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Pharmacological Awakening: An indispensable tool for Awake Craniotomy: A Case Report

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1. Abstract

Awake craniotomy allows safe and effective resection of brain tumours near eloquent areas. However, achieving timely and reliable intraoperative awakening is crucial, particularly when pre-existing pathologies and sedative agents delay emergence. This case report highlights a unique instance of pharmacological awakening using etophylline and sodium bicarbonate in a patient undergoing asleep-awake-asleep craniotomy for a left frontal glioma, demonstrating its utility in neurasthenic practice.

2. Introduction

Awake craniotomy has evolved significantly since Wilder Penfield and André Pasquet first introduced it for epilepsy surgery in the early 20th century. Their technique, aimed at preserving eloquent cortex during resection, became a cornerstone of neurosurgical practice globally [1]. The awake-asleep-awake protocol is particularly valuable in lesions involving critical cortical regions like the left frontal lobe.The left frontal lobe governs key executive functions such as decision-making, planning, and working memory [2]. Lesions in this region may disrupt initiation, organization, and adaptive responses, complicating both surgical and functional recovery. Moreover, memory processesparticularly temporal ordering and free recallalong with language functions are frequently impaired [3]. Such impairments can hinder postoperative rehabilitation and necessitate meticulous intraoperative mapping and awake testing.In recent years, pharmacologic agents such as amantadine, methylphenidate, and modafinil have demonstrated potential to facilitate awakening in comatose or sedated patients [4-7]. Despite this, their intraoperative utility remains underexplored. Pharmacologic awakening may be particularly valuable in bridging delayed emergence during awake craniotomy, especially when standard anesthetic weaning proves insufficient.We report a case of delayed arousal in a patient undergoing awake craniotomy for a left frontal glioma, where pharmacological stimulation using etophylline and sodium bicarbonate successfully facilitated timely intraoperative awakening.

3. Case Presentation

A 37-year-old right-handed male presented with occasional headaches and focal seizures over the past six months. MRI revealed a 3.2 x 3.3 x 3.8 cm left frontal glioma abutting the inferior frontal gyrus (Figure 1).Neuropsychological evaluation was within normal limits, with no baseline language or executive deficits. In view of the lesion's proximity to eloquent cortex, the patient was scheduled for an awake craniotomy using our institutional asleep-awake-asleep protocol. After informed consent, the patient was premedicated with intravenous midazolam (0.5 mg) and glycopyrrolate (0.2 mg).

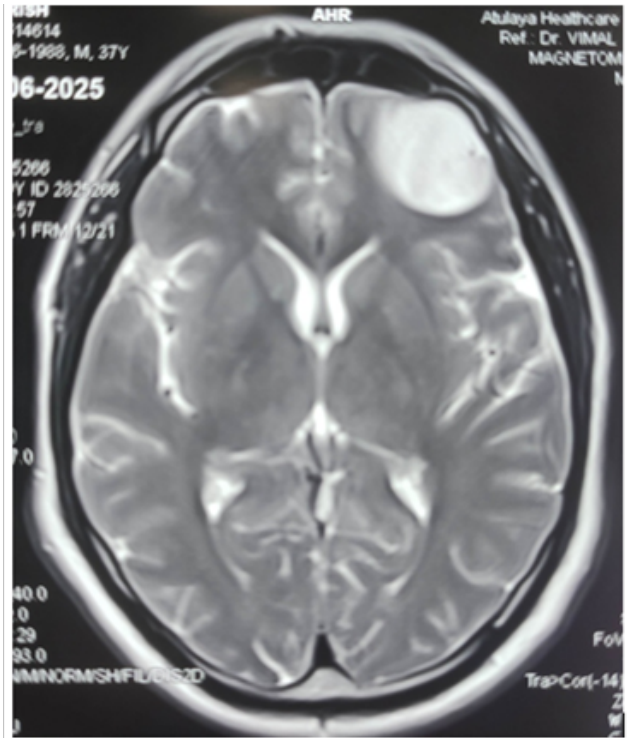

Figure 1: Axial slice of T2 weighted FLAIR image taken at the level of basal ganglia depicting the lesion in frontal lobe.

3.1. Asleep Phase 1

This case report adheres to the CARE (Case Report) guidelines of EQUATOR network. After arrival of patient in the operating room, he was positioned supine on the operation table. Once the venous line and arterial line was secured, the table was adjusted to the requirement of surgical exposure needed for the glioma resection. Oxygen was delivered via nasal cannula from a Dräger Fabius GS anaesthesia workstation.Anaesthesia was induced using the integrated dexmedetomidine-sevoflurane algorithm (Figure 2) [8]. Dexmedetomidine was initiated at 0.6 mcg/kg/min , followed by introduction of sevoflurane as per the algorithm to facilitate scalp block administration. Thereafter bilateral ultrasound-guided scalp block was performed using 0.5% bupivacaine with adrenaline. Intravenous levetiracetam (1000 mg) was infused over 20 minutes, given the patient's history of seizures.Craniotomy was performed under stable hemodynamic, and osmotherapy with 20% mannitol was initiated at dural opening. Dexmedetomidine infusion was tapered to 0.2 mcg/kg/min and stopped before cortical exposure to allow emergence.

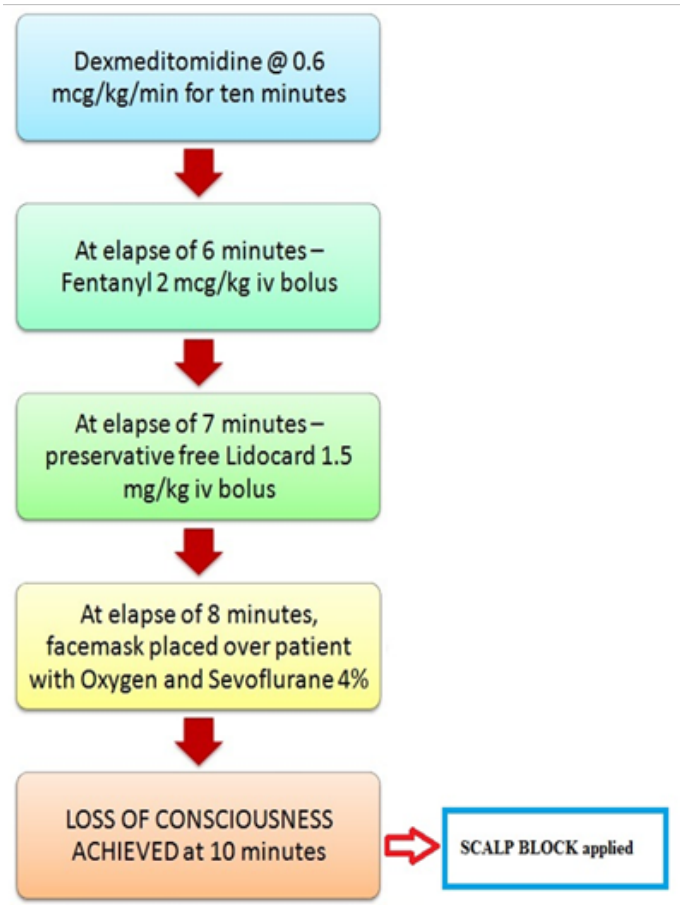

Figure 2: The Dexmedetomedine-Sevoflurane induction algorithm (Sharma et al 9].

3.2. Awake Phase - Crisis of Delayed Emergence

Despite cessation of sedatives and adequate ventilation, the patient remained unresponsive to verbal command for over 30 minutes. End-tidal sevoflurane was confirmed to be zero, and arterial blood gases ruled out metabolic or respiratory causes. At this point, pharmacological stimulation was considered.We administered intravenous etophylline followed by sodium bicarbonate (50 mEq). Within six minutes, the patient opened eyes to command and gave verbal responses. Subsequently, he was able to respond for the following tasks: (i) object naming; (ii) action naming; (iii) semantic association; (iv) sentence completion; (v) odd picture out; (vi) odd word out; (vii) logic and reasoning skill (viii) verb generation; (ix) grammaticality; (x) picture definition and (xi) conversation. The patient cooperated fully and responded accurately throughout. No intraoperative seizures occurred. Resection was completed uneventfully in 3 hours (Figure 3,4)

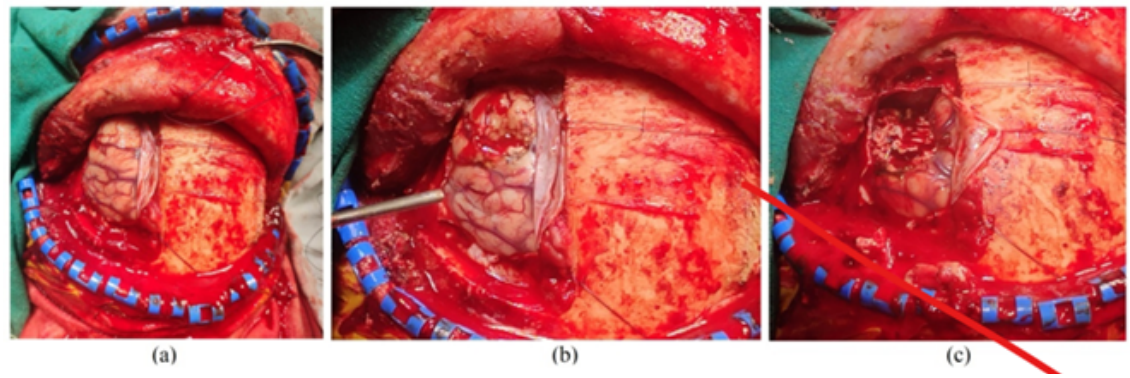

Figure 3 a,b,c: Chronologically arranged intraoperative phases of resection of glioma.

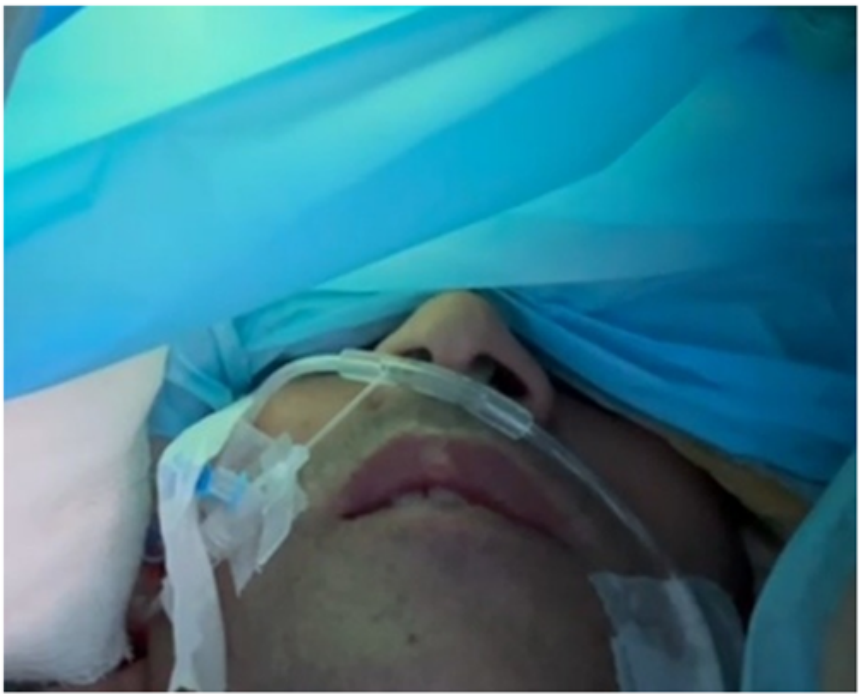

Figure 4 a: Intraoperative condition of patient during awake craniotomy.

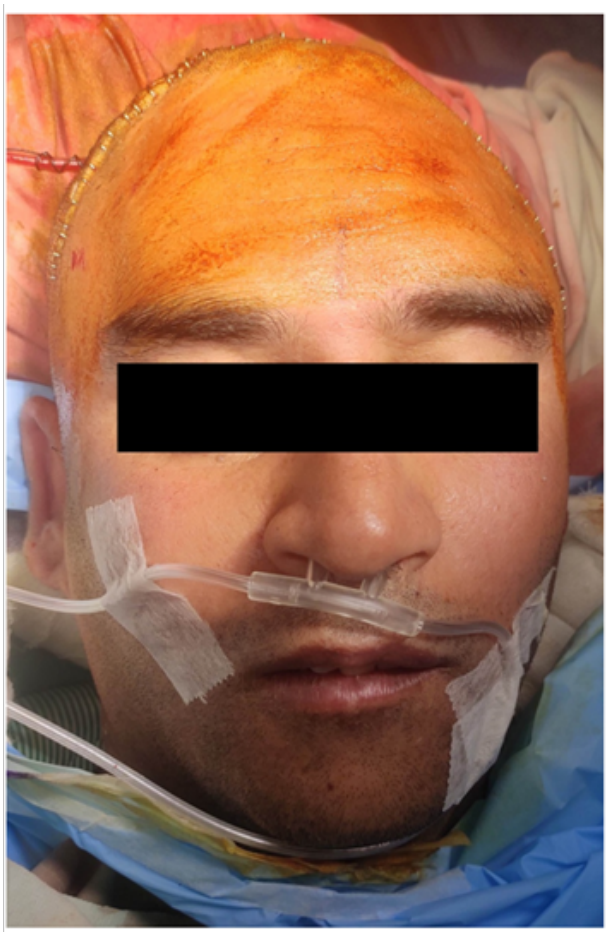

Figure 4b: Patient status after the completion of surgical procedure.

3.3. Asleep Phase 2

At dural closure, dexmedetomidine was re-initiated (0.6 mcg/kg/min) for 10 minutes, followed by maintenance at 0.4 mcg/kg/min until skin suturing. All anaesthetics were discontinued at the end of surgery. The patient emerged with a Glasgow Coma Scale (GCS) of 15 and no new deficits.Total blood loss was 760 ml; urine output was 950 ml. Final fluid balance was +150 ml. Postoperative assessments on day 2 and 7 confirmed preserved language and executive function.

4. Discussion

The successful outcome in this case underscores the importance of timely intraoperative arousal in awake craniotomy, particularly when anesthetic clearance alone is insufficient. Dexmedetomidine, while ideal for conscious sedation, can unpredictably prolong sedation due to its action on α_2-adrenergic receptors in the locus coeruleus [9,10]. Unlike GABAergic sedatives, dexmedetomidine minimally suppresses cortical EEG activity and preserves respiratory drive. However, in some patients—especially with pre-existing cortical compromisereturn of consciousness may lag, posing a threat to the surgical timeline [11].Epothilone is a methylxanthine and adenosine receptor antagonist. It acts by enhancing dopaminergic neurotransmission and stimulating the central nervous system, particularly the basal ganglia [12,13] By counteracting adenosine-induced suppression, it facilitates arousal, motor function, and vigilance. Its role in reversing aesthetic-induced suppression of thalamo-cortical circuits is particularly relevant in neuroanesthesia.In addition, etophylline promotes respiratory drive, cerebral perfusion, and synaptic activity, making it a versatile adjunct in emergence management. The adenosine-dopamine interplay in the basal ganglia, modulated by etophylline, supports faster reactivation of goal-directed behavior and cognitive responsiveness [14].Sodium bicarbonate's role is intriguing. The SLC4A10 gene, encoding a sodium-bicarbonate transporter, is involved in cortical excitability and seizure modulation.15 By modulating extracellular pH, sodium bicarbonate alters neuronal firing thresholds and ionic gradients. This can facilitate depolarization in dormant cortical regions and enhance aesthetic washout, particularly in patients with pre-existing hypoactivity. The combination of etophylline and bicarbonate thus provides dual stimulation—neurochemical and electrochemicalfacilitating arousal when standard aesthetic discontinuation is ineffective.

5. Conclusion

Pharmacological awakening using etophylline and sodium bicarbonate can serve as a rapid and effective solution to delayed emergence during awake craniotomy. In this case, their administration enabled successful language mapping and tumour resection without compromising surgical goals. We propose that pharmacological stimulation be considered an essential tool in the neuroanesthesiologist's armamentarium, particularly when facing emergence delays under dexmedetomidine-based protocols. Further prospective studies and harmonized regional protocols are warranted to establish safe, evidence-based algorithms for intraoperative pharmacologic awakening.

References

1. Bulsara KR, Johnson J, Villavicencio AT. Improvements in brain tumor surgery: the modern history of awake craniotomies. Neurosurg Focus. 2005;18(4):e5.
2. Eslinger PJ, Grattan LM, Geder L. Impact of frontal lobe lesions on rehabilitation and recovery from acute brain injury. NeuroRehabilitation. 1995;5(2):161-82.
3. Laura Brown, Jessica Fish, Daniel C. Mograbi, Keyoumars Ashkan, Robin Morris. The self and self-knowledge after frontal lobe neurosurgical lesions. Cortex. 2023;162:12-25.
4. Lehnerer SM, Scheibe F, Buchert R, Kliesch S, Meisel A. Awakening with amantadine from a persistent vegetative state after subarachnoid haemorrhage. BMJ Case Rep. 2017; 2017:bcr2017220305.
5. Zand Z, Zand F, Asmarian N, Sabetian G, Masjedi M, Beizavinejad Z. Efficacy of oral modafinil on accelerating consciousness recovery in adult patients with moderate to severe acute traumatic brain injury admitted to intensive care unit: a randomized double-blind clinical trial. Neurosurg Rev. 2024;48(1):2.

6. Reynolds JC, Rittenberger JC, Callaway CW. Methylphenidate and amantadine to stimulate reawakening in comatose patients resuscitated from cardiac arrest. Resuscitation. 2013;84(6):818-824.
7. Modi HR, Wang Q, Gd S, Sherman D, Greenwald E, Savonenko AV, Geocadin RG. Intranasal post-cardiac arrest treatment with orexin-A facilitates arousal from coma and ameliorates neuroinflammation. PLoS One 2017;12(9):e0182707.
8. Sharma KK, Chauhan B. Integrated dexmeditomidine-sevoflurane algorithm for anesthetic induction - A viable asset for neurosurgery. SurgNeurol Int. 2024;15:455.
9. Sharma KK, Sharma S, Takkar V, Devi M, Krishnaswami S. Neurocognition after Electroencephalography Guided Anesthetic Induction with Dexmeditomidine in Neurosurgical Patients: A Case Series. J. Neuroscience and Neurological Surgery. 2025;17(3):1-6.
10. Wang B, Wang Y, Wu Q, Huang HP, Li S. Effects of α2A Adrenoceptors on Norepinephrine Secretion from the Locus Coeruleus during Chronic Stress-Induced Depression. Frontiers in Neuroscience. 2017;11:243.
11. Donatiello V, Alfieri A, Napolitano A, Maffei V, Coppolino F, Pota V. Opioid sparing effect of intravenous dexmedetomidine in orthopaedic surgery: a retrospective analysis. J AnesthAnalg Crit Care. 2022;2(1):49.
12. Fuxe K, Ferré S, Genedani S, Franco R, Agnati LF. Adenosine receptor-dopamine receptor interactions in the basal ganglia and their relevance for brain function. PhysiolBehav. 2007;92(1-2):210-7.
13. Pardo M, Paul NE, Collins-Praino LE, Salamone JD, Correa M. The non-selective adenosine antagonist theophylline reverses the effects of dopamine antagonism on tremor, motor activity and effort-based decision-making. PharmacolBiochemBehav. 2020;198:173035.
14. Mirsadeghi MN, Biazar G, Soltanipour S, Rad RS, Madani ZH, Nikbin L. The effect of aminophylline on the recovery profile after hysterectomy: A randomized controlled double-blinded study. Health Sci Rep. 2023;6(6):e1362.
15. Gurnett CA, Veile R, Zempel J, Blackburn L, Lovett M, Bowcock A. Disruption of Sodium Bicarbonate Transporter SLC4A10 in a Patient with Complex Partial Epilepsy and Mental Retardation. Arch Neurol. 2008;65(4):550-553.