. doi:10.1016/j.anclin.2007.05.009
18. Wajekar AS, Oak SP, Shetty AN, Jain RA. A prospective, comparative, randomized, double-blind study on the efficacy of the addition of clonidine to 0,25% bupivacaine in scalp block for supratentorial craniotomies. Indian J Anesth. 2016;60(1):39-43.
19. Kerfeld MJ, Hambsch ZJ, Mcentire DM, Kirkpatrick DR, Cai J, Youngblood CF. Physiologic advantages of peripheral nerve blockade translate to decreased length of stay and improved patient satisfaction. Anesthesiol Open J. 2016;1(1):4-14.
20. Moharari RS, Emami P, Neishaboury M, Sharifnia SH, Kianpour P, Hatam M, et al. Scalp nerve block for enhanced pain control and analgesic optimization in elective craniotomy: A randomized controlled trial with analgesia nociception index monitoring. World Neurosurg. 2024;1-6. doi:10.1016/j.wneu.2024.05.144
21. Chia PA, Cannesson M, Bui CC. Opioid free anesthesia: Feasible? Curr Opin Anesthesiol. 2020;33(4):512-7. doi:10.1097/ACO.0000000000000878
22. Krisna IB, Sutawan J, Putu I, Suarjaya P, Juwita N, Prabowo Y. Teknik anestesi bebas opioid dalam mendukung konsep ERAS pada kraniotomi reseksi tumor metastasis otak opioid free anesthetic technique in supporting the ERASConcept in brain metastatic tumor resection craniotomy. J Neuroanestesi Indones. 2023;12(3):149-58.
23. Bohringer C, Astorga C, Liu H. The benefits of opioid-free anesthesia and the precautions necessary when employing it. Transl Perioper Pain Med. 2020;7(1):152-7.
24. Anupama AS, Kaushal A, Waindeskar V, Saigal S, Jain A, Kumar H. Comparison of opioid-based versus opioid-sparing anesthesia in patients undergoing glioma surgery. Cureus. 2024;16(2):1-8. doi:10.7759/cureus.54153
25. Christian B, Carlos A, Hong L. The benefits of opioid free anesthesia and the precautions necessary when employing it. Transl Perioper Pain Med. 2019;7(1):152-7. doi:10.3390/cancers15010064
26. Shiferaw AA, Negash AY, Tirsit A, Kunapaisal T, Gomez C, Theard MA, et al. Perioperative care and outcomes of patients with brain tumors undergoing elective craniotomy: Experience from an ethiopian tertiary-care

hospital. World Neurosurg. 2024;181:e434-46. doi:10.1016/j.wneu.2023.10.077
27. Bugada D, Drotar M, Finazzi S, Real G, Lorini LF, Forget P. Opioid-free anesthesia and postoperative outcomes in cancer surgery: A systematic review. Cancers (Basel). 2023;15(1):1-9. doi:10.3390/cancers15010064
28. Olausson A, Svensson CJ, Andréll P, Jildenstål P, Thörn SE, Wolf A. Total opioid-free general anaesthesia can improve operative outcomes after surgery, without evidence of adverse effects on patient safety and pain management: A systematic review and meta-analysis. Acta Anaesthesiol Scand. 2022;66(2):170-85. doi:10.1111/aas.13994
29. Belouaer A, Cossu G, Papadakis GE, Gaudet JG, Perez MH, Chanez V, et al. Implementation of the enhanced recovery after surgery (ERAS®) program in neurosurgery. Acta Neurochir (Wien). 2023;165(11):3137-45. doi:10.1007/s00701-023-05789-y
30. Mishra R, Kapoor I, Mahajan C, Prabhakar H. Enhanced recovery after surgery: Neuroanaesthetic perspective. J Neuroanaesth Crit Care. 2017;04(01):017-22.
31. Liu B, Liu S, Zheng T, Lu D, Chen L, Ma T, et al. Neurosurgical enhanced recovery after surgery ERAS for geriatric patients undergoing elective craniotomy: A review. Medicine (Baltimore). 2022;101(33):e30043.
32. Uribe AA, Stoicea N, Echeverria-Villalobos M, Todeschini AB, Gutierrez AE, Folea AR, et al. Postoperative nausea and vomiting after craniotomy: An evidence-based review of general considerations, risk factors, and management. J Neurosurg Anesthesiol. 2021;33(3):212-20.
33. Loo KY, Che Omar S, Mohamad Zaini RH, Wan Hassan WMN, Seevaunnamtum P. A comparison of the effects of prolonged infusion of propofol 2 % and 1 % during total intravenous anaesthesia using target-controlled infusion technique for elective neurosurgery. Malays J Med Sci. 2022;29(4):75-87.
34. Zhao Y, He J, Yu N, Jia C, Wang S. Mechanisms of dexmedetomidine in neuropathic pain. Front Neurosci. 2020;14:330. doi:10.3389/fnins.2020.00330
35. Liu X, Li Y, Kang L, Wang Q. Recent advances in the clinical value and potential of dexmedetomidine. J Inflamm Res. 2021;14:7507-27.
36. Liaquat Z, Xu X, Zilundu PLM, Fu R, Zhou L. The current role of dexmedetomidine as neuroprotective agent: An updated review. Brain Sci. 2021;11(7).
37. Wang K, Wu M, Xu J, Wu C, Zhang B, Wang G, et al. Effects of dexmedetomidine on perioperative stress, inflammation, and immune function: Systematic review and meta-analysis. Br J Anaesth. 2019;123(6):777-94. doi:10.1016/j.bja.2019.07.027
38. Nguyen A, Mandavalli A, Diaz MJ, Root KT, Patel A, Casauay J, et al. Neurosurgical anesthesia: Optimizing outcomes with agent selection. Biomedicines. 2023;11(2):372.
39. Butterworth JF, David CM, John DW. Morgan & Mikhail's clinical anesthesiology. 7th Edition. McGraw Hill LCC. United States; 2022.
40. Zeng M, Xu X, Li R, Zhang X, Ma T, Cui Q, et al. Dexmedetomidine prevents chronic incisional pain after brain tumor resection: A secondary analysis of the randomized control trial. Anesth Analg. 2024;138(4):839-47. doi:10.1213/ANE.0000000000006563
41. Asgari S, Behnaz F, Ommi D, Zandpazandi S, Mirahmadi Eraghi M. The effect of Dexmedetomidine on suppression of the bispectral index score and hemodynamic response during laryngoscopy and intubation in addicted patients in supratentorial brain tumor surgery, a randomized double-blinded controlled trial. Tren Anaesth Crit Care. 2023;53.
42. Sriganesh K, Syeda S, Shanthanna H, Venkataramaiah S, Palaniswamy SR. Effect of opioid versus non-opioid analgesia on surgical pleth index and biomarkers of surgical stress during neurosurgery for brain tumors: Preliminary findings. Neurol India. 2020;68(5):1101-5. doi:10.4103/0028-3886.294559
43. Kaye AD, Chernobylsky DJ, Thakur P, Siddaiah H, Kaye RJ, Eng LK, et al. Dexmedetomidine in enhanced recovery after surgery (ERAS) protocols for postoperative pain. Curr Pain Headache Rep. 2020;24(5).
44. Aditiarso C, Laksono BH. Perioperative management of neuroanesthesia in patients with supratentorial tumors who have excised tumors using neuroprotection technique and total intravenous anesthesia. J Anaesth Pain. 2024;5(2):45-50.
45. Esmaeeli S, Motayagheni N, Bastos AB, Ogilvy CS, Thomas AJ, Pollard R, et al. Propofol-based anesthesia maintenance and / or volatile anesthetics during intracranial aneurysm repair: A comparative analysis of neurological outcomes. J Clin Med. 2023;12(21):6954. doi:10.3390/jcm12216954
46. Irwin MG, Chung CKE, Ip KY, Wiles MD. Influence of propofol-based total intravenous anaesthesia on peri-operative outcome measures: A narrative review. Anaesthesia. 2020;75:e90-e100. doi:10.1111/anae.14905
47. Kannabiran N, Bidkar PU. Total intravenous anesthesia in neurosurgery. J Neuroanaesthesiol Crit Care. 2018;5(03):141-9. doi:10.1055/s-0038-1673544
48. Santos CMT, Pereira CU, Chaves PHS, Tôrres PTR de L, Oliveira DM da P, Rabelo NN. Options to manage postcraniotomy acute pain in neurosurgery: No protocol available. Br J Neurosurg. 2021;35(1):84-91. doi:10.1080/02688697.2020.1817852
49. Bisri DY, Hallis IK, Saputra TA, Bisri T. Brain relaxation score on craniotomy brain tumour removal with adjuvant thiopental and dexmedetomidine: A case report. J Adv Pharmacy Educ Res. 2023;13(3-2023):73-8. doi:10.51847/CTKVDUSITR
50. Fernández-Méndez R, Wan Y, Axon P, Joannides A. Incidence and presentation of vestibular schwannoma: A 3-year cohort registry study. Acta Neurochir (Wien).

2023;165(10):2903-11. doi:10.1007/s00701-023-05665-9

51. Jagannathan S, Krovvidi H. Anaesthetic considerations for posterior fossa surgery. Contin Educ Anaesthesia, Crit Care Pain. 2022;14(5):202-6. doi:10.1093/bjaceaccp/mkt056
52. Menegaz de Almeida A, Viana P, Marinheiro G, Hoffmann Relvas J, Lopes L, Lima Guilherme G, et al. Hypertonic saline solution versus mannitol for brain relaxation during craniotomies: A systematic review and updated meta-analysis. Neurosurgery. 2024;95(3):517-26.
53. Pérez de Arriba N, Antuña Ramos A, Martin Fernandez V, Rodriguez Sanchez M del C, Gonzalez Alarcon JR, Alvarez Vega MA. Risk factors associated with inadequate brain relaxation in craniotomy for surgery of supratentorial tumors. Cureus. 2022;14(5):e25544.
54. Ng JH, Maheshwari D. Anaesthesia for posterior cranial fossa surgery. World Fed Soc Anaesthesiol. 2023;(August):1-8.
55. Hayes SJ, Nijs K, Venkatraghavan L. Year in review: Synopsis of selected articles in neuroanesthesia and neurocritical care from 2023. J Neuroanaesth Crit Care. 2024.