Annals of Medicine and Surgery 78 (2022) 103783

Contents lists available at ScienceDirect

Annals of Medicine and Surgery

journal homepage: www.elsevier.com/locate/amsu

Systematic Review / Meta-analysis

Ketamine as a component of multimodal analgesia for pain management in bariatric surgery: A systematic review and meta-analysis of randomized controlled trials

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ARTICLE INFO

Keywords:
Ketamine
Obesity
Bariatric surgery
Pain management
Opioid-sparing

ABSTRACT

Introduction: Anaesthesia in morbidly obese people is challenging with a high dose of opioid consumption. This systematic review and meta-analysis of randomised controlled trials (RCTs) summaries evidence comparing ketamine to placebo for pain management after bariatric surgery.

Methods: We used PRISMA 2020 and AMSTAR 2 guidelines to conduct this study. The random-effects model was adopted using Review Manager Version 5.3 for pooled estimates.

Results: Seven RCTs published between 2009 and 2021 were eligible, including a total of 412 patients (202 patients in the ketamine group and 210 patients in the control group). In the ketamine group total opioid consumption during the first 24 h postoperatively was reduced (mean difference, MD = −5.89; 95% CI [-10.39, −1.38], p = 0.01), lower pain score at 4 h (MD = −0.81; 95% CI [-1.52, −0.10], p = 0.03), pain score at 8 h (MD = −1.00; 95% CI [-1.21, −0.79], p < 0.01), and shorter hospital stay (MD = −0.10; 95% CI [-0.20, −0.01], p = 0.03). There was no significant difference between the two groups regarding duration of anaesthesia (MD = −3.42; 95% CI [-8.62, 1.82], p = 0.20), or sedation score (MD = −0.02; 95% CI [-0.21, 0.17], p = 0.84). As concern the postoperative complications, risks of postoperative nausea and vomiting(OR = 0.75; 95% CI [0.27, 2.04], p = 0.56), hallucinations (OR = 5.47; 95% CI [0.26, 117.23], p = 0.28), dizziness (OR = 1.05; 95% CI [0.14, 7.78], p = 0.96), and euphoria (OR = 5.77; 95% CI [0.65, 51.52], p = 0.12) were not different between the two groups either.

Conclusion: Ketamine could be an effective and safe technique for pain management following bariatric surgery. It reduces opioid consumption, postoperative pain, and hospital stay.

RegistrationThis review was registered in PROSPERO (CRD42022296484).

1. Introduction

During the last decades, bariatric surgery has been increasingly used in parallel to the epidemic of obesity, and mini-invasive surgical approaches have been widespread [1]. Currently, surgery is effective for weight loss and control of comorbidities [2]. However, some postoperative analgesia modalities remain subject to controversy. Morphine, tramadol, and paracetamol were used in many studies. Postoperative pain management is crucial; it decreases postoperative morbidity, including cardiovascular and respiratory complications, and allows early ambulation [3]. The Enhanced Recovery After Surgery (ERAS) society guidelines for bariatric surgery, published in 2016, reported that a multimodal analgesic approach should be considered the gold standard [4]. Surely, this multimodal analgesia should be opioid-free as much as possible. Taylor et al. [5] showed that 77% of opioid-related side effects occur during the first postoperative 24 h, especially in case

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https://doi.org/10.1016/j.amsu.2022.103783
Received 27 March 2022; Received in revised form 8 May 2022; Accepted 10 May 2022
Available online 14 May 2022

of a medical history of obstructive sleep apnea. In addition, obese patients presented a higher risk of developing opioid dependence [6]. Several studies investigated different measures to reduce postoperative opioid consumption. They used clonidine [7], dexmedetomidine [8], or pregabalin [9].

Ketamine has been reported as an effective analgesic means due to N-methyl-D-aspartate (NMDA) receptor [10]. It has been used for analgesia following upper abdominal, thoracic, and major orthopaedic surgeries with encouraging results [10]. However, data on its efficacy after bariatric surgery is limited. So far, only a few studies have evaluated ketamine efficacy in postoperative pain management and opioid-sparing in obese patients. Therefore, we performed a systematic review with a meta-analysis of randomised clinical trials (RCTs) to provide a higher level of evidence concerning ketamine efficacy and safety.

This systematic review and meta-analysis aimed to compare the efficacy and safety of ketamine for pain management following bariatric surgery compared to a placebo.

2. Methods

We conducted a systematic review and meta-analysis according to the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) guidelines 2020 [11] and AMSTAR 2 (Assessing the methodological quality of systematic reviews) Guidelines [12]. This review was registered in PROSPERO (CRD42022296484).

Electronics searches: We performed a computer-based investigation of the relevant literature on June 15, 2021, on publications during the last two decades. We did not use language restrictions. We sought trials in the Cochrane Library's Controlled Trials Registry and systematic review database, Embase, National Institute of Health PubMed/MEDLINE, and Google Scholar databases. We used the following keywords: "analgesia", "pain management", "ketamine", "placebo", "bariatric surgery", "gastric bypass", "sleeve gastrectomy", and "randomized-controlled trials". We checked the reference list of relevant reviews for eligible clinical trials.

Inclusion criteria: We retained only RCTs comparing ketamine infusion or bolus with placebo for postoperative pain management following open or laparoscopic bariatric surgery for adults (>18-year-old). We excluded trials using an adjuvant with ketamine or when ketamine was compared to another analgesic regimen different from the placebo. Only articles published in peer-reviewed journals were considered. Data from non-randomised clinical trials, non-comparative studies, review articles, editorials letters, abstract only, comments, and case series (fewer than ten cases) were excluded.

3. Outcomes measures

The primary outcome was total opioid consumption in IV morphine equivalent during the first 24 h postoperatively. The secondary outcomes were visual analogue pain scores (VAS) at rest at different periods (4 h H4, 8 h H8, 12 h H12, and 24 h H24), duration of anaesthesia, sedation score (1 = awake and anxious, agitated, or restless; 2 = awake and cooperative, oriented and tranquil; 3 = asleep, responsive to commands; 4 = asleep with fast response to stimuli (light and noise); 5 = asleep with response only to pain; 6 = no response to any stimuli), postoperative nausea and vomiting (PONV), length of hospital stay, and postoperative complications (hallucination, euphoria, and dizziness).

Study Selection: Two authors (MAD and MAC) independently reviewed all abstracts. We retained all studies accompanied by the full text that met the inclusion criteria. After consulting a third review team member (GP), the discussion resolved disagreements.

Data Extraction: Two authors extracted the data independently (MAD and MAC), and the senior author (GP) settled any disparity after discussion. Included studies were fully matched for the first author's name, year of publication, country, body mass index (BMI), sample size (ketamine group and control group), age, sex ratio, administration protocol of ketamine (bolus or infusion), type of surgery, supplemental analgesic, and follow-up.

Missing data: We contacted authors by e-mail regarding unclear bias domains or missing primary outcomes information for our meta-analysis. If some data were not reported numerically, we extracted them from the figures.

Assessment of study quality and risk of bias assessment: All studies that met the selection criteria were appraised independently by two authors (MAD and MAC). We used the CONSORT (Consolidated Standards of Reporting Trials) scale for RCT quality assessment [13]. We excluded studies with a score <14/25. We used the Cochrane tool for bias assessment to assess the risk of bias in randomised trials (RoB2) [14]. We evaluated the bias in five distinct domains (A. randomisation process, B. deviations from intended interventions, C. bias in the measurement of outcome, D. bias to missing outcome data, E. bias in selecting the reported results, and F. overall bias). Within each domain, one or more signaling questions led to judgments of "low risk of bias," "some concerns," or "high risk of bias". Results were presented in the forest plot of each outcome.

Handling continuous data: Continuous data were analysed using Review Manager 5.3.5 statistical package from Cochrane collaboration for meta-analysis [15]. When mean and standard deviation (SD) were not reported, they were estimated from the provided interquartile range (IR) and median based on the formula described by Hozo et al. [16]. If the sample size was >25 patients, the mean was considered equal to the median. In addition, SD was calculated as IR/4 for sample size <70 patients and IR/7 for sample size >70 patients.

Assessment of heterogeneity: To assess heterogeneity, we used the Cochrane Chi^2 test (Q-test), the I^2 statistic, and the variance TAU^2 to estimate the degree of heterogeneity [17]. Funnel plots identified studies responsible for heterogeneity. A subgroup analysis was performed when all the included studies reported the outcome. It was performed to assess the opioid consumption in a ketamine infusion subgroup or ketamine bolus subgroup.

Summary of findings: Two authors (MAD and MAC) independently assessed the certainty of the evidence. We used The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) [18]. We considered the study limitations constancy of effect, imprecision, indirectness, and publication bias. We assessed the certainty of evidence as high, moderate, low, or very low. If appropriate, we considered the following criteria for upgrading the evidence: large effect, dose-response gradient, and plausible confounding effect. We used the methods and recommendations described in sections 8.5 and 8.7 and chapters 11 and 12 of the Cochrane Handbook for Systematic Reviews of Interventions. We used the GRADEpro GDT software to prepare the summary of findings tables. We explained the reasons for downgrading or upgrading the certainly of included studies using footnotes with comments.

Evaluation of effect size: We used the RevMan 5.3.5 statistical package from the Cochrane collaboration for meta-analyses [15]. We selected the mean difference (MD) as an effective measure for continuous data. For dichotomous variables, odds ratios (OR) with 95% confidence intervals (95% CI) were calculated. Random effects model was used. The threshold of statistical significance was set to 0.05.

4. Results

Literature search: In the initial research, 28 papers were identified from the electronic database. After full-text checking, we retained seven eligible RCTs [7,19–24] published between 2009 and 2021 (Fig. 1). Three studies were excluded for the following reasons: one study was a letter to the editor [25], one study was a case series[26], and one study was a systematic review[27]. The seven identified studies were published as full papers in English. They involved 412 patients (202 patients in the ketamine group and 210 in the control group). The mean BMI was between 41 and 53.5 kg/m^2. The mean age was between 28 and

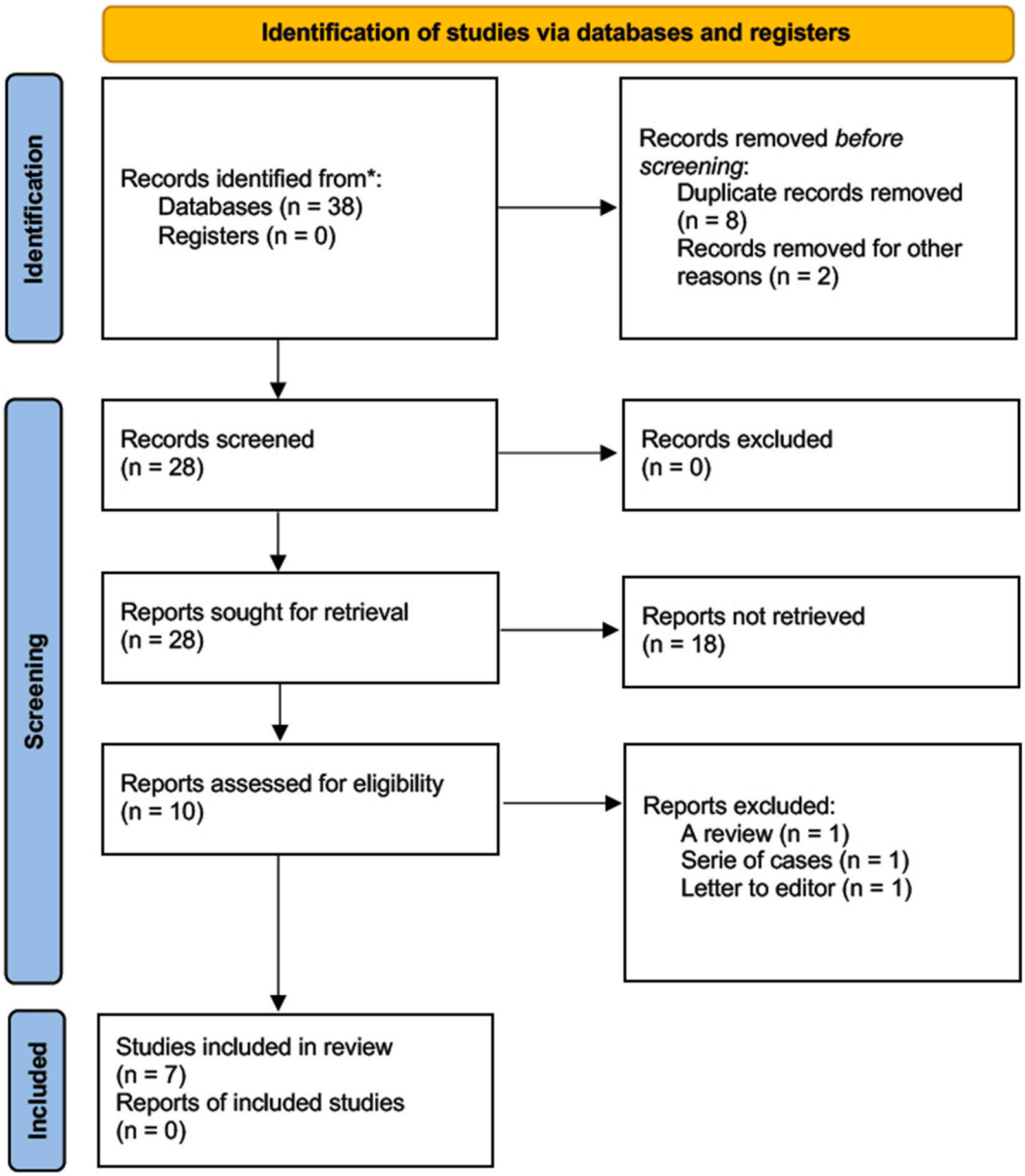

Fig. 1. Flow diagram of the studies research.

45.5-year-old. Five studies used the laparoscopic approach [19–22,24], and only one study used open surgery [7,23]. Six studies [19–24] have used morphine with the ketamine in a multimodal analgesia protocol, and one study [7] has used Tramadol in the multimodal analgesia protocol. Study characteristics with quality assessment and the summary of evidence findings were reported in Tables 1 and 2, respectively.

4.1. Primary outcome: total opioid consumption

Seven studies mentioned total opioid consumption during the first 24 h after surgery [7,19–24]. It was significantly lower in the ketamine group (MD = −5.89; 95% CI [-10.39, −1.38], p = 0.01). There was a high heterogeneity rate among the studies $Tau^2 = 29.16$ ($I^2 = 91\%$) (Fig. 2). We performed a subgroup analysis comparing the infusion group and the perfusion group. Three studies reported opioid consumption in the infusion group [21,23,24]. They included 77 patients in each group. There was no difference between groups in terms of opioid consumption (MD = −11.29; 95% CI [-30.31, 7.74], p = 0.24). Four studies reported opioid consumption in the bolus group [7,19,20,22]. They included 125 patients in the ketamine bolus group and 210 patients in the control group. There was lower opioid consumption in the ketamine group compared to the control group (MD = −5.44; 95% CI [-9.68, −1.19], p = 0.01).

4.2. Secondary outcomes

4.2.1. Visual analogue pain scores

Seven studies reported data on VAS 4 h after bariatric surgery. They included 202 patients in the ketamine group and 210 patients in the control group. The VAS-H4 was lower in the ketamine group compared to the control group (MD = −0.81; 95% CI [-1.52, −0.10], p = 0.03). There was no heterogeneity among the studies $Tau^2 = 0.89$ ($I^2 = 98\%$) (Fig. 3 and Table 3).

Concerning the VAS score at H8, it was reported in two studies [7, 20]. They included 66 patients in the ketamine group and 70 patients in the control group. Pooled results demonstrate any lower VAS score at H8 in the ketamine group (MD = −1.00; 95% CI [-1.21, −0.79], p < 0.01) **(Table 3)**.

Table 1
Included studies characteristics.

Author	Year	Country	BMI	Sample Size (ketamine/ placebo)	Age Sex (M/ F)	Ketamine Bolus/ infusion	Type of surgery	Supplemental analgesic	Follow-up	CONSORT
Mehta et al.	2020	USA	44.65	54 (27/27)	-(10/ 44)	20 mg bolus followed by 5 μg/kg/min infusion	Laparoscopic Roux-en-Y	Acetaminophen + morphine	48 h	21/25
Adhikary et al.	2020	Australia	44.5	86 (43/43)	42.0 –	Bolus 0.5 mg/kg after endotracheal intubation	Laparoscopic sleeve gastrectomy	PCA morphine	24 h	22/25
Wang et al.	2018	USA	42.75	90 (44/46)	40.2 (18/62)	Bolus 0.4 mg/kg	Laparoscopic gastric bypass/sleeve	Paracetamol + PCA morphine	48 h	20/25
Sollazzi et al.	2009	Italy	53.5	50 (23/27)	38.5 (18/32)	Bolus 0.5 mg/kg before induction	Open biliopancreatic diversion	Tramadol	24 h	15/25
Kasputyté et al.	2020	Lithuania	44.55	32 (15/17)	45.5 (9/ 23)	Bolus 0.15 mg/kg pre-incisional	Laparoscopic gastric bypass	Morphine	24 h	17/25
Jabbour et al.	2019	Lebanon	42.86	40 (20/20)	32.77 (19/21)	Bolus 0.2 mg/kg followed by 0.15 mg/ kg/h infusion	Open gastric bypass	Paracetamol + morphine	48 h	17/25
Hasanein et al.	2011	Egypt	41.0	60 (30/30)	28.0 (32/28)	1 μg/kg/min infusion	Laparoscopic gastric bypass	PCA morphine	24 h	14/25

The same two studies assessed the VAS score at H12 [7,20]. They included 66 patients in the ketamine group and 70 patients in the control group. There was no difference between the two groups (MD = 0.35; 95% CI [-0.34, 1.03], p = 0.32)**(Table 3)**.

Three studies reported data on the VAS score at H24 [19–21]. They included 114 patients in the ketamine group and 116 patients in the control group. There was no significant difference between the ketamine and the control group (MD = −0.17; 95% CI [-0.47, 0.13], p = 0.26) **(Table 3)**.

4.2.2. Duration of anaesthesia

Six studies assessed data on the duration of anaesthesia (7,19,20,22–24). They included 175 patients in the ketamine group and 183patients in the control group. There was no difference between the two groups (MD = −3.42; 95% CI [-8.62, 1.82], p = 0.20). There was high heterogeneity among the studies $Tau^2 = 18.30$ ($I^2 = 64\%$)(Fig. 4).

4.2.3. Postoperative sedation score

Two studies reported data on postoperative sedation scores(20,24). They included 73 patients in the ketamine group and 73 patients in the control group. There was no difference between the ketamine and the control group (MD = −0.02; 95% CI [-0.21, 0.17], p = 0.84) **(Table 3)**.

4.2.4. Postoperative nausea and vomiting (PONV)

Three studies assessed data on PONV [19,22,24]. Eight out of 89 patients presented PONV in the ketamine group and 11 out of 93 patients in the control group. There was no difference between the two groups (OR = 0.75; 95% CI [0.27, 2.04], p = 0.56)**(Table 3)**.

4.2.5. Lengths of hospital stay (LOS)

Two studies reported data on the length of hospital stay [19,21]. They included 71 patients in the ketamine group and 73 patients in the control group. LOS was shorter in the ketamine group than in the control group (MD = −0.10; 95% CI [-0.20, −0.01], p = 0.03) **(Table 3)**.

4.2.6. Postoperative complications

Data on postoperative hallucinations were reported in four studies [19,21,22,24]. Two patients reported this complication out of 116 in the ketamine group, and none of the 120 patients in the control group, but the difference between the two groups was not statistically significant (OR = 5.47; 95% CI [0.26, 117.23], p = 0.28).

It was assessed by three studies [19,21,22] concerning postoperative euphoria, including 86 patients in the ketamine group and 90 patients in the control group. Two patients from each group reported this side effect; there was no significant difference between the two groups (OR = 1.05; 95% CI [0.14, 7.78], p = 0.96).

Two studies assessed data on postoperative dizziness [19,21]. This side effect was found in five patients out of 71 in the ketamine group and one out of 73 patients in the control group, and the difference was not statistically significant (OR = 5.77; 95% CI [0.65, 51.52], p = 0.12).

5. Discussion

This systematic review with meta-analysis of RCTs comparing ketamine infusion or bolus with placebo for pain management following bariatric surgery demonstrated that ketamine was associated with lower opioid consumption during the 24 h postoperatively, decreased VAS scores at H4 and H8, and shorter hospital stay. However, there was no difference between the ketamine and control groups regarding the duration of anaesthesia, postoperative sedation scores, PONV, and postoperative complications (hallucinations, headache, euphoria and dizziness).

Bariatric surgery is more and more often performed. Obese patients are more prone to postoperative complications (pulmonary, cardiovascular, and thromboembolic). Early recovery and ambulation are crucial and depend on effective postoperative analgesia. According to the Canadian Consensus Statement, a multimodal approach with reduced opioid use has been strongly recommended after bariatric surgery [28]. Reducing opioid consumption may decrease the side effects such as nausea, vomiting, ileus, and respiratory depression [29]. It may also minimise the duration of hospital stay. That is why, to increase opioid-sparing, ketamine has been proposed among several adjuvants.

Since 1970, ketamine has been described as an anaesthetic drug. It has gained interest as part of a multimodal approach to acute pain management [30,31]. Its analgesic function was mostly explained by blocking the NMDA receptors involved in inflammatory and nociceptive pain transmission [32]. However, ketamine has been associated with untoward side effects such as hallucinations, headache, euphoria, and dizziness. Therefore, the best ketamine administration and the optimal dose are still controversial. A systematic review assessed that low doses of ketamine (no more than 1.2 mg/kg/h when used as continuous infusion and no more than 1 mg/kg when given as bolus) reduced opioid consumption and pain scores without major complications up to 48 h after surgery [33]. In our systematic review with meta-analysis, low doses of ketamine were used in the seven included studies (three RCTs used only one bolus of ketamine, three RCTs used ketamine bolus followed by continuous infusion, and only one RCT used a continuous infusion of ketamine without an initial bolus).

Table 2
Summary of findings table.

Ketamine compared to Control group for Obesity Surgery

Patient or population: Obesity Surgery
Setting: **Intervention**: Ketamine Vs. **Comparison**: Control group

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with Control group	Risk with Ketamine			
Opiod's consumption	The mean opiod's consumption was **0**	MD **5.89 lower** (10.39 lower to 1.38 lower)	-	412 (7 RCTs)	⨁⨁◯◯ LOW [a,b,c]
VAS H4	The mean VAS H4 was **0**	MD **0.81 lower** (1.52 lower to 0.1 lower)	-	412 (7 RCTs)	⨁⨁◯◯ LOW [a,b,c]
VAS H8	The mean VAS H8 was **0**	MD **1 lower** (1.21 lower to 0.79 lower)	-	136 (2 RCTs)	⨁⨁⨁◯ MODERATE [c]
VAS H12	The mean VAS H12 was **0**	MD **0.35 higher** (0.34 lower to 1.03 higher)	-	136 (2 RCTs)	⨁⨁◯◯ LOW [a,b,c]
VAS H24	The mean VAS H24 was **0**	MD **0.17 lower** (0.47 lower to 0.13 higher)	-	230 (3 RCTs)	⨁⨁◯◯ LOW [a,c]
Time to extubation	The mean time to extubation was **0**	MD **3.42 lower** (8.67 lower to 1.82 higher)	-	358 (6 RCTs)	⨁⨁◯◯ LOW [a,b,c]
Hospital stay	The mean hospital stay was **0**	MD **0.1 lower** (0.2 lower to 0.01 lower)	-	144 (2 RCTs)	⨁⨁⨁◯ MODERATE [c]
Sedation score	The mean sedation score was **0**	MD **0.02 lower** (0.21 lower to 0.17 higher)	-	146 (2 RCTs)	⨁⨁◯◯ LOW [a,c]
Nausea/vomiting	118 per 1 000	**90 per 1 000** (35 to 215)	**OR 0.74** (0.27 to 2.04)	182 (3 RCTs)	⨁⨁⨁◯ MODERATE [c]
Hallucinations	0 per 1 000	**0 per 1 000** (0 to 0)	**OR 5.47** (0.26 to 117.23)	236 (4 RCTs)	⨁⨁⨁◯ MODERATE [c]
Euphoria	22 per 1 000	**23 per 1 000** (3 to 150)	**OR 1.05** (0.14 to 7.78)	176 (3 RCTs)	⨁⨁⨁◯ MODERATE [c]
Dizziness	14 per 1 000	**74 per 1 000** (9 to 417)	**OR 5.77** (0.65 to 51.52)	144 (2 RCTs)	⨁⨁⨁◯ MODERATE [c]

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **MD:** Mean difference; **OR:** Odds ratio

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Explanations

a. I^2>50%,
b. Significant p value of heterogeneity
c. Small sample size

We have performed a subgroup analysis regarding the high heterogeneity rate in opioid consumption between the seven studies. This analysis reported a similar opioid consumption after ketamine infusion and a significantly lower opioid consumption in the ketamine bolus group. These findings could explain the heterogeneity among the studies since heterogeneity was reduced in the bolus subgroup analysis.

Concerning postoperative complications related to ketamine administration, we did not find any difference between the two groups.

Anaesthetic time is defined as the time from the induction to the endotracheal extubation. It depends on many factors, including residual muscle block, opioid dose, and level of consciousness. Ketamine, as an anaesthetic drug, has been reported to increase sedation and probably delay endotracheal extubation [34]. However, our results support the evidence that ketamine does not delay endotracheal extubation after surgery, and we thought this is probably due to the low dose of ketamine.

Regarding postoperative pain scores, we found that ketamine reduced the VAS scores only at H4 and H8. The pharmacokinetics of ketamine may explain these findings. Therefore, some authors suggested using magnesium as an adjuvant to ketamine. Even Liu et al. called the association of these two drugs a "super-additive effect". According to the meta-analysis of De Oliveira Jr et al., systemic administration of perioperative magnesium reduced postoperative pain and opioid consumption [35]. Thus, further studies are needed to assess the efficacy of adding magnesium to ketamine in improving pain management for bariatric surgery patients.

This study is the first systematic review with meta-analysis of RCTs comparing ketamine with placebo for acute pain management following bariatric surgery to the best of our knowledge. Several limitations should be considered. We included only RCTs in this systematic review, but only seven trials were published in the literature, so for this reason, the sample size was small (412 patients). We have included these two studies in the meta-analyses to enlarge the sample size of patients. In addition, after the pooled analysis and the sensitivity analysis, these two studies were not sources of heterogeneity in the different outcomes. Then these two studies allow a higher level of evidence.

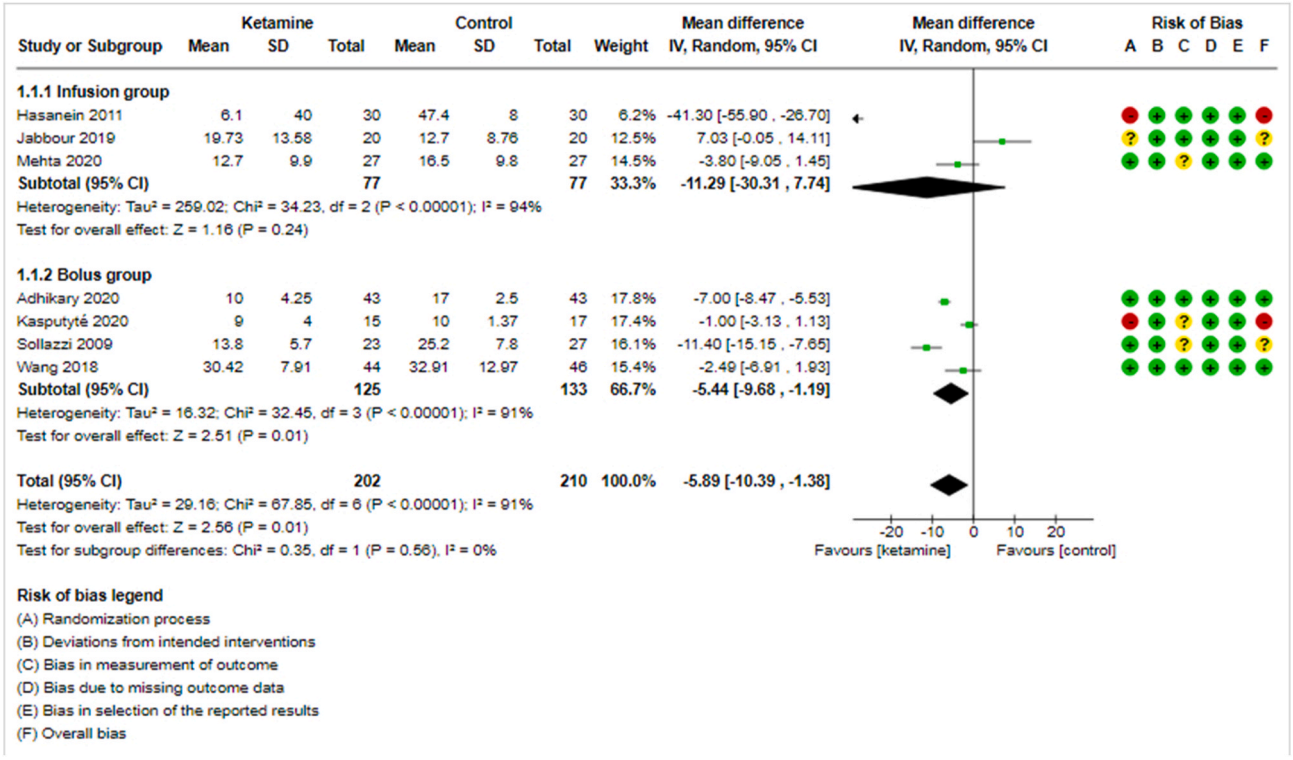

Fig. 2. Forest plots of opioid consumption.

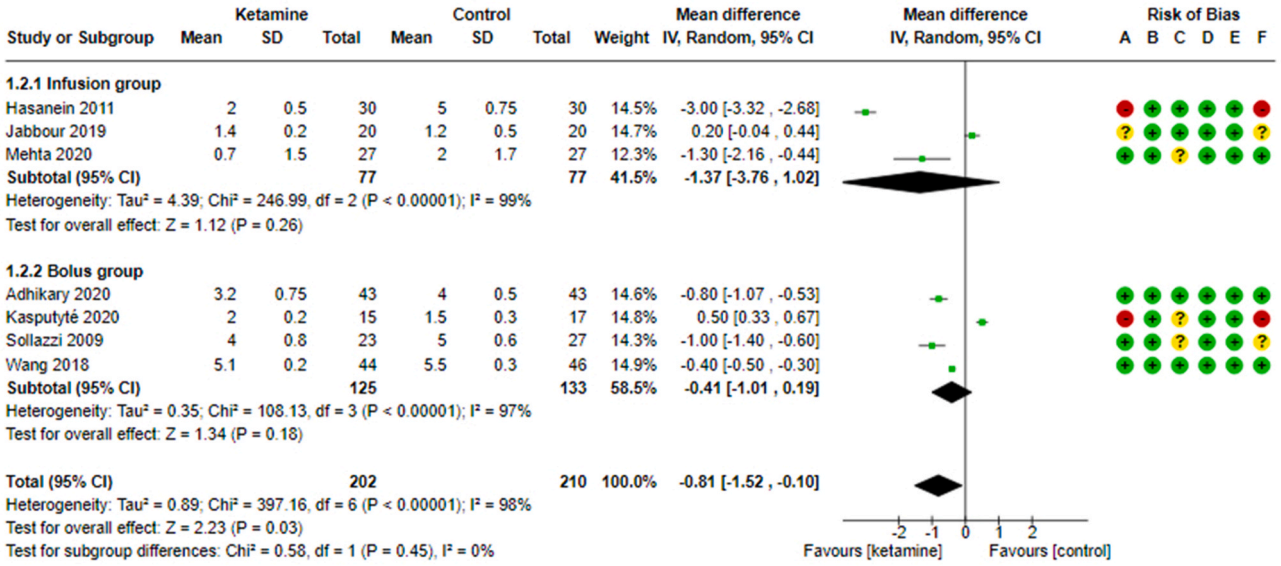

Fig. 3. Forest plots of pain scores at H4.

Furthermore, when there was heterogeneity among the studies, it was impossible to perform subgroup analyses for the outcomes. The risk of bias was assessed using the 5-piece Cochrane Handbook recommendation and the CONSORT to evaluate the quality of retained studies to overcome these limitations. We have tried to standardise, but some outcomes were not reported or well-defined. These findings should be considered cautiously and require confirmation in a larger group of patients. Besides, several postoperative data were not reported or missed. Finally, only acute pain management was assessed, so further trials studying the impact of ketamine on chronic pain are needed.

6. Conclusion

The primary outcome was opioid consumption for pain management following bariatric surgery: we can conclude with a high level of evidence that administration of ketamine decreased opioid consumption compared with placebo when it is administrated as a bolus. Furthermore, it reduced the VAS scores at H4 and H8 and the length of hospital stay. Thus, our systematic review's overall level of evidence can be graded 2a with a grade B of recommendation [36]. However, further studies with larger sample sizes are needed to address the superior effectiveness and safety of ketamine in pain management following

Table 3
Summary of secondary outcomes.

Outcomes	Number of studies	Participants (Ketamine/ placebo)	Relative effect (95% CI)	Tau^2	I^2	P value
VAS at H8	2 RCTs	136 (66/70)	OR = −1.00 [-1.21, −0.79]	0.00	0%	**< 0.01**
VAS at H12	2 RCTs	136 (66/70)	OR = −1.00 [-1.21, −0.79]	0.23	93%	0.32
VAS at H24	3 RCTs	230 (114/ 116)	OR = −0.17 [-0.47, 0.13]	0.04	67%	0.26
Sedation score	2 RCTs	146 (73/73)	OR = −0.02 [-0.21, 0.17]	0.01	63%	0.84
LOS	2 RCTs	144 (71/73)	OR = −0.10 [-0.20, −0.01]	0.00	0%	**0.03**

VAS: visual analogue scale; H8: 8 h; H12: 12 h; H24: 24 h; LOS: length of hospital stay; PONV: postoperative nausea and vomiting; RCT: a randomized controlled trial.

bariatric surgery.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Ethical Approval

This research involved human participants. This retrospective analysis of published cases did not require informed consent. Ethics approval and consent to participate were not included in this review.

Author contribution

MAC, MAD, MCB, and HO :study concept or design.
MAC, MAD, and SU: data collection.
MAC,MAD,MCB: data analysis or interpretation.
MAC, MCB, HO, GP: writing the paper.
MAD, JMF, OS, MB, GP, and HO Approved the final version.

Registration of Research Studies

Name of the registry: PROSPERO
Unique Identifying number or registration ID: CRD42022296484
Hyperlink to your specific registration (must be publicly accessible and will be checked): https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=296484

Compliance with ethical standards

This research involved human participants. This retrospective analysis of published cases did not require informed consent. Ethics approval and consent to participate were not included in this review.

Funding

Any institution did not support this work.

Availability of data and materials

All data generated or analysed during this study are included in this published article.

Trial registry number

Name of the registry: PROSPERO. Unique Identifying number or registration ID: CRD42022296484. Hyperlink to your specific registration (must be publicly accessible and will be checked): https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=296484.

Consent

No Ethical Approval or consent is required as this research project is a systematic review of previous studies.

Guarantor

The Guarantor is the one or more people who accept full responsibility for the work and/or the conduct of the study, had access to the data, and controlled the decision to publish.
Mohamed Ali CHAOUCH

Availability of data, code and other materials

None.

Author disclosures

No conflict of interest or support to disclose.

Compliance with ethical standards

Ethics approval and consent to participate in this retrospective research involving human participants are not applicable in this review.

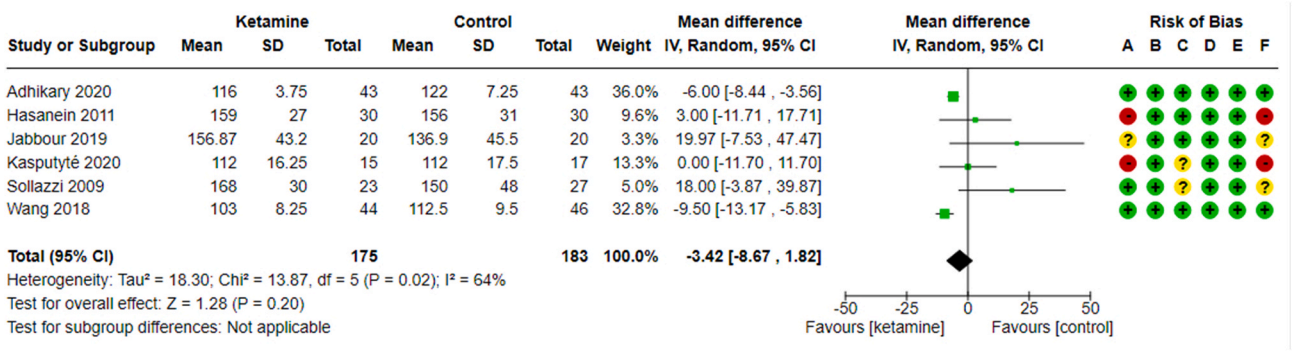

Fig. 4. Forest plots of the duration of anaesthesia.

Declaration of competing interest

The authors declare that they have no conflict of interest.

Acknowledgements

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2022.103783.

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