Review Article

DOI: 10.7860/JCDR/2026/85046.23421

Optimising Perioperative Care in Craniotomy Patients : A Narrative Review of Opioid-free Anaesthesia Approaches

Anaesthesia Section

PAYODHI MODI[1], SANJOT NINAVE[2]

ABSTRACT

Opioid-free Anaesthesia (OFA) for craniotomy is a method employed increasingly for intraoperative and postoperative pain management with reduced opioid side-effects. Standard opioid regimens, although best for analgesia, cause respiratory depression, sedation, nausea and emesis. OFA employs multimodal therapy and utilises regional modalities, such as scalp blocks and systemic non opioid analgesics, including dexmedetomidine, ketamine, lidocaine, acetaminophen, Non Steroidal Anti-Inflammatory Drugs (NSAIDs) and gabapentinoids, in an effort to preserve stable cerebral physiology and thereby prevent stress reactions. This approach aims to achieve a stable haemodynamic and analgesic profile. The intraoperative management of OFA is supported by titration of the anaesthetics mentioned above, with vigilant observation and add-on depth monitoring of anaesthesia and nociception to maintain analgesia during prolonged and severe stimulation, such as skull pinning, dura opening and incision. Postoperative multimodal pain control is extended for a sufficient time to avoid opioids but encourages recovery and allows early neurologic evaluation. OFA reduces opioid side-effects, optimises patient comfort and even hospital stay, but heterogeneity of population, protocol and outcome necessitates individual treatment and close observation. Risk with OFA is also present, such as haemodynamic instability, residual sedation and insufficiency of analgesia and therefore necessitates close observation and management by rescue analgesic therapy. This narrative review aims to evaluate OFA in terms of pharmacology, intraoperative technique, postoperative outcome, theoretical advantage and limitation and value added in the capacity to differentiate a global view, aggregate deficits of knowledge and build lines of future research with the objective of systematising treatment and maximising perioperative care of neurosurgery patients. The scope of this review extends to examining the broader implications of OFA protocols in the context of reducing opioid use, promoting patient safety and optimising postoperative recovery. It also emphasises the need for future research to establish standardised, evidence-based guidelines that could further enhance the efficacy and safety of OFA in neurosurgery.

Keywords: Analgesics, Cerebral perfusion, Dexmedetomidine, Neurosurgery, Postoperative pain

INTRODUCTION

The OFA for craniotomy is an immensely useful modality to administer sufficient intraoperative as well as postoperative analgesia without presenting the patient with any risk of inducing any notable opioid side-effects, such as respiratory depression, sedation, nausea and neurologic examination impairment. The rationale for doing so is that they have specialised neurosurgical needs, whereby stable cerebral physiology, balanced neurologic assessment and protection against respiratory compromise are of paramount importance. Through integration of the use of non opioid and regional drug regimens, anaesthesiologists try to administer analgesia under haemodynamic stability regardless of opioid use. Local block or scalp infiltration blocks are the foundation upon which such procedures are based, obliterating the nociceptive burst associated with craniotomy [1-4].

Multimodal drug administration, such as ketamine, lidocaine and dexmedetomidine, is given regularly for analgesia, blunting stress response and haemodynamic stability. Multimodal adjuvant drug supplementation with NSAIDs, gabapentinoids and acetaminophen is given. The drugs are titrated to the depth of anaesthesia with nociception monitoring in an attempt at having maximal analgesia with the minimum amount of impairment of brain relaxation and uncontrolled sedation with high levels of stimulus, such as skull pinning and incision. Postoperatively, the rescue opioid dose has been lower, with fewer opioid-related complications and excellent recovery profiles. The effects remain limited, inconsistent and of minimal benefit, especially considering the widespread issues of pain and distress, including refractory sedation and haemodynamic instability caused by some adjuvants [5,6].

This review aims to evaluate the role of OFA use in craniotomy, document pharmacologic and regional techniques utilised their impact on intraoperative care and postoperative recovery and outline research avenues. This serves as a proposal to evaluate the potential effectiveness and limitations of the intervention and to identify key areas for further research aimed at optimising protocols and improving patient outcomes in neurosurgical care.

DISCUSSION

Challenges in Physiologic and Pharmacologic Management During Craniotomy

Control of anaesthesia during craniotomy is very challenging. The primary targets are maintaining cerebral perfusion pressure, controlling Intracranial Pressure (ICP) and ensuring autoregulation. While opioids are efficient for pain relief, their use is complicated by side-effects such as respiratory depression, which can lead to hypercapnia, cerebral vasodilatation and rising ICP. These factors are particularly critical during neurosurgical procedures, as maintaining optimal cerebral blood flow and preventing ICP increases are essential for patient safety [1]. Sedation and emesis prolong neurologic recovery and assessment, which complicates the early detection of neurological deficits and renders other interventions more appealing to neurosurgeons. The pharmacological principles of OFA during craniotomy include maintaining uninterrupted medication control to provide analgesia and stabilise autonomic function without interfering with cerebral physiology [7,8].

Ketamine and dexmedetomidine are sympatholytic drugs with preserved ventilation effort and must be tightly controlled for

their haemodynamic effect. Ketamine, while effective in providing analgesia and preventing sympathetic hyperactivity, can cause dose-dependent increases in blood pressure and heart rate, which require careful management in craniotomy patients to avoid elevated ICP [9,10]. Intravenous lidocaine produces analgesia and an anti-inflammatory effect. However, it can also have potential side-effects such as neurotoxicity if used inappropriately in large doses and gabapentinoids, NSAIDs and acetaminophen provide systemic adjuvants in the management of central sensitisation and postoperative pain. These drugs are generally well-tolerated but can cause side-effects like gastrointestinal irritation (NSAIDs) or sedation (gabapentinoids) [11]. They form the cornerstone of OFA by incorporating native techniques, such as scalp blocks, which help target specific neural areas to reduce pain perception while maintaining haemodynamic stability. This approach aims to balance smooth recovery, cerebral protection and effective analgesia in patients undergoing craniotomy. Despite their efficacy, the challenge remains in ensuring that these agents disrupt the brain's delicate balance of perfusion, oxygenation and pressure regulation during surgery [9,12,13].

Components of an OFA Regimen

An OFA craniotomy regimen is based on a multimodal regimen with regional techniques, systemic adjuvants and anaesthetic medication titration for the attainment of balanced analgesia with opioid sparing. Scalp or surgical site local block, regional anaesthesia, or direct blocking of scalp and periosteal nociceptive nerve fibers is most useful. Regional methods radially anaesthetise incision-stimulated haemodynamic response, craniotomy and skull pinning and decrease postoperative opioid use and pain [1,12,14].

Systemic medication is selected to complement the local blocks and provide additional analgesia, sedation and haemodynamic stabilisation. Supplementation with dexmedetomidine causes anxiolysis, analgesia and sympatholysis without respiratory depression. Ketamine, through blockade of N-methyl-D-aspartate (NMDA) receptors, has an opioid-sparing action and maximal analgesia employed in states of hyperstimulation. Infusions of lidocaine are administered for adjunct analgesic and anti-inflammatory action and blunting of central sensitisation. NSAIDs, gabapentinoids and acetaminophen in the multimodal regimen supplement them. Titration of anaesthetic depth requires nociception monitoring to optimise drug delivery without over-sedation. These drugs represent an integrated practice of prevention of opioid dependence at the expense of proper analgesia, cerebral stability and optimal postoperative recovery [7,9,12,15]. [Table/Fig-1] depicts the various components that can be used in OFA [2,6,9,11,16-23].

Component/ Technique	Typical dose/ Regimen	Clinical role/ Rationale	Considerations
Scalp Block [11,16]	2-3 mL of 0.5% ropivacaine or bupivacaine per nerve, targeting key scalp nerves bilaterally	Provides regional analgesia for scalp incision, skull pinning and craniotomy; attenuates nociceptive input and haemodynamic responses	Must respect maximum local anaesthetic doses; anatomical precision is essential
Dexmedetomidine [17,18]	Loading dose: 1 µg/kg over 10 min, Maintenance: 0.3-0.7 µg/kg/h	Provides sedation, anxiolysis and analgesia without respiratory depression; blunts sympathetic responses	May cause bradycardia or hypotension; requires close haemodynamic monitoring
Ketamine [9,19]	Loading dose: 0.25 mg/kg, Maintenance: 0.0625-0.125 mg/kg/h	NMDA receptor antagonism reduces central sensitisation and has an opioid-sparing effect, especially useful in hyperalgesic states	Monitor for emergence reactions or sympathomimetic effects; avoid in elevated ICP unless closely managed
Lidocaine [20]	Loading dose: 1.5 mg/kg, Maintenance: 0.5 mg/kg/h	Provides systemic analgesia and anti-inflammatory effects; reduces postoperative pain and opioid need	Monitor for signs of systemic toxicity; avoid in patients with cardiac conduction abnormalities
NSAIDs (e.g., Ketorolac) [21]	Ketorolac 30 mg i.v. intraoperatively or postoperatively	Provides analgesia via COX inhibition; reduces prostaglandin-mediated pain and inflammation	Caution in patients with bleeding risk, renal impairment, or gastrointestinal disease
Acetaminophen (Paracetamol) [22]	1 g i.v. every 6-8 hours	Baseline non opioid analgesia with a good safety profile; complements other agents in a multimodal approach	Monitor cumulative dose to prevent hepatotoxicity, especially in patients with liver dysfunction
Gabapentinoids (e.g., Gabapentin) [23]	600 mg orally the night before and 2 hours preoperatively	Modulates calcium channels to reduce neuropathic pain and central sensitisation; supports opioid sparing	May cause sedation or dizziness; dose adjustment needed in renal impairment
Multimodal Integration Strategy [2,6]	Customised combination of regional and systemic agents	Achieves effective analgesia, minimises opioid use and supports stable cerebral and haemodynamic physiology	Requires careful planning and individualised dosing to avoid drug interactions or adverse effects

[Table/Fig-1]: Various components employed in OFA [2,6,9,11,16-23].

Intraoperative Planning and Monitoring

Intraoperative care of OFA during craniotomy is to optimise the analgesia, haemodynamic stability and cerebral function for uneventful surgery. Adjuvants such as dexmedetomidine and ketamine bolus supplementation must be preemptively controlled at main noxious stimulus incisions, including scalp, skull pinning and dural opening, by incorporating regional intervention. Scalp infiltration or block is particularly useful at such sites to eliminate sympathetic response and manage systemic drug dependence. However, careful management of haemodynamics is crucial, as dexmedetomidine can induce hypotension, which may require the use of vasoactive agents to maintain stable blood pressure during surgery. Emergence from anaesthesia is also significant, as quick and consistent neurologic screening must be performed following cranial surgery. OFA protocols, by reducing opioid use, can facilitate faster and clearer neurologic evaluations during emergence, minimising sedation and respiratory depression that may mask important neurological deficits. Intraoperative care and monitoring are of the greatest significance. Depth of anaesthesia can be measured by processed electroencephalographic monitors and nociception monitors to titrate non opioid analgesics with extremely unreliable stimulation. Cerebral perfusion pressure and infusion rates are maintained without modification and titrated vasoactive support as needed. Ventilation must be rigorously regulated to prevent normocapnia or mild hypocapnia from escaping the harmful effect of hypercapnia on ICP. Ketamine and lidocaine's effects on CO_2 reactivity further complicate the ventilation strategy, as both can alter respiratory drive and blood gas dynamics, making precise ventilation management even more critical to ensure proper cerebral oxygenation and ICP control. Both these practices are synergistically used to combine multimodal non opioid drugs, regional anaesthesia methods and monitoring equipment for effective use. The goals are to maintain stable intraoperative analgesia, preserve cerebral physiology and ensure the best possible postoperative recovery, which have been achieved to varying degrees with opioid type anaesthetics [16,24,25].

Postoperative Analgesia and Recovery

Postoperative recovery following craniotomy is especially difficult, with effective analgesia achieved without disrupting neurologic monitoring and without producing sedation that will result in a delay in the detection of complications. OFA regimens utilise multimodal, synergistic methods to complement scalp block, fixed-

dose oral dosing of NSAIDs and acetaminophen and intravenous administration of drugs such as dexmedetomidine or lidocaine for a few hours of early recovery, if necessary. These are the interventions implemented in an effort to assist in achieving additional pain control with reduced utilisation of rescue opioids. Clinical practice shows that OFA patients exhibit fewer side-effects of nausea, vomiting and respiratory depression compared to opioid treatment. Satisfactory pain relief will be achieved; however, careful observation must be performed to detect and manage breakthrough pain promptly. Low levels of short-acting opioids are feasible to use on an as-needed basis as rescue therapy without sacrificing the entire opioid sparing regimen. Heterogeneity of action of the adjunct drugs on pain and sedation reminds us to individualise and be cautious. Proper planning guarantees that the intraoperative OFA advantage is realised in recovery, quality outcome and patient safety. Setiadi I et al., (2024), Saputra TA et al., (2024), Krishna JS (2022) and all found that OFA resulted in significant improvements in postoperative recovery, with patients reporting reduced pain levels and fewer complications such as opioid-related side-effects. The use of non opioid analgesics, such as dexmedetomidine, lidocaine and regional techniques, enhanced pain control while minimising the need for opioids. The studies highlighted that the incorporation of OFA into clinical practice led to faster recovery, more stable vital signs and lower incidences of postoperative nausea and vomiting, supporting the efficacy of opioid-free regimens in improving patient outcomes across various surgical procedures [8,26-30].

Advantages, Disadvantages and Limitations of OFA in Neurosurgery

Opioid reduction or withdrawal protocols help prevent respiratory depression, hypercapnia and elevated ICP, all of which are known to disrupt normal brain physiology. Increased postoperative neurologic examination, decreased sedation and fewer opioid side-effects, such as nausea, vomiting and constipation, also benefit patients. They form the foundation of speeded recovery protocols and can inform more effective recovery strategies after surgery in neurosurgery [1,24,31].

Adjuvant non opioids such as ketamine and dexmedetomidine may induce haemodynamic instability in the form of bradycardia, hypotension, or sympathetically mediated stimulation and need to be intraoperatively closely monitored. The sedative effect of some drugs extends into the postoperative period and makes late extubation or neurologic examination invalid. Adequate pain control continues to be a problem, particularly in such patients with augmented pain tolerance or on less-than-optimal multimodal regimens and rescue analgesia needs to be reserved. While the technique itself shows promise, challenges such as variations in dosing, inconsistent multimodal regimens and outcome heterogeneity further complicate the optimisation of OFA protocols. Heterogeneity of dosage, regimen and outcome decreases dosage comparability. Cost considerations, the need for specialised resources and gaps in training can influence the feasibility of implementing OFA in clinical practice. OFA protocols require a well-equipped perioperative setting, as well as staff familiar with multimodal pain management and advanced monitoring techniques, which may not be universally available, especially in lower-resource environments [1,24,31].

Future Directions

Large-scale randomised controlled trials and everyday practice must be done before making OFA an accepted standard of care for craniotomy in the event of initial positive results. The priority and direction of future research in OFA for craniotomy would be to generate high-level evidence with the assistance of adequately conducted randomised controlled trials. Systemic adjunct dose and combined multimodal regimens must become routine to control and maintain optimal reproducibility during the procedure to allow for precise opioid-based comparisons. Objective nociceptive and analgesic efficacy is contrasted with haemodynamics and cerebral physiology to allow dosing and safety on an individual basis. Long-term results, such as the impact on chronic post-craniotomy pain, patient satisfaction and outcome, are poorly followed up and are of greatest interest to examine in future research. Research must place greater emphasis on long-term outcomes, including chronic post-craniotomy pain, cognitive recovery and patient satisfaction, as these are emerging areas of focus that directly impact the quality of life after surgery. Comparison measurement among individual non opioid drugs, infusion treatment regimens and modes also logically best establishes their relative worth and limitations to answer long-term outcomes, such as chronic post-craniotomy pain and cognitive recovery, which deserve more detail, as these are emerging research interests [1,12,24,31].

CONCLUSION(S)

The OFA is a promising strategy in neurosurgical care that provides valid analgesia with decreased opioid-related morbidity and maintains the quality of postoperative neurologic evaluation. By combining local anaesthesia, oxygenation techniques and general anaesthetics within a multimodal regimen, OFA facilitates stable cerebral physiology and enhances more uniform perioperative recovery. Optimal results depend on careful patient selection, customised regimen design and close intraoperative observation. With increasing clinical experience, continuous refinement of OFA protocols will establish best practices and improve patient care within neurosurgery.

REFERENCES

[1] Kutum C, Lakhe P. Opioid-free anesthesia in craniotomy – Current evidence and gaps in implementation. Brain Spine. 2025;5:104287.
[2] Negm EM, Younus MA, Morsy AA, El Gammal SMS, El-Harrisi MA, Sameaa FAA, et al. Opioid-sparing multimodal analgesia for post-craniotomy pain: A randomized, double-blind, placebo-controlled trial. BMC Anesthesiol. 2025;25(1):437.
[3] 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):152-57.
[4] Benyamin R, Trescot AM, Datta S, Buenaventura R, Adlaka R, Sehgal N, et al. Opioid complications and side-effects. Pain Physician. 2008;11(2):S105-S120.
[5] Elvir-Lazo OL, White PF. The role of multimodal analgesia in pain management after ambulatory surgery. Curr Opin Anaesthesiol. 2010;23(6):697-703.
[6] Ban VS, Bhoja R, McDonagh DL. Multimodal analgesia for craniotomy. Curr Opin Anaesthesiol. 2019;32(5):592-99.
[7] Kim SH, Choi SH. Anesthetic considerations for awake craniotomy. Anesth Pain Med. 2020;15(3):269-74.
[8] Setiadi I, Alifahna MR, Halimi RA, Bisri DY. Opioid-free anesthesia in enhanced recovery after supratentorial craniotomies: A case series. J Med Life. 2024;17(12):1061-66.
[9] Abdollahpour A, Saffarieh E, Zoroufchi B. A review on the recent application of ketamine in management of anesthesia, pain, and health care. J Fam Med Prim Care. 2020;9(3):1317-24.
[10] Banik S, Madavi S. Exploring the role of ketamine sedation in critically ill patients: A comprehensive review. Cureus. 2024;16(7):e65836.
[11] Chen Y, Ni J, Li X, Zhou J, Chen G. Scalp block for postoperative pain after craniotomy: A meta-analysis of randomized control trials. Front Surg. 2022;9:1018511.
[12] McCullough IL, Shteamer JW, Erwood AM, Spektor B, Boorman DW, Sharifpour M, et al. Opioid-free anesthesia for craniotomy. J Neurosurg Anesthesiol. 2023;35(1):80-85.
[13] Afonso J, Reis F. Dexmedetomidine: Current role in anesthesia and intensive care. Braz J Anesthesiol. 2012;62(1):118-33.
[14] Chakrabarti R, Tewari A, Sinha A, Ghazanwy M. Awake craniotomy: A qualitative review and future challenges. Saudi J Anaesth. 2014;8(4):529.
[15] Aryan HE, Box KW, Ibrahim D, Desiraju U, Ames CP. Safety and efficacy of dexmedetomidine in neurosurgical patients. Brain Inj. 2006;20(8):791-98.
[16] 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;189:e55-e60.
[17] Kallapur B, Bhosale R. Use of dexmedetomidine infusion in anaesthesia for awake craniotomy. Indian J Anaesth. 2012;56(4):413-15.
[18] Akavipat P, Sookplung P, Lekprasert V, Kasemsiri C, Lerdsirisophon S. Dexmedetomidine for awake craniotomy: Systematic review and meta-analysis. J Clin Neurosci. 2024;127:110765.
[19] Dengler BA, Karam O, Barthol CA, Chance A, Snider LE, Mundy CM, et al. Ketamine boluses are associated with a reduction in intracranial pressure and an increase in cerebral perfusion pressure: A retrospective observational study of patients with severe traumatic brain injury. Tran QK, editor. Crit Care Res Pract. 2022;2022:3834165.

[20] Chandra S, Pryambodho P, Omega A. Evaluation of continuous intravenous lidocaine on brain relaxation, intraoperative opioid consumption, and surgeon's satisfaction in adult patients undergoing craniotomy tumor surgery: A randomized controlled trial. Medicine (Baltimore). 2022;101(36):e30216.
[21] Sriram S, Miller P, Reilly T, Ebrahim G, Ali M, Chowdhury MAB, et al. Safety and efficacy of ketorolac after craniotomy for tumor resection. World Neurosurg. 2025;194:123339.
[22] Graham GG, Davies MJ, Day RO, Mohamudally A, Scott KF. The modern pharmacology of paracetamol: Therapeutic actions, mechanism of action, metabolism, toxicity and recent pharmacological findings. Inflammopharmacology. 2013;21(3):201-32.
[23] Türe H, Sayin M, Karlikaya G, Bingol CA, Aykac B, Türe U. The analgesic effect of gabapentin as a prophylactic anticonvulsant drug on postcraniotomy pain: A prospective randomized study. Anesth Analg. 2009;109(5):1625-31.
[24] Rani US, Panda NB, Chauhan R, Mahajan S, Kaloria N, Tripathi M. Comparison of the effects of Opioid-free Anesthesia (OFA) and Opioid-based Anesthesia (OBA) on postoperative analgesia and intraoperative hemodynamics in patients undergoing spine surgery: A prospective randomized double-blind controlled trial. Saudi J Anaesth. 2024;18(2):173-80.
[25] Mieszczan´ski P, Górniewski G, Ziemian´ski P, Cylke R, Lisik W, Trzebicki J. Comparison between multimodal and intraoperative opioid free anesthesia for laparoscopic sleeve gastrectomy: A prospective, randomized study. Sci Rep. 2023;13(1):12677.
[26] Nasr YM, Waly SH, Morsy AA. Scalp block for awake craniotomy: Lidocaine-bupivacaine versus lidocaine-bupivacaine with adjuvants. Egypt J Anaesth. 2020;36(1):07-15.
[27] Liu Y, Ma W, Zuo Y, Li Q. Opioid-free anaesthesia and postoperative quality of recovery: A systematic review and meta-analysis with trial sequential analysis. Anaesth Crit Care Pain Med. 2025;44(1):101453.
[28] Qin J, Zhang J, Bo J, Ma X, He X. Impact of the absence of opioid anesthesia on postoperative outcome indicators: A systematic review and meta-analysis. Front Med. 2025;12:1639968.
[29] 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.
[30] Krishna J S. Case series: Opioid free anaesthesia. Indian J Clin Anaesth. 2022;9(3):379-81.
[31] Wei Q, Xia M. The progress in the clinical application of opioid-free anesthesia: A narrative review. J Oral Maxillofac Anesth. 2022;1:7.

PARTICULARS OF CONTRIBUTORS:
1. Junior Resident, Department of Anaesthesiology, AVBRH, Datta Meghe Institute of Higher Education and Research, Wardha, Maharashtra, India.
2. Professor, Department of Anaesthesiology, AVBRH, Datta Meghe Institute of Higher Education and Research, Wardha, Maharashtra, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Payodhi Modi,
Junior Resident, Department of Anaesthesiology, AVBRH, Datta Meghe Institute of Higher Education and Research Sawangi, Wardha, Maharashtra-442001, India.
E-mail: payodhimodi@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Oct 25, 2025
- Manual Googling: Jan 30, 2026
- iThenticate Software: Feb 02, 2026 (1%)

ETYMOLOGY: Author Origin

EMENDATIONS: 6

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was informed consent obtained from the subjects involved in the study? No
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Oct 23, 2025**
Date of Peer Review: **Dec 13, 2025**
Date of Acceptance: **Feb 05, 2026**
Date of Publishing: **May 01, 2026**