Impact of intra-operative ketamine on postoperative outcomes in abdominal surgery: a narrative review

Daniela Kerguelen Murcia[1#], Joy S. Li[1#], Uma R. Phatak[2^]

[1]School of Medicine, University of Texas Medical Branch, Galveston, TX, USA; [2]Department of Surgery, University of Texas Medical Branch, Galveston, TX, USA

Contributions: (I) Conception and design: All authors; (II) Administrative support: UR Phatak; (III) Provision of study materials or patients: All authors; (IV) Collection and assembly of data: All authors; (V) Data analysis and interpretation: All authors; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work and should be considered as co-first authors.

Correspondence to: Uma R. Phatak, MD, MS. Department of Surgery, University of Texas Medical Branch, 301 University Blvd., Galveston, TX 77555, USA. Email: urphatak@utmb.edu.

Background and Objective: Ketamine offers a promising solution to common postoperative issues in abdominal surgery, including pain, nausea, opioid use, and opioid-related side effects. The purpose of this literature review is to analyze the benefits and potential adverse effects associated with the intraoperative utilization of ketamine during abdominal surgeries.

Methods: A comprehensive search of PubMed and Ovid MEDLINE was conducted by two independent reviewers. Studies were included if they targeted adult patients and evaluated intra-operative use of ketamine for abdominal operations.

Key Content and Findings: We identified 13 studies of intraoperative use of ketamine in abdominal surgery. The results of these studies showed improved pain management as demonstrated by lower pain scores, decreased hyperalgesia, and a decreased need for additional analgesics. The results also demonstrated a decrease in opioid consumption during the critical 24-hour postoperative period. However, a few studies reported undesirable side effects such as hallucinations and delirium.

Conclusions: The intraoperative use of ketamine holds promise as a valuable adjunct to anesthesia during abdominal surgeries. Studies support its use in improving post-operative pain and decreasing opioid consumption. Due to risks of adverse effects, further studies in larger patient populations may help identify which patients will benefit the most. This review offers a succinct selection of the pertinent literature.

Keywords: Ketamine; intraoperative; abdominal surgery

Received: 11 November 2023; Accepted: 01 February 2024; Published online: 26 March 2024.

doi: 10.21037/tgh-23-97

View this article at: https://dx.doi.org/10.21037/tgh-23-97

Introduction

Acute pain management stands as a cornerstone in anesthetic care, with inadequate analgesia being linked to adverse postoperative outcomes such as immunosuppression, hyperglycemia, and the potential onset of chronic pain. While opioids remain the primary option for acute pain management, their application is often supplemented with adjuncts including non-steroidal anti-inflammatory drugs (NSAIDs), acetaminophen, gabapentin, and regional anesthesia techniques to foster more comprehensive pain management and reduce opioid consumption.

^ ORCID: 0000-0003-4382-8572.

Ketamine is a dissociative anesthetic and analgesic agent that primarily exerts its effects through binding to the N-methyl-D-aspartate receptor (NMDAR), disrupting the transmission of pain signals in the central nervous system. It has been increasingly recongized for its therapeutic potential in various medical conditions, with its ability to interact with several opioid receptors, specifically μ, δ, and κ, enhancing its analgesic properties. S-ketamine, the S-enantiomer of ketamine, binds to NMDARs with four times the affinity of ketamine, resulting in more potent effects at lower doses and fewer psychotropic side effects. In a recent study, ketamine has been shown to improve treatment-resistant chronic pain, improving pain severity, mood, and quality of life (1).

Ketamine has also been investigated for its potential in preventing postoperative delirium and treating refractory asthma exacerbations, yet these results have been inconsistent (2,3). While some studies suggest benefits in delirium prevention, others indicate increased risk, necessitating cautious evaluation (2). In asthma care, the evidence for ketamine's efficacy remains inconclusive, highlighting the need for further research in these areas (3).

Notably, ketamine has been extensively discussed in the literature as a supplemental analgesic for perioperative pain control. Some reviews highlight the effectiveness of ketamine or S-ketamine in improving acute pain in perioperative settings, noting reduced pain scores (4,5). Other studies indicate a statistically significant reduction in opioid analgesic consumption with the use of ketamine (6,7). However, whether this holds true specifically for intraoperative administration of ketamine in abdominal surgery remains uncertain.

Ketamine and its more potent enantiomer, S-ketamine, have emerged as notable agents for reducing pain (8). Because S-ketamine exhibits higher NMDAR affinity as well as fewer psychotropic effects than ketamine, it is progressively replacing it in clinical settings (9,10). Additionally, low-dose ketamine serves as a promising candidate for pain management regimens, offering analgesic benefits that are yet to be fully understood (11). It can be administered through several routes, including continuous intravenous (IV) infusion, intravenous patient-controlled analgesia (IV-PCA), or epidural infusion (8). However, defining the optimal dosing and duration remains a complex task, despite its acknowledged morphine-sparing effects during intraoperative periods.

Typical postoperative challenges for abdominal surgery include pain management, postoperative nausea and vomiting (PONV), and adverse effects secondary to opioid administration. Ketamine may address these challenges effectively, as studies have shown that it use reduces morphine consumption substantially in the initial 24-hour postoperative window with little to no severe adverse events (12). Despite the emergence of minor side effects such as vague feelings and hallucinations, its benefits seemingly outweigh the risks, opening avenues for deeper exploration into its applicative benefits in abdominal surgeries (8).

Previous research into the intraoperative use of ketamine in abdominal surgeries has produced inconclusive results, partly due to the heterogeneity of study designs. Our study aims to fill this gap by focusing exclusively on randomized controlled trials (RCTs) that investigate the intraoperative administration of these agents in abdominal surgery. We further differentiate our review by including a sub-analysis on the timing of administration, a critical factor in drug efficacy yet underexplored in the existing literature.

The goal of this review is to carefully analyze the benefits and potential adverse effects of the intraoperative utilization of ketamine and its S-enantiomer, S-ketamine, in the pain management regimen during abdominal surgeries. This analysis draws on a diverse range of administration techniques and emphasizes RCTs to ensure a robust evaluation. This rigorous approach facilitates a deeper understanding of pain management strategies in abdominal surgeries and provides insights into secondary outcomes such as morphine/opioid consumption and the occurrence of PONV. We present this article in accordance with the Narrative Review reporting checklist (available at https://tgh.amegroups.com/article/view/10.21037/tgh-23-97/rc).

Methods

Two independent reviewers conducted a narrative review by conducting a systematic search (D.K.M. and J.S.L.) of PubMed and Ovid (MEDLINE). The search strategies included "abdominal surgery", "ketamine", and "intraoperative" and were restricted to RCTs and clinical trials (*Table 1*). We combined the results of the searches and duplicates were eliminated. Articles were screened by title and abstract by two reviewers. Discrepancies were resolved by a third reviewer (U.R.P.). Studies were included if they targeted adult patients and evaluated intra-operative use of ketamine for abdominal operations. We excluded descriptive articles including commentaries, editorials, and reviews to maintain the focus on primary research. Two reviewers assessed each article included for full-text review

Table 1 Search terms used in PubMed

Database	PubMed
Date	15/09/2023
Strategy	#1 and #2, duplicates were eliminated
#1	(Ketamine[Mesh] OR "ketamine") AND (Abdomen/surgery[Mesh] OR "abdominal surgery" OR "abdominal procedures" OR "abdominal operations" OR "abdominal surgeries")
#2	(("Ketamine" [Mesh] OR "ketamine" [tiab] OR "Ketalar" [tiab] OR "CI-581" [tiab] OR "CI 581" [tiab]) AND ("Intraoperative Care" [Mesh] OR "intraoperative" [tiab] OR "during surgery" [tiab] OR "during operation" [tiab] OR "intra-operative"[tiab]) AND ("Abdomen/surgery" [Mesh] OR "abdominal surgery" [tiab] OR "laparotomy" [tiab] OR "laparoscopy" [tiab]) AND ("Pain" [Mesh] OR "pain management" [tiab] OR "analgesia" [tiab] OR "satisfaction" [tiab])

Table 2 The search strategy summary

Items	Specification
Date of search	Sep 15, 2023
Databases and other sources searched	PubMed and MEDLINE via (Ovid)
Search terms used	Ketamine, abdominal surgery, intraoperative See *Table 1*
Timeframe	Jan 1, 1993 to Sep 15, 2023
Inclusion and exclusion criteria	Inclusion: RCTs and clinical trials in English Exclusion: pediatric intervention, descriptive articles
Selection process	D.K.M. and J.S.L. conducted the search independently, consensus was obtained with discussion with U.R.P.

RCTs, randomized controlled trials.

based on relevance and significance. The search strategy can be found in *Table 2*.

In this narrative review, we exclusively included RCTs for their gold standard status in establishing causal relationships between interventions and outcomes. These trials offer high internal validity by minimizing selection bias and controlling for confounding variables. Thus, by focusing solely on RCTs, this review aims to provide the most reliable and ethically sound insights into the role of intraoperative ketamine in anesthesia.

Results

We identified 13 studies that met our criteria (*Table 3*). The main outcomes measured across these studies include postoperative pain intensity at various time points, analgesic effects, and opioid consumption, while secondary outcomes encompass factors such as hemodynamics, side effects, and cognitive function.

Pain and analgesia

The major outcomes studied in the intraoperative administration of ketamine included pain scores and quality of analgesia. One commonly used method to determine pain is the visual analog scale (VAS), which is a pain rating scale that represents a continuum between "no pain" (0 cm of the scale) and the "worst pain" at the end of the scale (10 cm) (25). Studies have shown that the intraoperative administration of ketamine lowers VAS pain scores postoperatively (7,13-15). Bilgin *et al.* (2005) investigated the influence of ketamine administration timing on postoperative pain relief (13). The study revealed that pain scores were lower at 2 and 4 hours postoperatively in the group that received ketamine before and during surgery. Moreover, VAS scores were significantly lower after 24 hours in the groups that administered intraoperative ketamine compared to preoperative administration alone (13). Zhang *et al.* (2023) also found a statistically significant reduction in pain scores after 24 hours (14).

Table 3 List of included studies

No.	Authors	Title of paper	Year	Outcomes	Main results	Reference No.
1	Zakine J, Samarcq D, Lorne E, Moubarak M, Montravers P, Beloucif S, Dupont H	Postoperative Ketamine Administration Decreases Morphine Consumption in Major Abdominal Surgery: A Prospective, Randomized, Double-Blind, Controlled Study	2008	Opioid consumption and pain scores (VAS)	Low-dose ketamine improved postoperative analgesia with a significant decrease of morphine consumption when its administration was continued for 48 h postoperatively	(7)
2	Bilgin H, Ozcan B, Bilgin T, Kerimoğlu B, Uçkunkaya N, Toker A, Alev T, Osma S	The influence of timing of systemic ketamine administration on postoperative morphine consumption	2005	Pain scores (VAS)	Lower pain scores in the ketamine group at 2 and 4 hours; sustained reduction after 24 hours compared to preoperative administration alone	(13)
3	Zhang T, Yue Z, Yu L, Li S, Xie Y, Wei J, Wu M, Liu H, Tan H	S-ketamine promotes postoperative recovery of gastrointestinal function and reduces postoperative pain in gynecological abdominal surgery patients: a randomized controlled trial.	2023	Time to first flatus and pain scores (VAS)	S-ketamine accelerated postoperative GI recovery and reduced 24 h postoperative pain in patients undergoing open gynecological surgery	(14)
4	Jipa M, Isac S, Klimko A, Simion-Cotorogea M, Martac C, Cobilinschi C, Droc G	Opioid-Sparing Analgesia Impacts the Perioperative Anesthetic Management in Major Abdominal Surgery	2022	Pain scores (VAS)	Significant decrease in VAS scores for both multimodal analgesic regimens (ketamine group and epidural group compared to control)	(15)
5	Argiriadou H, Himmelseher S, Papagiannopoulou P, Georgiou M, Kanakoudis F, Giala M, Kochs E	Improvement of pain treatment after major abdominal surgery by intravenous S+-ketamine	2004	Pain scores, additional analgesic requirements, mood states	Patients who received repeated S(+)-ketamine reported smaller pain scores than those who received placebo, required additional analgesics, and reported being in a better mood after awakening	(16)
6	Webb AR, Skinner BS, Leong S, Kolawole H, Crofts T, Taverner M, Burn SJ	The addition of a small-dose ketamine infusion to tramadol for postoperative analgesia: a double-blinded, placebo-controlled, randomized trial after abdominal surgery	2007	Opioid consumption (PCA) and pain scores (VRS)	Median PCA morphine use was significantly lower in the ketamine group during the 0–24 h period and the 24–48 h period compared to the control group. Pain scores (VRS) were significantly lower at rest and with movement over 48 h in the ketamine group	(17)
7	Bornemann-Cimenti H, Wejbora M, Michaeli K, Edler A, Sandner-Kiesling A	The effects of minimal-dose versus low-dose S-ketamine on opioid consumption, hyperalgesia, and postoperative delirium: a triple-blinded, randomized, active- and placebo-controlled clinical trial	2016	Opioid consumption, hyperalgesia, and postoperative delirium	Patients in the placebo group had the highest cumulative opioid consumption and the largest normalized areas of hyperalgesia at the incisional site, while those in the low-dose group had the highest delirium scores	(18)

Table 3 *(continued)*

Table 3 *(continued)*

No.	Authors	Title of paper	Year	Outcomes	Main results	Reference No.
8	Joly V, Richebe P, Guignard B, Fletcher D, Maurette P, Sessler DI, Chauvin M	Remifentanil-induced postoperative hyperalgesia and its prevention with small-dose ketamine	2005	Hyperalgesia	Remifentanil-induced hyperalgesia was prevented by small-dose ketamine, implicating an N-methyl-d-aspartate pain-facilitator process	(19)
9	Fu ES, Miguel R, Scharf JE	Preemptive ketamine decreases postoperative narcotic requirements in patients undergoing abdominal surgery	1997	Opioid consumption	Patients in the preemptive group had significantly lower morphine consumption on postoperative days 1 and 2	(20)
10	Guignard B, Coste C, Costes H, Sessler DI, Lebrault C, Morris W, Simonnet G, Chauvin M	Supplementing desflurane-remifentanil anesthesia with small-dose ketamine reduces perioperative opioid analgesic requirements	2002	Opioid consumption	The ketamine patients required postoperative morphine later and received less morphine during the first 24 postoperative h	(21)
11	Edwards ND, Fletcher A, Cole JR, Peacock JE	Combined infusions of morphine and ketamine for postoperative pain in elderly patients	1993	Side effects	Increasing the dose of ketamine resulted in an increased incidence of postoperative dreaming	(22)
12	Wu CT, Yeh CC, Yu JC, Lee MM, Tao PL, Ho ST, Wong CS	Pre-incisional epidural ketamine, morphine and bupivacaine combined with epidural and general anaesthesia provides pre-emptive analgesia for upper abdominal surgery	2000	Pain scores (VAS), opioid consumption, and adverse effects	Pre-incisional ketamine group resulted in decreased pain scores, one incidence of delirium but no hallucinations	(23)
13	Subramaniam K, Subramaniam B, Pawar DK, Kumar L	Evaluation of the safety and efficacy of epidural ketamine combined with morphine for postoperative analgesia after major upper abdominal surgery	2001	Pain scores (VAS) and side effects	Ketamine group reported faster onset of analgesia, requirement of analgesia was longer, required less morphine postoperatively, and had higher sedation scores, without any side effects	(24)

VAS, visual analog scale; PCA, patient-controlled analgesia; VRS, verbal rating scale.

Other studies have emphasized the improved analgesic effects of intraoperative ketamine administration determined by various metrics like a reduced need for additional analgesics, reporting better analgesia, a smaller area of hyperalgesia, and lower verbal pain scores in the verbal rating scale (VRS) (16-18). Argiriadou *et al.* (2004) demonstrated the effectiveness of repeated intraoperative s(+)-ketamine administration in improving postoperative pain relief and mood after abdominal surgery, with patients in the intraoperative group reporting lower pain scores, reduced need for additional analgesics, and improved mood states compared to single pre-incisional s(+)-ketamine and placebo groups (16). Webb *et al.* (2007) revealed that ketamine administration led to a significantly higher proportion of patients reporting excellent analgesia during the 0–24-hour postoperative period, and reduced pain scores (VRS) at rest and with movement over 48 hours (17). Bornemann-Cimenti *et al.* (2016) found a significantly smaller area of hyperalgesia in groups receiving intraoperative ketamine, signifying its potential to reduce hyperalgesia following surgery (18). Moreover, the postoperative hyperalgesia that results from a large dose of intraoperative remifentanil can be alleviated with a small dose of ketamine as studied by Joly *et al.* (2005), and even minimized morphine consumption (19).

Opioid consumption

Patient-controlled analgesia (PCA) is a method of self-administration of pain medication during the postoperative period. It allows for monitored tracking of a patient's opioid consumption, from the time of administration to the number of doses. Webb *et al.* (2007) found that compared to a control group, the addition of intraoperative ketamine and postoperative infusion significantly lowered PCA morphine use by up to 48 hours post-surgery. Additionally, they noted that the control group required a significantly more frequent need for analgesic interventions during the 0–24 h period compared to the ketamine group, decreasing the need for physician intervention (17). Similarly, Fu *et al.* (1997) studied morphine consumption in two groups that received ketamine either intraoperatively or at wound closure. They found that cumulative morphine consumption was reduced by approximately 40% in the intraoperative group up to 48 hours, long after the normal expected duration of ketamine's pharmacological action (20). Guignard *et al.* (2002) not only measured morphine consumption but also the time to first morphine administration and found that the ketamine group had a delay in requesting morphine (21). They also found lower morphine consumption in the ketamine group up to 24 hours postoperatively. Other studies also support the evidence from the findings above consistently demonstrating that intraoperative ketamine significantly reduces opioid consumption during the postoperative period (13,15,18).

Side effects

Several psychological side effects were noted. Bornemann-Cimenti *et al.* (2016) evaluated delirium using the Intensive Care Delirium Screening Checklist (ICDSC) 48 hours postoperatively (18). This tool gives eight points for eight different dimensions of delirium, including level of consciousness, inattention, disorientation, hallucination-delusion-psychosis, psychomotor agitation or retardation, inappropriate speech or mood, sleep/wake cycle disturbance, and symptom fluctuation (26). Delirium was defined as a score of more than three. Postoperative delirium scores were highest in the more conventional low-dose group, with no significant difference in delirium scores between the minimal dose and placebo groups (18). Similarly, Edwards *et al.* (1993) reported a significant correlation between higher doses of ketamine and an increase in postoperative dreaming. One of the patients in the highest dose ketamine group (20 $mg{\cdot}hr^{-1}$) found these dreams to be very distressing and had to be withdrawn from the study (22). Similarly, Webb *et al.* (2007) noted that although the incidence of brief, non-disturbing hallucinations were not significantly increased in the ketamine group compared to the control group, three out of fifty-six patients in the ketamine group had to be withdrawn due to experiences of disturbing hallucinations/confusion. Additionally, they reported no significant increases in postoperative dreaming between the ketamine and control groups (17). Wu *et al.* (2000) found one incidence of psychomimetic emergence delirium from ketamine but no incidence of hallucinations (23). Zakine *et al.* (2008) observed no difference in, psychiatric disorders, delusions, nightmares, and sleep disorders between the intraoperative ketamine, perioperative (intraoperative and postoperative ketamine), and control groups (7).

Other postoperative analgesic-related side effects varied between the studies. The ketamine group in Webb *et al.* (2007) was found to have lower median sedation scores compared to the control group in the 0–24-hour period, but other side effect data, including nausea score, antiemetic administration, psychomotor, sleep quality, and Trail Making test scores were not significantly different between the two groups (17). Zakine *et al.* (2008) found no difference in sedation scores between their groups but reported that significantly lower nausea and vomiting scores in the perioperative group compared to the control group (7). Subramaniam *et al.* (2001), in contrast, noted elevated sedation scores in the initial two hours following surgery, though no hallucinations or respiratory depression were observed. Pruritis, nausea, and vomiting were similar between in both their groups (24). Wu *et al.* (2000) reported with no serious analgesic-related adverse effects as well as no significant difference in nausea, vomiting, urinary retention, and respiratory depression between their ketamine and control groups (23). Zhang *et al.* (2023) found no postoperative delirium, oliguria, or emergence agitation in the S-ketamine group. Additionally, side effects including dizziness, nausea, vomiting, or flatulence/bloating adverse events were comparable between the S-ketamine and control groups (14).

Postoperative recovery

Notably, Zhang *et al.* (2023) found that S-ketamine improved postoperative gastrointestinal (GI) recovery, reflected by a significantly shorter time of first postoperative flatus. The mean first postoperative flatus time for the S-ketamine group (50.3 hours) was 6.2 hours earlier than in the control group (56.5 hours) (14). However, additional research is essential to further elucidate effects of ketamine on postoperative GI recovery.

Discussion

Pain and analgesia

The results from the included studies collectively highlight the efficacy of intraoperative ketamine in improving pain outcomes. The consistent reduction in pain scores, as measured by VAS and VRS illustrate the potential of intraoperative ketamine to provide effective pain relief during the crucial early postoperative period following abdominal surgery (13-15,17). Furthermore, the observed improvements extend beyond subjective pain scores, encompassing metrics such as, reduced need for additional analgesics, reporting better analgesia, alleviation of hyperalgesia, and improved mood (16,18). Ketamine may also prove essential in comprehensive pain management strategies as demonstrated by its ability to alleviate hyperalgesia, and counteract the hyperalgesic effects of remifentanil (18,19).

Opioid consumption

Another major outcome studied in the intraoperative administration of ketamine is the level of opioid consumption postoperatively. Studies have shown that ketamine use reduces morphine consumption substantially in the initial 24-hour postoperative window with little to no severe adverse events (17). This reduction in opioid consumption reflects improved pain management and patient comfort and aligns with the broader healthcare goal of minimizing opioid usage. Additionally, a reduced need for opioids may mitigate opioid-related side effects, such as respiratory depression and ileus following abdominal surgery, thus promoting a faster and safer recovery for patients.

Notably, in the study by Fu *et al.* (1997) the reduced incremental use of morphine later in the study period is strongly suggestive of the sustained analgesic effect of intraoperative ketamine use. The time to morphine administration can also assess decreased opioid consumption as it reflects how quickly a patient requires pain relief and the effectiveness of pain management (20). The use of PCA as a self-administering method further supports the sustained analgesic effect of ketamine. The observed delay in time to first morphine administration and reduced need for physician intervention in the ketamine groups suggests prolonged and effective postoperative pain relief (17,21). These findings are indicative of improved pain management and reduced opioid consumption following intraoperative ketamine use.

Side effects

In evaluating the side effects associated with intraoperative ketamine, diverse findings have been reported across the medical literature, ranging from psychological and physical impacts to no adverse effects at all. The intraoperative use of ketamine is considered generally safe, but it has been associated with varying side effects such as delirium and hallucinations that could complicate post-operative care after abdominal surgery.

Overall, there were variable psychiatric side effects observed in these studies. Most mentioned minimal psychiatric side effects, but a few patients reported disturbing hallucinations or distressing dreams, resulting in their withdrawal of the study (17,22). However, there was no mention of the effect of these psychiatric side effects on postoperative recovery in these patients. These studies support minimal side effects with the use of intraoperative ketamine rather than serious adverse effects that would significantly impact postoperative recovery.

Ketamine's adverse effects are predominantly dose-dependent, with more severe effects in subcutaneous infusions compared to oral intake (27). These include psychotomimetic effects like euphoria and hallucinations, as well as physical symptoms including hypertension and tachycardia. Notably, it can cause urinary tract toxicity, which can manifest as increased frequency, urgency, urge incontinence, dysuria, and hematuria (28). High doses in anesthesia are linked to tonic-clonic movements in a significant number of patients, highlighting the importance of stringent dosing and vigilant monitoring when administering ketamine (27).

Strengths and limitations

The use of two independent reviewers for study selection and the use of multiple databases enhances the validity and reliability of our conclusions. Additionally, we limited our results to randomized studies with the hope of decreasing selection bias and confounding.

However, there are several limitations to consider. We exclusively used PubMed and Ovid (MEDLINE) for our literature search, potentially omitting relevant studies published in other databases. The narrative format of the review, while informative, precludes a quantitative meta-analysis of the data. Finally, the focus on adult patients undergoing abdominal surgeries limits the generalizability of our conclusions to other patient populations.

Conclusions

In this review we highlight the findings from RCTs, which point to ketamine as a beneficial adjunct for managing post-operative pain and reducing opioid consumption. Additionally, ketamine was shown to extend the time until the first administration of morphine after surgery, reflecting the sustained analgesic effects of ketamine. While ketamine's benefits are promising, these findings highlight the importance of adopting a systematic approach for further validation. Given the differences in study methodologies and patient demographics, a comprehensive meta-analysis would be essential to solidify our understanding of ketamine's effects and inform clinical guidelines, ensuring its use in abdominal surgeries optimally balances efficacy with safety.

Acknowledgments

Funding: None.

Footnote

Reporting Checklist: The authors have completed the Narrative Review reporting checklist. Available at https://tgh.amegroups.com/article/view/10.21037/tgh-23-97/rc

Peer Review File: Available at https://tgh.amegroups.com/article/view/10.21037/tgh-23-97/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tgh.amegroups.com/article/view/10.21037/tgh-23-97/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

1. Al Mukhaizeem S, Nasa A, Waldron D, et al. Investigating the effectiveness of oral ketamine on pain, mood and quality of life in treatment resistant chronic pain. Front Pain Res (Lausanne) 2023;4:1268985.
2. Ghazaly HF, Hemaida TS, Zaher ZZ, et al. A pre-anesthetic bolus of ketamine versus dexmedetomidine for prevention of postoperative delirium in elderly patients undergoing emergency surgery: a randomized, double-blinded, placebo-controlled study. BMC Anesthesiol 2023;23:407.
3. La Via L, Sanfilippo F, Cuttone G, et al. Use of ketamine in patients with refractory severe asthma exacerbations: systematic review of prospective studies. Eur J Clin Pharmacol 2022;78:1613-22.
4. Xie M, Liang Y, Deng Y, et al. Effect of S-ketamine on Postoperative Pain in Adults Post-Abdominal Surgery: A Systematic Review and Meta-analysis. Pain Physician 2023;26:327-35.
5. Wang X, Lin C, Lan L, et al. Perioperative intravenous S-ketamine for acute postoperative pain in adults: A systematic review and meta-analysis. J Clin Anesth 2021;68:110071.
6. Bell RF, Dahl JB, Moore RA, et al. Peri-operative ketamine for acute post-operative pain: a quantitative and qualitative systematic review (Cochrane review). Acta Anaesthesiol Scand 2005;49:1405-28.
7. Zakine J, Samarcq D, Lorne E, et al. Postoperative ketamine administration decreases morphine consumption in major abdominal surgery: a prospective, randomized, double-blind, controlled study. Anesth Analg 2008;106:1856-61.
8. Weinbroum AA. Non-opioid IV adjuvants in the perioperative period: pharmacological and clinical aspects of ketamine and gabapentinoids. Pharmacol Res 2012;65:411-29.
9. Pfenninger EG, Durieux ME, Himmelseher S. Cognitive

impairment after small-dose ketamine isomers in comparison to equianalgesic racemic ketamine in human volunteers. Anesthesiology 2002;96:357-66.
10. Bonaventura J, Lam S, Carlton M, et al. Pharmacological and behavioral divergence of ketamine enantiomers: implications for abuse liability. Mol Psychiatry 2021;26:6704-22.
11. Jouguelet-Lacoste J, La Colla L, Schilling D, et al. The use of intravenous infusion or single dose of low-dose ketamine for postoperative analgesia: a review of the current literature. Pain Med 2015;16:383-403.
12. De Kock M, Lavand'homme P, Waterloos H. 'Balanced analgesia' in the perioperative period: is there a place for ketamine? Pain 2001;92:373-80.
13. Bilgin H, Ozcan B, Bilgin T, et al. The influence of timing of systemic ketamine administration on postoperative morphine consumption. J Clin Anesth 2005;17:592-7.
14. Zhang T, Yue Z, Yu L, et al. S-ketamine promotes postoperative recovery of gastrointestinal function and reduces postoperative pain in gynecological abdominal surgery patients: a randomized controlled trial. BMC Surg 2023;23:74.
15. Jipa M, Isac S, Klimko A, et al. Opioid-Sparing Analgesia Impacts the Perioperative Anesthetic Management in Major Abdominal Surgery. Medicina (Kaunas) 2022;58:487.
16. Argiriadou H, Himmelseher S, Papagiannopoulou P, et al. Improvement of pain treatment after major abdominal surgery by intravenous S+-ketamine. Anesth Analg 2004;98:1413-8, table of contents.
17. Webb AR, Skinner BS, Leong S, et al. The addition of a small-dose ketamine infusion to tramadol for postoperative analgesia: a double-blinded, placebo-controlled, randomized trial after abdominal surgery. Anesth Analg 2007;104:912-7.
18. Bornemann-Cimenti H, Wejbora M, Michaeli K, et al. The effects of minimal-dose versus low-dose S-ketamine on opioid consumption, hyperalgesia, and postoperative delirium: a triple-blinded, randomized, active- and placebo-controlled clinical trial. Minerva Anestesiol 2016;82:1069-76.
19. Joly V, Richebe P, Guignard B, et al. Remifentanil-induced postoperative hyperalgesia and its prevention with small-dose ketamine. Anesthesiology 2005;103:147-55.
20. Fu ES, Miguel R, Scharf JE. Preemptive ketamine decreases postoperative narcotic requirements in patients undergoing abdominal surgery. Anesth Analg 1997;84:1086-90.
21. Guignard B, Coste C, Costes H, et al. Supplementing desflurane-remifentanil anesthesia with small-dose ketamine reduces perioperative opioid analgesic requirements. Anesth Analg 2002;95:103-8, table of contents.
22. Edwards ND, Fletcher A, Cole JR, et al. Combined infusions of morphine and ketamine for postoperative pain in elderly patients. Anaesthesia 1993;48:124-7.
23. Wu CT, Yeh CC, Yu JC, et al. Pre-incisional epidural ketamine, morphine and bupivacaine combined with epidural and general anaesthesia provides pre-emptive analgesia for upper abdominal surgery. Acta Anaesthesiol Scand 2000;44:63-8.
24. Subramaniam K, Subramaniam B, Pawar DK, et al. Evaluation of the safety and efficacy of epidural ketamine combined with morphine for postoperative analgesia after major upper abdominal surgery. J Clin Anesth 2001;13:339-44.
25. Alexander I. Electronic medical records for the orthopaedic practice. Clin Orthop Relat Res 2007;457:114-9.
26. Bergeron N, Dubois MJ, Dumont M, et al. Intensive Care Delirium Screening Checklist: evaluation of a new screening tool. Intensive Care Med 2001;27:859-64.
27. Quibell R, Prommer EE, Mihalyo M, et al. Ketamine. J Clin Anesth 2011;41:640-9.
28. Chu PS, Ma WK, Wong SC, et al. The destruction of the lower urinary tract by ketamine abuse: a new syndrome? BJU Int 2008;102:1616-22.

doi: 10.21037/tgh-23-97
Cite this article as: Kerguelen Murcia D, Li JS, Phatak UR. Impact of intra-operative ketamine on postoperative outcomes in abdominal surgery: a narrative review. Transl Gastroenterol Hepatol 2024;9:25.

