Mechanistic Interplay of Ketofol Versus Propofol: Implications for Neurocognition, Analgesia, and Post-Operative Recovery

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ABSTRACT

Post-operative cognitive dysfunction (POCD) is a significant complication following surgical procedures, with implications for patient recovery and overall quality of life. The selection of anesthetic agents, particularly during induction and maintenance, plays a crucial role in influencing post-operative outcomes. Propofol is commonly utilized due to its rapid onset and favorable safety profile; however, it presents limitations such as respiratory depression, hypotension, and lack of analgesia. These drawbacks necessitate the exploration of alternative or adjunct anesthetic approaches. A systematic literature review was conducted to evaluate the comparative efficacy of propofol and ketofol in post-operative cognitive function, pain management, and functional recovery. The search strategy employed predefined keywords and Boolean operators across major databases, including Web of Science, PubMed, and Scopus. Inclusion criteria were restricted to peer-reviewed, English-language studies presenting empirical data or systematic analyses. Non-peer-reviewed sources, conference abstracts, and studies with methodological deficiencies were excluded. Emerging evidence suggests that ketofol, a combination of ketamine and propofol, may offer enhanced hemodynamic stability and superior analgesic effects compared to propofol alone. The combination appears to mitigate the adverse effects associated with each individual agent while potentially reducing post-operative opioid requirements. Furthermore, preliminary findings indicate a possible reduction in POCD incidence with ketofol use. Ketofol demonstrates promise as an effective anesthetic alternative, with potential benefits in cognitive preservation, pain control, and recovery. However, further high-quality research is needed to establish its long-term safety, optimal dosing, and applicability across diverse surgical populations

KEYWORDS: Anesthetic agent, cognition, hemodynamic stability, pain management, tolerability.

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INTRODUCTION

Post-operative Cognitive Decline or Dysfunction (POCD)

Post-operative cognitive decline or dysfunction (POCD) is a condition in which there may be a decline in the cognitive abilities of the patient immediately following surgery. It may last for weeks to months or even years [1, 2]. This condition may also resolve itself. Post-operative cognitive dysfunction is characterized by a decrease in the cognitive functioning of the patients relating to many areas of cognition, like memory, attention, visuospatial or executive functioning, naming, language, abstraction, and orientation [3–5]. Many factors are involved in the development of post-operative cognitive dysfunction, including patient age, type of surgical procedure, concurrent medication use, underlying comorbidities, the anesthesia regimen followed during surgery, and intensity of pain [6]. Post-operative cognitive decline has a prevalence of 40% within 1 week of any cardiovascular surgery and can remain as high as 17% even 3 months later [6]. Since POCD may last from several weeks to years, it is associated with the patient's decreased health-related quality of life and increased healthcare costs due to prolonged hospitalization. The development of POCD involves a deeply interconnected blend of complex factors and may be a significant challenge for clinicians and patients.

Pain Management in Post-Surgical Patients

The main problem that most of the patients face immediately after surgery is dealing with pain. Almost half of the patients undergoing surgery experience post-operative pain [7]. Usually, post-operative pain is treated by IV or oral analgesics like non-steroidal anti-inflammatory drugs (NSAIDs), opioids, or sometimes just acetaminophen may be sufficient. However, the use of non-steroidal anti-inflammatory drugs and opioids is accompanied by various adverse effects [8, 9], like gastric irritation, abdominal discomfort, pruritis, and excessive drowsiness. Furthermore, opioid use can lead to potential abuse and dependence. Although these risks are present, opioids are sometimes considered to be the best option to treat moderate to severe pain. Pain management in such patients requires a multimodal approach [10, 11] and must be treated adequately to avoid the negative effects of chronic pain on a patient's health. Inadequate pain management tends to have other adverse health effects like decreased ability to sleep and perform routine chores [12]. In fact, about 75% of the patients undergoing any surgical procedure have reported acute post-operative pain [12]. If pain control is optimized, it will result in reduced length and hospitalization costs and better patient satisfaction.

Role of Anesthesia in Post-Surgical Outcomes

One of the cornerstones of surgery is anesthesia. An optimal anesthetic regimen is required for the proper conduct of the surgery, but the role of these agents does not stop here; the impact of these anesthetic drugs can extend even after the patient has been discharged from the hospital. Anesthesia's influence is multifaceted, from providing the appropriate depth of sedation during surgery to enhanced patient recovery post-operatively. Greater depth of anesthesia increases the risk of a higher incidence of post-operative delirium and longer recovery time but may result in reduced post-operative pain [13]. Anesthetic drugs tend to have their own complications, which also need to be taken into consideration when selecting the right anesthetic agent that matches the patient's conditions and needs. Anesthetic drugs' residual effects can increase the risk of post-operative mortality, besides prolonging recovery, and the consideration of the number of agents to be used is also very important [14]. Inadequate anesthesia or poor anesthetic choice may lead to cognitive decline, excessive opioid consumption, post-operative delirium, and delayed mobilization [15]. Anesthesia also affects the human body's response when triggered by factors like inflammation, stress, or tissue trauma. Particularly, the combination of anesthesia and surgery may result in neuroinflammation, which is closely linked to post-operative cognitive dysfunction and delirium, especially in older adults and younger children [16–21]. When deciding on the right anesthetic plan, anesthesiologists must also consider the complete drug profile, including the pharmacokinetic and pharmacodynamic properties. Thus, optimizing an anesthetic regimen is crucial in improving patient care outcomes, and the anesthetic drug should not be considered as merely used for sedation purposes.

METHODOLOGY:

A methodologically rigorous and unbiased approach was employed to identify and synthesize relevant literature on ketofol vs propofol in post-operative cognitive function, pain management, and functional recovery. A comprehensive systematic literature search was executed using well-defined keywords and Boolean operators across multiple high-impact academic databases, including Web of Science, PubMed, and Scopus. This search strategy was carefully designed to capture empirical studies examining the multifaceted effects of Ketofol and Propofol in post-operative contexts. To maintain scientific rigor and ensure the credibility of the evidence base, the inclusion criteria were restricted to peer-reviewed, English-language publications presenting original data or rigorous systematic analyses. Sources such as conference abstracts, non-peer-reviewed materials, and studies lacking methodological clarity were deliberately excluded. The initial screening process involved title and abstract reviews, followed by full-text evaluations of studies meeting the inclusion criteria. Subsequently, a detailed critical appraisal of the selected literature was conducted to identify recurring patterns, novel insights, and existing gaps in the field. This thorough evaluation culminated in an analytically robust synthesis of the current scientific evidence, offering a comprehensive overview of the comparative impacts of Ketofol and Propofol on cognitive outcomes, pain control, and functional recovery in the post-operative setting.

Table 1. Pharmacological Comparison between Propofol and Ketamine

Table 1. Pharmacological effects of propofol vs ketamine		
Organ system/effects	Propofol	Ketamine
Central nervous system	Dose-dependent decrease in consciousness Cognitive depression Decreased cerebral blood flow Decreased ICP Decreased cerebral O_2 consumption	Amnesia with only light sleep Dissociation from the surrounding environment Hallucinations Confusion Euphoria

	Transient excitatory phenomena – choreiform movements and opisthotonus	
Cardiovascular system	Vasodilation Mild depression of myocardial contractility Hypotension	Increased HR, BP, cardiac output Hypertension and tachycardia
Respiratory system	Dose-dependent respiratory depression Induction dose-related apnea	No observed respiratory depression
Others	Increased antiemetic action No analgesia Loss of muscle tone	Decreased antiemetic action Produces analgesia Reflexes and muscle tone are maintained

As depicted in Table 1, propofol and ketamine are two anesthetic drugs that are completely opposite in nature. Ketamine is unique because it is pharmacologically similar to the hallucinogen phencyclidine, thus producing a state of dissociation from the body and the surroundings [22]. The use of each drug is associated with its own positive and negative health effects.

Mechanisms of Anesthetic Impact on Cognitive Function

Both of these anesthetic agents have exhibited neurotoxic and neuroprotective effects. Because of the ability of propofol to decrease intracranial pressure, cerebral blood flow, and oxygenation, it is commonly used in neurosurgical procedures [23]. Propofol slows down the production of pro-inflammatory cytokines like TNF-α and IL-6 and also tends to decrease the NF-κB signaling, affecting microglial activation [23]. However, other factors like autophagy and apoptosis act as a two-edged sword, potentially leading to neurotoxicity and neuroprotection. The positive and negative neuronal consequence is separated by a thin line between how propofol induces autophagy and apoptosis. Wang et al. [23] stated that propofol can either inhibit or promote hippocampal autophagy, and activation of autophagy triggers the apoptotic cascade, leading to neuronal cell death.

On the other hand, excessive autophagy can be useful in neurodegenerative diseases, protecting neuronal cell death [23]. In another study conducted to assess the effects of propofol on a neurotoxic model, it was found that propofol increased the levels of the reactive oxygen species (ROS) and suppressed the expression of the brain-derived neurotrophic factor, ultimately resulting in neurotoxicity [24]. Propofol-induced neurotoxicity, as explained through various molecular studies, has been explicitly demonstrated in Figure 1.

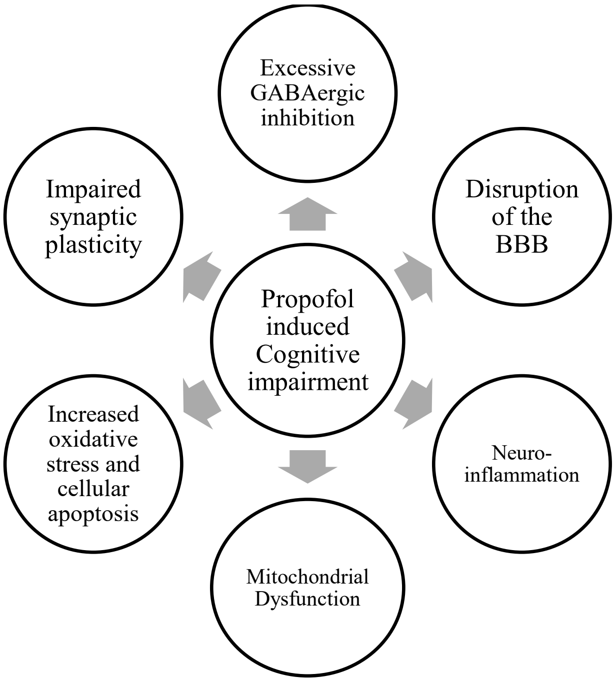

Figure 1. Pathways through which propofol exerts its neurotoxic effects.

Ketamine's neurotoxic or neuroprotective effects are mainly based on the dose. At higher doses, ketamine exhibits neurotoxicity, but at sub-anesthetic doses, it protects the neuronal cells from damage and destruction. The upregulation of mTOR and its downstream regulators is responsible for the dose-dependent neurotoxicity of ketamine, and thus, inhibition of this pathway safeguards against ketamine-induced toxicity [23, 25]. Although ketamine has shown neurotoxicity in rat models and other experiments, recent research has highlighted that ketamine's neuroprotective effects are worth investigating and can be a helpful treatment for acute neuronal injuries and neuropsychiatric disorders. Figure 2 depicts the various neuroprotective effects of Ketamine.

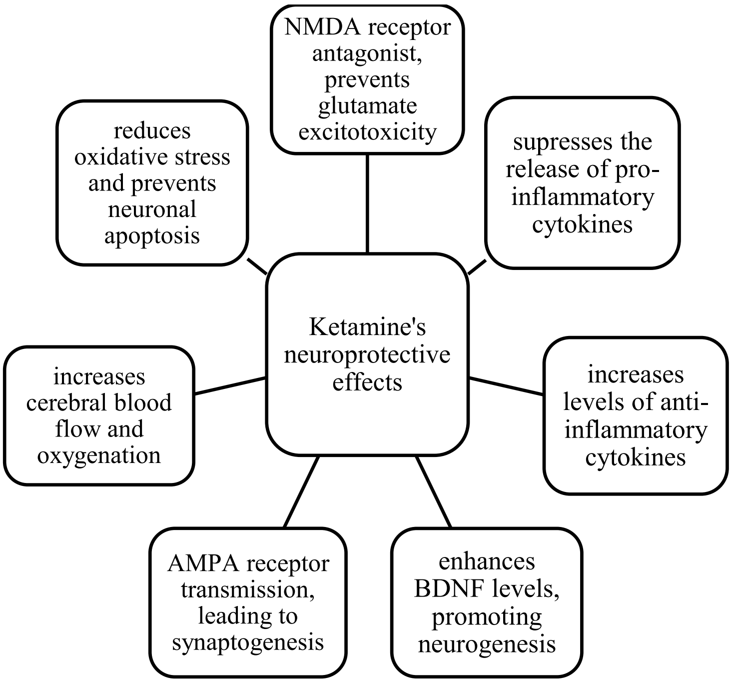

Figure 2. Mechanisms of Ketamine induced neuroprotection.

Ketofol: A promising anesthetic approach

Ketofol is a mixture of ketamine and propofol and has been of interest due to the numerous ways in which it offsets the effects of propofol. Ketofol can be a promising combination because it provides the additive properties of both the anesthetic agents while reducing the dose and disadvantages associated with each one individually [26, 27]. This review article analyzes the efficacy of ketofol and propofol on cognition and functional outcomes and assesses pain with reference to evidence on the benefits of ketofol. Although propofol and ketofol are popular in modern anesthesia practice, there is still a notable lack of knowledge on the effects of these agents on integrated post-operative outcomes — particularly cognitive function, pain control, and functional recovery. Although individual studies have explored these drugs in isolation or with a limited focus on sedation quality and hemodynamic profiles, a comprehensive synthesis addressing their broader neurocognitive implications is not entirely available. The review seeks to fill this gap by synthesizing the current evidence across a wide range of surgical procedures to elucidate a better perspective on how anesthetic selection may shape early recovery and long-term patient-centered outcomes. The comparative study of ketofol and propofol presented in this article will help improve anesthetic selection, resulting in enhanced recovery after surgery (ERAS) to avoid possible post-operative cognitive dysfunction and other complications.

Cognitive Function and Postoperative Recovery

Neuropsychological recovery after anesthesia is an important factor in the general postoperative management of patients. The neurocognitive disorder is a common postanesthetic complication that is increasingly reported in elderly patients or those with baseline cognitive pathology. Sedated groups are identified through propofol, but it has the disadvantage of being related to postoperative cognitive dysfunction (POCD), affecting recovery [28]. It is hypothesized that POCD is due to neuroinflammation, oxidative stress, and anesthetic neurotoxicity. Propofol's sedative effect works by enhancing the effects of agonists acting at the GABAA receptor, which gives rise to neuroinflammatory changes that limit cognition. For example, Matas et al. [29] established that patients who received high doses of propofol had higher concentrations of pro-inflammatory cytokines in the cerebrospinal fluid as compared to the patients given low doses of propofol, and they had a lower cognitive status in the postoperative period. This phenomenon can be particularly alarming for elderly patients, who might have lower CR even before the onset of the disease. Ketamine, which is used in ketofol, has some protective properties for the neurons that could prevent the deterioration of cognitive functions caused by anesthetic agents, including propofol. Another mechanism is that ketamine is an N-methyl-D-aspartate (NMDA) receptor antagonist, which indicates that ketamine reduces excitotoxicity, one of the main sources of neuroinflammation [30]. Furthermore, ketamine regulates cytokine production, which may also safeguard the brain and its synapses from anesthesia-induced neurotoxicity. From the literature, the idea that ketofol affords a better protective effect against encephalopathy when compared to propofol alone is well substantiated. Mehri et al. [31] looked at patients who were part of a random, controlled study after surgery and found that patients who received ketofol had better Kearns-Sayre syndrome for cognitive improvement within 48 hours of surgery compared to patients who got propofol. This was particularly apparent in elderly patients, who are especially vulnerable to the amnesic-like effects of the anesthetic agents. To prevent the neurotoxic activation of propofol, ketofol reduces the quantity of the agent used in order to achieve the desired effect.

The effect of ketofol on cognition influences patient care in risky populations, for example, elderly people or patients undergoing surgeries. By supplementing with ketofol, postoperative cognition may be enhanced within the first hours of surgery, and the detrimental effects of long-term propofol on cognition may be minimized. In this regard, ketofol might be an innovative strategy for providing efficient sedation during surgery and excluding an increased risk of POCD.

Opioid Sparing Strategies: Role of Analgesic Anesthetics

Pain management during the peri-operative phase is crucial to reducing the use of opioids as its increased use is one of the major health concerns in the world. The opioid epidemic seems to be on the rise, with opioids being more frequently prescribed and administered to patients on a routine basis. Although opioids have a great potential to relieve pain, the increased use of opioids has been associated with abuse and dependence. A link has been associated between intra-operative and post-operative use of opioids with a clinical condition called "opioid use disorder," abbreviated as OUD [32]. Thus, it is highly recommended that a multimodal approach be incorporated to pain management, and this kind of approach can be initiated from the most appropriate use of an anesthetic agent with analgesic features. Multimodal analgesia (MMA) refers to the use of multiple pharmacological drugs that can act through various mechanisms to reduce and control pain in a patient while attempting to minimize the adverse effects of individual medications [33]. In this manner, the selection of an efficient anesthetic with inherent analgesic properties plays a vital role in reducing the need for opioid use both during and after surgery. Opioid-sparing anesthesia (OSA) and opioid-free anesthesia (OFA) seem to be effective strategies within the context of multimodal analgesia and anesthesia. Traditional opioid anesthesia was compared with opioid-sparing techniques, and the review found that OSA is a more practical approach to reducing the complications associated with opioid consumption without affecting patient safety drastically [34]. Choi et al. [35] compared OFA with ketamine and OSA with remifentanil and found that visual analog scores, as well as the number of patients requiring rescue analgesics, were lower in the OFA group. However, patients who received OFA required a longer time to gain consciousness after anesthesia, and although it wasn't clinically significant, they concluded that OFA with ketamine was feasible [35]. This study, therefore, adds to the fact that ketamine can be an effective drug to use intraoperatively to reduce opioid consumption.

Because of ketamine's side effects, ketofol seems to be a better anesthetic combination that aligns with this approach. Ketamine's NMDA antagonism provides sufficient intraoperative and post-operative analgesia [36–38]. Thus, the combination of ketofol can contribute to reduced post-operative pain and opioid consumption. Integrating ketofol into perioperative anesthetic protocols can act as a possible starting point in the multimodal approach to pain management in post-surgical patients.

Functional Recovery and Pain Management

The performance of functional recovery, which is the movement capacity of these patients after surgery, is a key reason why these patients' recovery is believed to have been successful. As a short-acting drug, propofol is often used in surgeries or operations where patients need to be awakened soon after the operation [39]. However, it does not have an analgesic effect, thus the requirement of using opioids for pain relief during and after surgical procedures. Opioids used for pain control result in side effects like sedation, nausea and vomiting, respiratory depression, and other complications that go a long way in prolonging the recovery period. Li and Chen [40] noted that the intravenous administration of ketamine can result in a significant reduction in pain scores and opioid consumption during the post-operative period, which implies that the administration of ketofol may also result in decreased pain levels following surgery. This holds a lot of concern, especially for patients who undergo major operations or patients with high pain numerical values, where long-term opioid administration may limit their progress to normalcy.

Ketofol is a mixture that exhibits the same level of sedation as propofol and the analgesic effect of ketamine. Ketamine, because of its reliable pain control, means that opioids can be minimized, thus bringing down undesired effects of opioid use. In another study evaluating the analgesic effect of ketofol, the patients who received ketofol were found to have lower visual analog scores compared to those who were anesthetized with propofol alone [41]. Therefore, the consumption of rescue opioids was lower in the ketofol group than in the propofol group. Abbasi et al. [42] investigated the impact of ketofol on patients admitted for orthopedic procedures. The authors of the study established that those who had been administered ketofol had a 25% faster recovery than people who were given propofol. Therefore, patients can become accustomed to reduced postoperative pain due to an extended analgesic duration of ketamine, which allows the patients to mobilize and engage in physical therapy more quickly. This accelerated recovery was especially advantageous in those patients who had joint replacement or spinal surgeries, as early mobilization helps to avoid the development of DVT and muscle wasting.

Besides improving pain management, ketofol's sedation and analgesia also play a role in improving the overall outcome of patients by reducing the use of other drugs. The reduction in the use of opioids does not only eliminate side effects associated with opioids but also enhances early awakening. Also, ketamine stimulates the sympathetic system in the body, which prevents the occurrence of hypotension that is normally associated with the use of propofol during surgery [43, 44]. Ketofol reduces the total dose of propofol [45–47] required in many surgeries, thus avoiding the dose-dependent adverse effects of propofol. Of clinical interest is that this promotes hemodynamic stability and decreases the necessity to apply vasopressors while improving the recovery of patients' status, especially those with cardiovascular diseases or high-risk surgeries.

Table 2. Quantitative Summary of Analgesic Parameters

Author (Year)	Study Design	Sample Size	Clinical/Surgical Setting	Key Findings	Outcome Trend
Khosa et al. (2022)	RCT	100	Lower Segment Cesarean Section	Intra-operative fentanyl was required in 6% of the patients in Group P and only 2% in Group KP. Post-operative fentanyl was	No significant difference

				required in only 8% of Group KP.	
Karki et al. (2017)	Prospective comparative study	100	Minor surgical procedures	From a total of 100 patients, 23 required analgesia: 9 patients from the ketofol group and 14 from the propofol group	Ketofol
Chaouch et al. (2022)	Meta-analysis	412	Bariatric surgery	Total opioid consumption was lower in the ketamine group after 24 hours (95% Cl, p = 0.01). VAS-H4 and VAS-H8 were lowered with ketamine use.	Ketamine-based regimens
Li and Chen (2019)	Meta-analysis	244	Total Knee Arthroplasty	Pooled data revealed ketamine demonstrated lower pain scores at 6, 12 and 24 hours (p = 0.003, p = 0.001, and p = 0.001 respectively). Total morphine consumption was also lower in ketofol group (p = 0.040).	Ketamine-based regimens
Abdelhalim et al. (2016)	Randomized double-blind study	200	Cervical dilation and currettage	Patients in propofol group required rescue pain medications and VAS was higher at the 5th and 10th minute.	Ketofol
Abbasi et al. (2024)	Randomized double-blind clinical trial	296	Orthopedic procedures	The average pain intensity and mitigation, based on VAS, were similar between the groups.	No significant difference
Ferguson et al. (2016)	Randomized double-blind clinical trial	573	Emergency deep sedation procedures	Ketofol group demonstrated lower pain scores 30 minutes after the procedure, but both agents were similar in most parameters.	No significant difference

Table 2 refers to the different studies evaluating particular pain parameters with the help of visual analog scale (VAS), where only 4 (57%) of the studies demonstrated a clear analgesic benefit with ketofol or ketamine-based regimens. These studies suggested that patients receiving an anesthetic regimen involving ketamine showed better post-operative pain scores and lower opioid consumption during or after the surgical procedure. The remaining 3 studies (43%) reported no major difference between ketofol and propofol, warranting further research to understand the true analgesic effects of ketamine in combination with propofol. Quantitatively, studies favoring ketofol or ketamine reported an average reduction of 1-2 points in the VAS score and at least a 20% decrease in opioid requirements within the first 6 hours after surgery.

Hemodynamic Stability

Maintaining hemodynamic stability during surgery has an important influence on post-operative patient outcomes, especially functional recovery. Stable vitals, including heart rate, blood pressure, respiratory rate, and oxygen saturation, are necessary to ensure adequate blood flow to the organs, thus preventing the risk of post-operative complications and promoting healing [48, 49]. Since hemodynamic stability is a crucial aspect of improving functional recovery after surgery, the anesthetic agent that results in better stabilization of vitals should be the ideal choice. There has been substantial evidence from various medical literature that ketofol provides better or at least similar hemodynamic stability in comparison to propofol. Raman et al. [50] found a statistically significant difference in HR, SBP, DBP, and MAP between ketofol and propofol, with ketofol showing better stability. Likewise, other studies have also concluded that ketofol offers a more favorable hemodynamic stability than propofol in different kinds of circumstances [51–60]. On the other hand, a research study suggested there was no significant difference between the two agents, and their effects on hemodynamic parameters were comparable [61, 62].

Table 3. Quantitative Summary of Hemodynamic Outcomes

Author (Year)	Study Design	Sample Size	Clinical/Surgical Setting	Key Findings	Outcome Trend
Raman et al. (2022)	Prospective randomized double-blind study	80	Laparoscopic Surgery	MAP and HR remained within ±10% of baseline with ketofol; propofol caused >20% MAP reduction (p<0.05).	Ketofol

El Mourad et al. (2021)	Prospective randomized double blind study	75	Transesophageal Echocardiography	Fewer hemodynamic alterations with ketofol, MAP and HR reductions were more significant in propofol group	Ketofol
Aslan et al. (2019)	Cross- sectional observational study	60	Tympanomastoidectomy	SAP, DAP, MAP, and HR values were significantly reduced in propofol group, however, Aldrete recovery score was higher for propofol	Ketofol
Gaddam et al. (2021)	Prospective randomized double blind study	30	Electroconvulsive Therapy	Recovery parameters were similar between both anesthetic agents.	No difference
Khandelwal et al. (2022)	Randomized double-blind study	38	Thoracolumbar spine surgery	MAP was significantly decreased in Group X (Propofol). No significant differences in HR between the two groups.	Ketofol
Aberra et al. (2019)	Prospective observational cohort study	120	Pediatric anesthesia (Laryngeal mask airway insertion)	Ketofol showed more stable MAP readings whereas significant drop in MAP observed in Propofol group ($p < 0.001$)	Ketofol
Sabertanha et al. (2019)	Randomized double-blind clinical trial	54	Orthopedic leg surgery	SBP, DBP, and MAP were significantly higher in ketofol group 10 – 60 minutes after induction. No significant difference in HR.	Ketofol
Bhardwaj et al. (2022)	Prospective RCT	40	Aneurysm Clipping	45% of patients receiving propofol experienced > 20% fall in MAP compared to only 15% of patients who received Ketofol.	Ketofol
Gandhi et al. (2024)	Retrospective observational study	30	Adult elective surgery	Ketofol and propofol demonstrated comparable hemodynamic parameters; ketofol resulted in longer recovery time.	Propofol

Table 3 displays the quantitative analysis of the 9 most relevant studies comparing hemodynamic parameters between ketofol and propofol among the broader literature reviewed. Across the 9 comparative studies analyzed, 7 (78%) of the studies demonstrated a favorable trend towards the use of ketofol, characterized by smaller fluctuations in blood pressure and mean arterial pressure (MAP) during induction and maintenance of anesthesia. One study (11%) suggested that the hemodynamic profiles were comparable between the two anesthetic agents, while only one study favored the use of propofol due to the prolonged recovery time noted in patients receiving ketofol. MAP reductions were 10-15% lower in the ketofol group than the propofol group when compared to the baseline readings.

Clinical Implications

The benefits of ketofol compared to propofol in aspects like cognitive preservation, functional regain, and postoperative pain indicate that ketofol is possibly preferred for several types of surgical processes. Propofol continues to be preferred for use in many brief operations and other outpatient surgical procedures because of the fast induction and the brief period the patient takes to regain consciousness [63]. Another advantage of propofol is the reduced post-operative nausea and vomiting compared to other anesthetic agents [64–70]. However, since ketofol has both sedative and analgesic effects with stability of hemodynamic parameters, the choice of its application is more suitable in cases of more complex surgeries or when a higher degree of pain is expected. Especially the combination of ketofol with a higher ratio of propofol to ketamine [71, 72] is suggested to provide better outcomes [73]. The fact that ketofol has the potential to enhance both early and delayed postoperative outcomes, mainly among vulnerable groups of patients, makes it one of the best anesthetic agents.

As much as there is an agreement that ketofol has a lot of advantages, several challenges are still present. While ketamine does help to decrease the number of opioids a patient is administered and supports walking again, its use is accompanied by some side effects, including hallucinations and dissociation at the high dose [74]. These side effects could be worse when experienced by particular patient groups, especially those with psychiatric conditions. To avoid the above effects, the use of this compound should be closely monitored, especially when adjusting the dosage. Moreover, ketofol was reported in numerous studies to enhance cognitive recovery and functional status, but the authors argued that further research is still needed to confirm these data in various surgeries and with more diversified patient populations [75].

Further Insights and Future Directions

This synthesis examines the potential benefits of ketofol over propofol in improving post-operative cognitive performance, like better pain control and rapid functional recovery. However, heterogeneity across existing studies, ranging from variability in dosing protocols to differences in outcome measurement, prevents the formation of definitive clinical conclusions. The review found that few studies investigated cognitive impairment, especially utilizing neuropsychological assessments like the Montreal Cognitive Assessment (MoCA) and comparing the test scores between the two drug groups. Although ketamine was proven to reduce post-operative pain in many studies, there was still limited research on ketofol's potential in relieving patients' pain. Moreover, many studies assessed short-term post-surgical outcomes with a small sample size rather than the long-term impact of the drugs. Therefore, future research should focus on long-term patient-centered outcomes involving a larger sample size and could even involve neuroinflammatory biomarkers, electrophysiological monitoring, and a combination of sensitive cognitive tests to understand the mechanisms underlying anesthesia-related cognitive changes.

CONCLUSION

Ketofol, a combination of ketamine and propofol, is much better than using propofol alone in terms of cognitive protection, better functional recovery from anesthesia, and improved pain control. Although propofol is still popular due to its fast induction and wake-up times, its drawbacks, which are a lack of pain relief and postoperative neurocognitive dysfunction, require further research. These two reasons are well handled by the synergistic effects of ketofol in that it provides better improvements in cognitive status, less opioid use, and faster functional restoration. As the depth of evidence endorsing ketofol increases, especially within the critical care population, its utilization may extend into general use within clinical practice. However, the entire program of investigations on its dosage schedules, long-term outcomes, and extended patient population remains to be continued. As ketofol anesthetic contribution continues to advance without serious side effects, it could advance post-surgical patient care and overall long-term patient health.

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Competing Interests

The authors have declared that no competing interests exist.

Author contribution

The authors confirm their contribution to the paper as follows: study conception and design: DPP, MP; data collection: MP, DPP, AY, DR; Data Analysis or Interpretation: MP, DPP, AY, DR, MR, KK, SP; methodology: MP, MR, investigation: MP, DPP, AY, DR; Original draft preparation: DPP, AY, DR; Revision and editing: KK, SP; Supervision: KK, SP. All authors reviewed the results and approved the final version of the manuscript.

Data availability

No datasets were generated or analysed during the study.

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