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Anesthesia for Brain Tumor Surgery: A Comparative Review of Target-Controlled Infusion Propofol with and without Dexmedetomidine

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ABSTRACT

Brain tumor surgeries pose significant challenges due to high morbidity and mortality rates, often resulting in extended intensive care unit stays and complications from neuroinflammation, such as postoperative cognitive dysfunction. This review compares the efficacy of two anesthesia techniques: target-controlled infusion propofol combined with dexmedetomidine versus propofol alone. It explores the impact of these approaches on immediate and long-term patient outcomes, focusing on inflammatory markers, cognitive function, cost-effectiveness, and the risk of propofol-related infusion syndrome. Total intravenous anesthesia with target-controlled infusion of propofol is preferred for its effectiveness in facilitating faster neurological recovery, reducing neuroinflammatory markers like interleukin-6 and S100B, promoting brain relaxation, and lowering intracranial pressure while preserving cognitive function. Although propofol is effective as a single hypnotic agent when used with opioids and muscle relaxants, there is increasing interest in dexmedetomidine as an adjunct. The combination of dexmedetomidine with propofol may enhance neuroprotection, further reduce inflammation, and lower the incidence of postoperative cognitive dysfunction while providing anesthetic-sparing effects that can reduce costs. Using dexmedetomidine can also mitigate the risk of propofol-related infusion syndrome by lowering propofol consumption, thus reducing the likelihood of lactic acidosis during lengthy surgeries. While initial medication costs may increase with dexmedetomidine, it could lead to long-term savings by minimizing complications and intensive care unit stays. The choice between propofol alone or in combination with dexmedetomidine should be tailored to individual patient needs and institutional resources. Further research is needed to understand the long-term outcomes and economic implications of this combination in brain tumor surgeries.

Keywords: *Target-Controlled Infusion, Propofol, Dexmedetomidine, Brain Tumor Surgery, Neuroanesthesia*.

1. INTRODUCTION

Brain tumor surgeries pose significant challenges due to the complex nature of the brain and the associated risks of morbidity and mortality. Studies indicate concerning outcomes, with a 30-day mortality rate of approximately 8.2% across various tumor types, and a 90-day mortality rate reaching 23% in some cohorts [1]. Complications are common, with an overall morbidity rate of 66%, significantly affecting 34.2% of patients [2]. These complications often lead to extended Intensive Care Unit (ICU) stays due to elevated inflammatory markers, prolonged recovery, cognitive dysfunction, and elevated intracranial pressure [3]. The economic impact is substantial, with median hospitalization cost after craniotomy for tumor resection was approximately $24,504, as length of stay being one of the primary drivers of these costs [4]. Furthermore, patients who developed infections often exacerbated by inflammatory responses which had an average ICU stay of 3.8 days and a mean hospitalization period of 12 days [5].

Propofol-based Total Intravenous Anesthesia (TIVA) is preferred in brain tumor surgeries over volatile anesthetics due to its ability to reduce intracranial pressure (ICP) and enhance brain relaxation, thereby minimizing cerebral swelling. A meta-analysis has demonstrated that propofol significantly lowers ICP compared to volatile anesthetics [6]. Maintaining optimal systemic circulatory parameters is critical for ensuring adequate cerebral perfusion pressure (CPP) during neurosurgery. Given its superior stability in mean arterial pressure, which directly influences CPP, target-controlled infusion is increasingly regarded as the preferred method of anesthesia for intracranial surgeries compared to manually controlled infusion [7]. While

propofol remains effective as a standalone hypnotic agent when combined with opioids and muscle relaxants, there is growing interest in the use of dexmedetomidine as an adjunct. Modern anesthesiologists are increasingly focused on mitigating inflammation and its associated complications. Dexmedetomidine, an alpha-2 adrenergic agonist, has gained attention for its potential to reduce inflammatory markers, enhance hemodynamic stability, decrease opioid requirements, improve recovery profiles, mitigate postoperative cognitive dysfunction (POCD), and ICU stays [8][9].

Despite the growing interest in dexmedetomidine as an adjunct in anesthesia, its necessity and the balance between risks and benefits remain subjects of debate. The economic implications and overall clinical outcomes associated with its use have not been comprehensively reviewed or fully established. Key considerations when comparing anesthesia techniques include their impact on inflammatory responses during surgery, the risk of POCD—a condition that can significantly impair patients' quality of life and the economic ramifications of resource allocation across different approaches [5] [10]. Addressing the risk of metabolic acidosis as a precursor to Propofol-Related Infusion Syndrome (PRIS) is critical to ensure patient safety during prolonged propofol administration in extended surgical procedures [11]. This review evaluates the efficacy and safety of propofol combined with dexmedetomidine compared to propofol alone in brain tumor surgeries, with a particular focus on how various anesthetic strategies influence both immediate and long-term patient outcomes.

2. NEUROANESTHESIA TECHNIQUES

In neuroanesthesia management for brain tumor surgery, the primary goals include enhanced recovery for faster neurological assessment, good hemodynamic stability, brain relaxation, and the ability to lower ICP while preserving cognitive function [6]. Two prominent techniques in neuroanesthesia are TIVA-based propofol and volatile anesthesia. While volatile anesthetics are cost-effective and widely used, they can increase cerebral blood flow and ICP. These effects are particularly pronounced at concentrations exceeding 1.5 mean alveolar concentration (MAC), where volatile anesthetics may impair cerebral autoregulation, increasing the risk of cerebral ischemia [12]. A systematic review and meta-analysis of 14 randomized controlled trials (1,819 patients) compared propofol-based anesthesia and volatile anesthetics for elective craniotomy. Brain relaxation scores were similar between groups after dural opening, but propofol was associated with lower ICP (weighted mean difference: -5.2 mmHg; 95% CI: -6.81 to -3.6) and higher CPP (weighted mean difference: 16.3 mmHg; 95% CI: 12.2 to 20.46). Recovery profiles and postoperative complications were comparable, though propofol led to less postoperative nausea and vomiting [13]. Propofol-based TIVA is considered the anesthesia of choice in neurosurgery due to its ability to reduce ICP, preserve cerebral autoregulation, provide hemodynamic stability, facilitate rapid recovery, reduce postoperative nausea and vomiting, and support intraoperative neuromonitoring (IONM) compatibility [6], [14], [15], [16]. These benefits contribute to improved surgical conditions and better patient outcomes compared to volatile anesthetics. However, prolonged use or high doses of propofol may lead to complications such as hypertriglyceridemia or PRIS [17]. To minimize propofol consumption and its associated side effects, several techniques have emerged as effective alternatives.

TIVA can be administered using two distinct methods: manually controlled infusion (MCI) or target-controlled infusion (TCI) [18]. MCI relies on the anesthesiologist to manually adjust the infusion rate of anesthetic drugs based on clinical observations and the patient's physiological responses [19]. In contrast, TCI utilizes a computerized system that calculates and automatically adjusts the infusion rate to achieve and maintain a specific target concentration of the drug in the blood or effect site [20]. There are limited studies directly comparing TCI and MCI in intracranial surgeries. A study of 50 patients (25 TCI, 25 MCI) with supratentorial intracranial pathology compared target-controlled infusion (TCI) and manually controlled infusion (MCI) for anesthesia. Patients in ASA grades III and IV or with circulatory diseases were excluded. Both groups were comparable in sex, age, BMI, operation time, and lesion volume. TCI-anaesthetised patients showed superior MAP stability across 14 critical time points, which has a direct effect on CPP, making TCI the preferred method for intracranial surgery [7]. Similarly, a study with 71 patients undergoing asleep-awake-asleep epilepsy surgery and found that TCI provided superior hemodynamic stability, with fewer cases of tachycardia (52.9% vs. 0%, $P = .001$) and hypertension (29.4% vs. 0%, $P = .064$) compared to MCI. TCI also enabled faster intraoperative awakening, with TCI patients waking in 12.82 ± 6.93 minutes versus 29.9 ± 9.04 minutes for MCI ($P < .001$) [21]. TCI systems utilize three-compartment pharmacokinetic models that incorporate patient-specific parameters such as age, weight, and sex to optimize drug delivery [22]. Advanced pharmacokinetic modeling, particularly the Schnider model, targets effect-site concentrations (e.g., brain), which is especially beneficial in neurosurgery [23]. TCI systems ensures precise dosing, reduces drug consumption thus prevents drug accumulation by maintaining steady-state concentrations without overshooting [24][25]. TCI demonstrates superior hemodynamic stability, and more precise drug delivery compared to MCI in intracranial surgeries. These advantages make TCI a preferred method for neurosurgical anesthesia, particularly due to its advanced pharmacokinetic modeling and individualized dosing. Furthermore, anesthesiologists can incorporate adjuvant drugs such as dexmedetomidine to further reduce propofol consumption, enhance hemodynamic and CPP stability, and, in this review context, mitigate inflammation and postoperative complications [9], [26], [27], [28].

3. NEUROINFLAMMATION

Brain tumor resection triggers a stress response with neuroendocrine, metabolic, and inflammatory changes. Activation of the hypothalamic-pituitary-adrenal axis and sympathetic nervous system releases stress hormones, causing inflammation through increased pro-inflammatory cytokines like IL-6 and TNF-α, which can persist post-surgery, worsening outcomes [29]. Mechanical craniotomy stress disrupts blood flow, alters intracranial pressure, and can lead to ischemia. Manipulation of brain tissue can cause hematomas and edema, activating inflammatory responses that alter systemic arterial pressure and cerebral blood flow, potentially decreasing cerebral perfusion and leading to ischemia and impaired brain function [30].

To assess inflammation and tissue damage during brain tumor surgery, several inflammatory markers can be measured. IL-6 is a key pro-inflammatory cytokine that increases rapidly after brain injury and correlates with tissue damage extent. C-reactive protein (CRP), an acute phase protein, also rises significantly following major surgery. S100 calcium-binding protein (S100B) is a calcium-binding protein released from damaged astrocytes that indicates blood-brain barrier disruption; elevated levels in serum or cerebrospinal fluid reflect astrocytic damage [31]. Neuron-specific enolase (NSE) provides insight into neuronal injury severity. Matrix metalloproteinases, involved in extracellular matrix remodeling during neuroinflammation, can be measured as indicators of ongoing inflammatory processes. High-mobility group box 1, a damage-associated molecular patterns (DAMPs) released from necrotic cells, propagates inflammation; its levels can be assessed to evaluate inflammatory status after surgery [32].

The Role of Propofol

Research has shown that propofol significantly reduces pro-inflammatory cytokines, such as IL-6 and TNF-α, during surgical procedures. In a randomized controlled trial of 50 patients undergoing robot-assisted laparoscopic radical prostatectomy, the effects of propofol (n=25) and desflurane (n=25) on inflammatory responses were compared. Serum IL-6 levels significantly increased from baseline at T2 (100 minutes after CO2 insufflation) and T3 (10 minutes after CO2 deflation), with propofol showing a lower increase (T2: 5.2 ± 1.1 pg/mL; T3: 6.1 ± 1.4 pg/mL) compared to desflurane (T2: 8.4 ± 2.0 pg/mL; T3: 9.6 ± 2.5 pg/mL) [33].

In another randomized controlled trial with 70 patients undergoing laparoscopic cholecystectomy, the effects of propofol (75 µg/kg/min) were compared to dexmedetomidine (0.5 µg/kg/hour). While dexmedetomidine significantly reduced heart rate and mean arterial pressure ($P < 0.001$), propofol was more effective in lowering serum epinephrine and blood glucose levels, with post-anesthesia epinephrine levels at 95.38 ± 8.14 in the propofol group versus 114.0 ± 14.58 in the dexmedetomidine group. These two findings suggest that while dexmedetomidine stabilizes hemodynamics, propofol alone is sufficient to mitigate stress-induced inflammatory responses during surgery [34].

The Role of Dexmedetomidine as Adjunct

The combination of propofol and dexmedetomidine has been shown to provide synergistic effects on inflammation, particularly in surgical settings. Research indicates that this combination can lead to lower levels of pro-inflammatory cytokines compared to propofol alone, which is significant during surgeries associated with substantial inflammatory responses. In a study involving patients undergoing digestive tract cancer surgery, participants received total intravenous anesthesia (TIVA) with propofol and remifentanil, along with a dexmedetomidine loading dose of 0.5 µg/kg over 10 minutes, followed by a maintenance dose of 0.5 µg/kg/hour. The control group was administered only propofol and remifentanil. Results demonstrated significant reductions in inflammatory markers in the intervention group. Interleukin-6 (IL-6) levels decreased by a standardized mean difference (SMD) of -2.71 (95% CI: -4.46 to -0.97), tumor necrosis factor-alpha (TNF-α) dropped by an SMD of -4.22 (95% CI: -5.91 to -2.54), and C-reactive protein levels were reduced by an SMD of -4.26 (95% CI: -6.16 to -2.36). These findings suggest that dexmedetomidine may help mitigate inflammation during brain tumor surgeries [35].

Another study evaluated dexmedetomidine as an adjunct to TIVA with propofol and sufentanil in patients undergoing coronary artery bypass graft (CABG) surgery. Participants were randomized into two groups: one receiving TIVA alone and the other receiving TIVA plus dexmedetomidine at 0.3 µg/kg/h. The results indicated significant reductions in inflammatory markers in the dexmedetomidine group, with IL-1 levels rising to 30 pg/mL compared to 45 pg/mL in the TIVA group, IL-6 increasing to 90 pg/mL versus 150 pg/mL, and TNF-α rising to 50 pg/mL versus 80 pg/mL in the TIVA group. However, this combination was also associated with increased oxidative stress, as indicated by elevated levels of thiobarbituric acid reactive substances (TBARS), rising to 8 nmol/L in the TIVA plus dexmedetomidine group compared to 5 nmol/L in the TIVA group. Although dexmedetomidine helps reduce neuroinflammation and may enhance cognitive recovery, its application during brain tumor surgery raises concerns regarding oxidative stress. Oxidative stress can lead to cellular damage, trigger inflammation, disrupt the blood-brain barrier, and impair recovery, highlighting the need for careful monitoring to enhance patient outcomes post-surgery [36].

A third study focused on patients with liver cirrhosis undergoing surgery, where participants received either dexmedetomidine or a control regimen without it. Stress hormones such as cortisol and aldosterone were significantly lower in the dexmedetomidine group, indicating its potential to modulate perioperative stress responses. Cortisol levels rose to 12.4 ± 2.1 µg/dL compared to 16.8 ± 3.2 µg/dL in controls, while aldosterone reached 120 ± 15 pg/mL versus 180 ± 20 pg/mL [37]. Lastly, a study comparing dexmedetomidine and propofol for sedation in non-brain injured patients on prolonged mechanical ventilation found that serum levels of neuroprotective markers were significantly lower in the dexmedetomidine group; S100B levels reached 0.25 ± 0.05 µg/L compared to 0.45 ± 0.07 µg/L for propofol [38].

Minimizing inflammatory responses during brain tumor surgeries is crucial due to the delicate nature of brain tissue and the potential for postoperative complications. Evidence suggests that while propofol effectively reduces inflammatory markers, combining it with dexmedetomidine may enhance protective effects against neuroinflammation. However, this combination requires careful monitoring for potential oxidative stress, which can lead to cellular damage, trigger inflammation, disrupt the blood-brain barrier, and impair recovery.

4. POSTOPERATIVE COGNITIVE DYSFUNCTIONS

The stress from craniotomy, particularly under general anesthesia, can lead to neuroinflammation and neuronal apoptosis, significant contributors to postoperative cognitive dysfunction (POCD) [30]. POCD impairs cognitive functions such as memory, attention, and language comprehension, diagnosable via the Mini-Mental State Examination (MMSE) [39]. Approximately 30-80% of POCD cases manifest within the first week after surgery, with 10-60% occurring in the following months [40][41]. A study on non-cardiac surgeries reported a 36,6% incidence of POCD, affecting younger patients as well [42]. The emotional and psychological effects of POCD can significantly disrupt daily activities and quality of life, with 10-30% of patients experiencing symptoms six months post-surgery [43]. Surgical procedures induce sterile trauma, releasing DAMPs that activate immune cells through Toll-like receptor 4 (TLR4) [44]. This triggers inflammatory pathways, producing cytokines like TNF-α and IL-6, which can harm the hippocampus and lead to POCD [45]. Reducing these markers may lower POCD risk.

A meta-analysis involving 26 randomized controlled trials has demonstrated that dexmedetomidine administration is associated with a significantly lower incidence of POCD compared to control groups receiving other anesthetic agents, including propofol. The pooled odds ratio for POCD incidence in the dexmedetomidine group was 0.49 (95% CI 0.39–0.63), indicating a substantial protective effect against cognitive dysfunction following surgery [46]. Additionally, patients receiving dexmedetomidine showed improved MMSE scores on the first postoperative day, further supporting its efficacy in enhancing cognitive function [46]. In specific comparisons, one study investigated the effects of dexmedetomidine as an adjunct to propofol in patients undergoing lobectomy under general anesthesia. This study found that patients who received dexmedetomidine exhibited higher scores on the Montreal Cognitive Assessment and lower incidences of delirium compared to those receiving propofol alone [47]. These findings suggest that dexmedetomidine may mitigate neuroinflammation—an important factor in the development of POCD, by reducing levels of inflammatory cytokines such as TNF-α and IL-6 [28].

Conversely, a randomized controlled trial involving elderly patients undergoing hip or knee arthroplasty indicated that the incidence of POCD was significantly lower in the propofol group (18.2%) compared to those receiving dexmedetomidine (40.0%) [48]. This suggests that while both agents have their merits, propofol may be more effective for short-term cognitive function immediately after surgery. While dexmedetomidine shows promise in reducing POCD and enhancing cognitive outcomes, particularly when used as an adjunct to propofol, further research is necessary to clarify its comparative effectiveness against propofol alone. The existing literature indicates potential neuroprotective benefits from combining these agents, but more direct comparisons are needed to optimize their use in preventing cognitive decline postoperatively.

5. ECONOMIC CONSIDERATIONS

The economic landscape of brain tumor surgeries is shaped by multiple factors influencing both direct and indirect costs. From an anesthesiologist's perspective, there are immediate and long-term costs associated with these procedures. Direct costs arise from the choice of anesthesia, particularly the debate between TIVA using propofol combined with dexmedetomidine versus propofol alone. This decision has significant implications for both cost and patient outcomes, as the use of dexmedetomidine, while more expensive initially, may reduce the need for other anesthetic agents, potentially leading to overall cost-effectiveness [49].

Indirect costs are influenced by the length of hospital stay, especially in inpatient settings with high bed occupancy rates, which significantly impacts total expenses [50], [51]. Balancing these financial considerations with clinical outcomes is crucial for effective patient care. Healthcare providers are increasingly focusing on strategies to minimize ICU time and reduce the risk of POCD, essential for achieving cost-effective treatment while maintaining high-quality care [49].

Direct Cost Benefit of Reduced Drug Used

The combination of dexmedetomidine with propofol-based TIVA demonstrates significant direct cost savings through reduced medication uses. Studies show that patients receiving dexmedetomidine required significantly less fentanyl for anesthetic induction (1.2 [1.0-1.4] vs 1.6 [1.1-2.8] μg/kg, P = 0.02) and 29% less propofol during maintenance (2.2 [1.5-3.0] vs 3.1 [2.4-4.5] mg/kg/h, P = 0.005). During maintenance anesthesia, remifentanil requirements showed a slight reduction, though not statistically significant (0.16 [0.09-0.17] vs 0.14 [0.13-0.21] μg/kg/h, P = 0.3). Furthermore, the dexmedetomidine-propofol combination significantly delayed the first postoperative request for morphine analgesia (median fourth hour vs first hour, P = 0.008), potentially reducing overall postoperative opioid requirements [52].

Another randomized, double-blind trial examined the propofol-sparing effects of dexmedetomidine in spine surgery [53]. The study compared two groups: both received standard anesthesia with propofol, fentanyl, and vecuronium for induction and maintenance, while the intervention group received additional dexmedetomidine (1 μg/kg loading dose, followed by 0.5 μg/kg/h maintenance). The results demonstrated substantial reductions in propofol requirements: induction doses decreased by 48.08% (from 2.37 ± 0.36 to 1.23 ± 0.41 mg/kg), and maintenance requirements reduced by 61.87% (from 12.89 ± 4.95 to 4.92 ± 1.23 mg/kg/h). Importantly, these significant reductions maintained adequate anesthesia depth (bispectral index of 40-60) and hemodynamic stability, with no adverse effects on recovery times or patient safety. These medication savings are particularly significant in neurosurgical procedures, where optimal anesthetic depth must be maintained while minimizing post-operative complications.

Optimal economic benefits in dexmedetomidine use involve a two-phase dosing strategy: a 0.5 μg/kg loading dose over 10 minutes, followed by 0.2 μg/kg/h maintenance infusion, offering the best cost-benefit ratio [54]. Moderate doses (0.6-0.8 μg/kg) control intubation responses and maintain hemodynamic stability, but higher doses increase the risk of bradycardia (4.0% at 0.4 μg/kg to 16.67% at 0.8 μg/kg) [55]. Balancing these factors minimizes other anesthetic use, optimizing patient outcomes while providing substantial cost savings compared to traditional sedation. While direct comparisons are lacking, these findings suggest that combining dexmedetomidine with propofol could optimize resource use and potentially improve patient outcomes, thereby reducing costs. However, conclusions drawn here are tentative, based on extrapolations from available data.

Indirect Cost Benefit: Reduced POCD and ICU Length of Stay

The economic burden of POCD is substantial, although specific costs for brain tumor surgery cases are not well-documented. POCD imposes substantial economic burdens. Patients face increased healthcare costs, with Medicare patients spending an additional $17,275 annually [56]. Caregivers incur out-of-pocket expenses and employment challenges. Healthcare systems bear significant costs, with POCD patients' median annual expenditures reaching $26,881.74 compared to $7,149.35 for non-POCD patients [57].

Recent research has focused on strategies to mitigate POCD risk and improve outcomes. A meta-analysis found that perioperative dexmedetomidine treatment was associated with a significantly reduced incidence of POCD (pooled OR = 0.59, 95% CI 0.45-2.95) and improved Mini-Mental State Examination scores (standardized mean difference = 1.74, 95% CI 0.43-3.05) on the first postoperative day [46]. These findings suggest that adding dexmedetomidine to propofol during brain tumor surgery could potentially reduce the long-term burden and costs associated with POCD. Furthermore, dexmedetomidine has been associated with shorter ICU stays. A meta-analysis comparing dexmedetomidine and propofol in cardiac surgery patients found that dexmedetomidine was linked to significantly shorter ICU stays (mean difference: 0.89 days, 95% CI: 0.04-1.74, p-value: 0.04) [58]. While this study focused on cardiac surgery, it suggests potential benefits in other surgical contexts, including brain tumor surgery.

A comprehensive cost-minimization analysis estimated the total cost per patient per ICU stay to be $21,115 for dexmedetomidine, compared to $27,073 for propofol [59]. Although not specific to brain tumor surgery, and comparing two single drugs (dexmedetomidine vs propofol for ICU sedation), this analysis demonstrates the potential for significant cost savings associated with dexmedetomidine use, primarily driven by reductions in ICU length of stay and required monitoring. Interestingly, a study on elderly patients undergoing hip or knee replacement surgery found that propofol sedation alone showed a significant advantage in terms of short-term POCD incidence compared to dexmedetomidine and midazolam (18.2% vs. 40.0% and 51.9%, respectively) [60]. This highlights the potential cognitive benefits of propofol, which may be further enhanced when combined with dexmedetomidine. Further research is necessary to evaluate the cost-effectiveness of the dexmedetomidine-propofol combination versus propofol alone in a more precise clinical setting. A direct head-to-head comparison of these two anesthetic techniques is crucial to determine their relative economic impacts.

6. RISK OF METABOLIC ACIDOSIS

Understanding propofol-related infusion syndrome (PRIS) is crucial for anesthesiologists during extended procedures like brain tumor surgeries where TCI propofol is often used for its cognitive preservation and ICP management benefits. PRIS, a rare but grave condition, can manifest as metabolic acidosis, cardiovascular dysfunction, rhabdomyolysis, and multi-organ failure, particularly with high-dose or prolonged propofol infusions, despite precise control via TCI [61]. Key risk factors include administration exceeding 48 hours, high doses (>4 mg/kg/hour), critical illness, young age, and concurrent use of catecholamines and glucocorticoids [62]. Early signs of PRIS often manifest as metabolic acidosis, indicated by elevated lactate levels due to mitochondrial dysfunction from the accumulation of long-chain fatty acids. Monitoring electrocardiograms and creatine kinase levels is essential for early detection, with immediate discontinuation of propofol upon identifying abnormalities being a critical intervention [63].

A study from January 2005 to September 2012 analyzed 390 patients undergoing elective neurosurgery, comparing total intravenous anesthesia (TIVA) with propofol to inhalation anesthesia with sevoflurane. Metabolic acidosis rates were similar (11% vs. 13%). Five TIVA patients developed severe metabolic acidosis (pH <7.30, elevated lactate) within 2 to 4 hours after starting propofol infusion, recovering upon discontinuation. While severe metabolic acidosis incidence was not significantly higher, patients receiving propofol may experience metabolic disturbances that could precede PRIS [11].

In another case report, a patient who underwent abdominal aortic aneurysm surgery developed PRIS after receiving propofol for sedation, exhibiting metabolic acidosis and rhabdomyolysis. The patient's condition improved significantly after stopping propofol [64]. Additionally, a neurosurgical patient receiving TCI propofol and remifentanil presented with increasing lactate levels and metabolic acidosis during a prolonged procedure, underscoring cumulative doses of propofol and infusion duration as significant risk factors for PRIS [65].

While some studies indicate a potential risk for metabolic acidosis and PRIS associated with high-dose or prolonged propofol use, others suggest that when used appropriately in surgical settings, propofol may not significantly increase lactate levels or lead to lactic acidosis. Dexmedetomidine may play a role in mitigating these risks due to its ability to reduce the requirement for propofol during anesthesia. In a randomized controlled trial involving 66 patients undergoing elective surgery, researchers found that those receiving dexmedetomidine required significantly less propofol for both induction (median dose reduced from 1.3 mg/kg in the placebo group to 1.0 mg/kg in the dexmedetomidine group, $P = 0.002$) and maintenance (29% reduction from 3.1 mg/kg/h to 2.2 mg/kg/h, $P = 0.005$) [66]. This reduction in propofol usage is clinically significant as lower doses may decrease the risk of developing PRIS.

Another relevant study focused on mechanically ventilated patients with septic shock, examining whether sedation with dexmedetomidine could enhance lactate clearance—a critical factor in assessing metabolic status and potential lactic acidosis. In this randomized controlled trial involving 111 patients, those receiving dexmedetomidine showed improved lactate clearance at six hours compared to those who did not receive it; although this difference was not statistically significant initially ($23.3 \pm 29.8\%$ vs. $11.1 \pm 54.4\%$, mean difference 12.2), it became significant after adjusting for baseline lactate levels (adjusted mean difference 18.5). This finding is particularly relevant as improved lactate clearance could indicate better metabolic stability and a lower risk of developing lactic acidosis or PRIS during prolonged sedation with propofol [67].

While there are indications that high-dose or prolonged use of propofol may lead to metabolic disturbances such as lactic acidosis and PRIS, studies also suggest that when used judiciously—potentially in combination with dexmedetomidine—propofol can be administered safely without significant adverse effects on metabolic status during extended surgical procedures.

7. FUTURE DIRECTIONS

Future research should prioritize developing standardized guidelines for TCI propofol with dexmedetomidine in brain tumor surgeries, focusing on clinical and economic outcomes. Current reviews often target specific populations, such as pediatric patients, or provide general recommendations for craniotomy in adults without comprehensive protocols for anesthetic management [68], [69]. While the World Federation of Societies of Anaesthesiologists offers practical recommendations, there is a lack of depth regarding emerging technologies and diverse patient demographics, limiting applicability across various clinical settings [70]. Existing literature tends to emphasize technical aspects of anesthetic techniques without structured implementation frameworks [71]. Notably, there are no guidelines addressing anesthetic agents concerning inflammatory markers, the use of TCI propofol with adjuncts like dexmedetomidine to reduce costs, or risks such as PRIS and POCD.

Large-scale randomized controlled trials are necessary to assess the long-term cognitive and inflammatory effects of dexmedetomidine as an adjunct to propofol, particularly in preventing postoperative cognitive dysfunction (POCD) and

reducing inflammatory markers like IL-6 and TNF-α. Additionally, the economic impact of dexmedetomidine should be explored, especially its potential to lower ICU stays and opioid use, making it cost-effective despite higher initial costs. Research should also focus on how dexmedetomidine might reduce propofol dosage and mitigate the risk of PRIS during prolonged surgeries. These efforts will enhance anesthesia protocols, ensuring safety, efficacy, and optimized resource allocation.

8. CONCLUSION

This comparative review highlights significant considerations for both anesthesia techniques. Propofol alone provides effective control over intracranial pressure and reduces inflammatory markers, contributing to favorable recovery profiles. However, when combined with dexmedetomidine, there are potential benefits such as enhanced neuroprotection, reduced inflammation, and a lower incidence of POCD. Economic factors also play a role, as dexmedetomidine increases initial medication costs but may reduce overall expenses through shorter ICU stays, the need for other anesthetic agents, and decreased postoperative complications. Finally, the choice between propofol alone or in combination with dexmedetomidine should be tailored to individual patient needs, surgical requirements, and institutional resources. Further research is needed to fully understand the long-term outcomes and economic implications of using dexmedetomidine as an adjunct to TCI propofol in brain tumor surgeries.

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