

The efficacy of intravenous ketamine in major abdominal surgery

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ABSTRACT:

The postoperative pain associated with major abdominal surgery by laparotomy is considered severe. It also involves peripheral and central sensitisation phenomena, defining primary and secondary hyperalgesia respectively, and allodynia phenomena. The perioperative administration of antihyperalgesic substances such as ketamine and the reduction of intraoperative opioid use in a multimodal anaesthesia and analgesia protocol has been the subject of numerous studies. The aim of this study is to evaluate the efficacy of intraoperative and postoperative IV ketamine in major abdominal surgery. A prospective, comparative, randomised, double-blind study was conducted in the general surgery department of the Mostaganem University Hospital. Over a two-year period from March 2023 to March 2025, 84 patients underwent major abdominal surgery by laparotomy, comparing two groups of patients. Group P1 (n=43) received an IV lidocaine bolus (bolus + continuous infusion) and group P2 (n=41) received ketamine (bolus + continuous infusion) in addition to lidocaine. Additional analgesia was provided by IV paracetamol and nefopam (ACUPAN) and titrated morphine to achieve the analgesic target ($EN \leq 3$). Data collected on morphine consumption 24 hours after surgery and DPO scores for coughing and resting at various post-operative times on the numerical scale (EN). Morphine consumption during the first 24 hours was reduced in both groups but significantly lower in the P2 group with lower DPO scores at rest and during mobilisation ($P < 0.001$). The results clearly demonstrated that the efficacy of ketamine in addition to xylocaine led to significant savings in morphine consumption 24 hours after surgery in a multimodal analgesia strategy and significantly reduced DPO scores in static and dynamic conditions.

Keywords: postoperative hyperalgesia, DPO, ketamine

INTRODUCTION:

Post-operative pain following major abdominal surgery is defined as severe. It is not solely the result of excessive nociception caused by damage to the viscera, muscles and skin, but also involves peripheral and central sensitisation phenomena[1]. Peripheral sensitisation corresponds to inflammation at the site of the injury, and the resulting hyperalgesia is known as primary hyperalgesia[2]. Central sensitisation corresponds to a state of hyperexcitability of spinal and supraspinal nociceptive neurons, the mechanisms of which are very similar to those of neuropathic pain, and the resulting hyperalgesia is known as secondary hyperalgesia [2]. Morphine derivatives used in the perioperative period amplify this hyperalgesia already induced by surgery, particularly in patients with chronic pain[3].

Primary and secondary hyperalgesia clinically manifest as very intense postoperative pain, leading to excessive consumption of morphine in the postoperative period, which increases its side effects (nausea and vomiting, sedation, ileus, confusion/delirium, respiratory depression, immunosuppression), thereby delaying the

patient's recovery[4].

The prevention of this postoperative hyperalgesia through the perioperative administration of antihyperalgesic substances and the reduction of intraoperative opioid use in multimodal anaesthesia and analgesia protocols has been the subject of numerous.

Study objectives:

To evaluate the effect of perioperative infusion of ketamine combined with IV lidocaine compared to IV lidocaine infusion alone on:

- Postoperative opioid consumption up to 24 hours postoperatively
- DPO scores up to 48 hours postoperatively (cough and rest)

MATERIALS AND METHODS:

This is a prospective, comparative, randomised, double-blind study conducted over a two-year period from March 2024 to March 2025. Eighty-four patients underwent major abdominal surgery for cancerous and non-cancerous conditions via a median subumbilical,

transverse or oblique laparotomy, which is associated with intense postoperative pain

Our study included adult patients > 16 years of age; informed and consenting; ASA class I, II and III; undergoing major abdominal surgery by laparotomy Under général anesthésia lasting more than two hours. The following were excluded from this study: pregnant or breastfeeding women, patients with mental disorders or who were uncooperative; repeat surgery; emergency surgery; ASA IV, V and VI patients with a post-operative life expectancy of less than 24 hours; Patients with a contraindication to IV lidocaine (allergy to the product, recurrent porphyria, uncontrolled epilepsy, haemodynamic instability, conduction disorder. atrioventricular block (AVB) with indication for pacemaker; patients unwilling to participate in the study, either because they do not understand the principle of the numerical scale or because they cannot count from 0 to 10; patients with a contraindication to ketamine (allergy to the product, uncontrolled hypertension, severe heart failure, preoperative cognitive impairment).

Study protocol

This is a prospective randomised study involving 96 patients divided into two groups:

1. Group P1 (n=43) received perioperatively lidocaine (2%) intravenously in a bolus dose of 1.5 mg/kg before anaesthetic induction, followed by continuous infusion via an auto-pulsed syringe at a rate of 2 mg/kg/h before surgical incision until 30 minutes to 1 hour before the end of surgery.
2. Group P2 (n=41) received lidocaine IVn bolus and continuous infusion as in group P1; after anaesthetic induction, patients received a ketamine bolus of 0.15-0.5 mg/kg followed by a continuous infusion via auto-pulsing syringe of 0.125-0.250 mg/kg before the surgical incision, continued until 30 minutes to 1 hour before the end of the surgical procedure.

Primary outcome measure:

Cumulative postoperative morphine consumption up to 24 hours

Secondary outcome measures:

- DPO scores at rest at different postoperative times (SSPI, H1, H2, H4, H6, H12, H24, H36, H 48).
- DPO scores at mobilisation at 24 hours postoperatively A score ≤ 3 is considered the threshold for optimal analgesia Both groups P1 and P2 received the same general anaesthesia protocol.

General anaesthesia was induced with propofol, fentanyl (1 to 1.5 μ g/kg) and rocuronium (0.6mg/kg). Anaesthesia was maintained with sevoflurane and a

mixture of 50% oxygen and 50% nitrous oxide (NO₂). During surgery, monitoring was performed using a five-parameter cardioscope (PANI, HR, ECG, SPO₂).

Analgesia was multimodal for both groups and was provided by:

Dexamethasone (DXM) administered intravenously at a dose of 0.1–0.2 mg/kg, with 4 mg for patients weighing less than 50 kg for both groups.

Group P1 received a bolus of lidocaine at 1.5 mg/kg prior to induction, followed by a continuous infusion of 2 mg/kg/h, which was stopped 30 minutes before the end of the surgical procedure.

Group P2 received, in addition to lidocaine (bolus and continuous infusion), a bolus of ketamine at a dose of 0.15–0.50 mg/kg after induction, followed by a continuous infusion at a dose of 0.10–0.20 mg/kg/h, which was stopped 30 minutes before the end of the surgical procedure.

Both groups received 1 g of paracetamol IV and 20 mg of nefopam (Acupan) and 100 mg of diclofenac injectable deep IM, except in cases of contraindications (gastroduodenal ulcer, surgery with anastomosis Postoperative pain with a score greater than or equal to 4 was controlled by morphine titration by a blinded nurse not participating in the study through intravenous administration of a 2 mg bolus every 5 minutes based on respiratory rate (FR ≥ 10 cycles/min) and the sedation score (score < 1) until a score of less than or equal to 3 on the numerical scale (EN ≤ 3) was obtained. Continuous infusions of IV lidocaine alone in SAP (group P1) or combined with ketamine (group p2) were reconnected in all patients with a sedation score of 0.

Group p1: IV lidocaine at a rate of 1.33 mg/kg/h continued in the surgical intensive care unit for 24 hours postoperatively (Table 1).

Group P2: IV lidocaine at a rate of 1.33 mg/kg/h and ketamine at a rate of 0.12-0.25 mg/kg/h for 24 hours postoperatively (Table 1). Additional multimodal analgesia was administered in both groups by combining IV paracetamol (Perfalgan) at a rate of 1 g every 6 hours and IV nefopam (Acupan) at a rate of 20 mg every 6 hours and 100 mg of diclofenac IM only if necessary. Morphine titration by 2 mg IV bolus was indicated only for patients with an EN score ≥ 4 up to

Measurement of Results:

- Our primary endpoint was a 50% reduction in morphine consumption at 24 hours.
- The DPO was assessed at various postoperative times at rest in the PACU at 48 hours.
- DPO scores at mobilisation at 24 hours.

In this study, we took the following parameters into account:

Gender; physical status (ASA classification); age; weight; height; body mass index; amount of morphine consumed during the first 24 hours post-operatively; DPO scores at rest, coughing, duration of surgery (min),

amount of fentanyl consumed intraoperatively (μ).

RESULTS:

Over a 24-month period from March 2024 to March 2025, a total of 96 patients were enrolled. Seven patients

were excluded from the outset, leaving 89 patients eligible for the study, who were then divided into two groups. Eleven other patients were excluded during the study (Figure 1).

Figure 1: Quantitative and qualitative variables for the two groups of patients P1 and P2

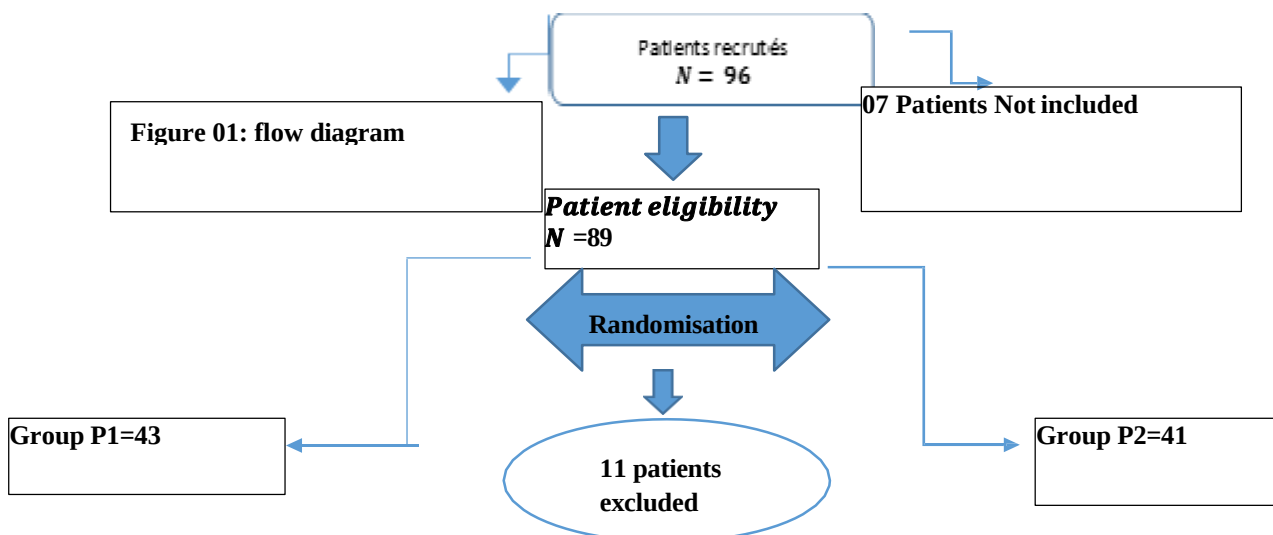


Table 01: Quantitative and qualitative variables for the two patient groups P1 and P2

Group P1 N=43

Group P2 N=43

			p-value
Age (years)	52.53 ± 15.20	8.68 ± 15.57	
Gender (M, F)%	37.2/62.8	34.1/65.9	
BMI (kg/m ²)	23.75 ± 5.09	22.52 ± 4.75	
ASA (I, II, III) (%)	42/44/14	56/32/12	
Type of surgery (%)			
Oesophageal surgery	2.37	1.60	
Gastric surgery	4.75	7.33	
Pancreatic surgery	5.95	5.95	
Colorectal surgery	24.99	8.33	
Kidney surgery	1.98	3.97	
Gynaecological surgery	2.38	5.95	
Adrenal surgery	00	2.38	
Hepatobiliary surgery	2.38	5.95	
Gastrointestinal	3.57	3.57	p > 0.5
surgery	00	1.19	
Splenic surgery	3.97	1.98	
Exploratory laparotomy	187.58 ± 58.50	200.07 ± 107.66	
- Duration of			
intervention (min)	127.44 ± 66.88	108.30 ± 53.75	
- Average dose			
of fentanyl (μ g)	7,5 ± 3,50	2,71 ± 3,0	
- Morphine dose (mg)			

Cumulative morphine consumption in the 24 hours following surgery :

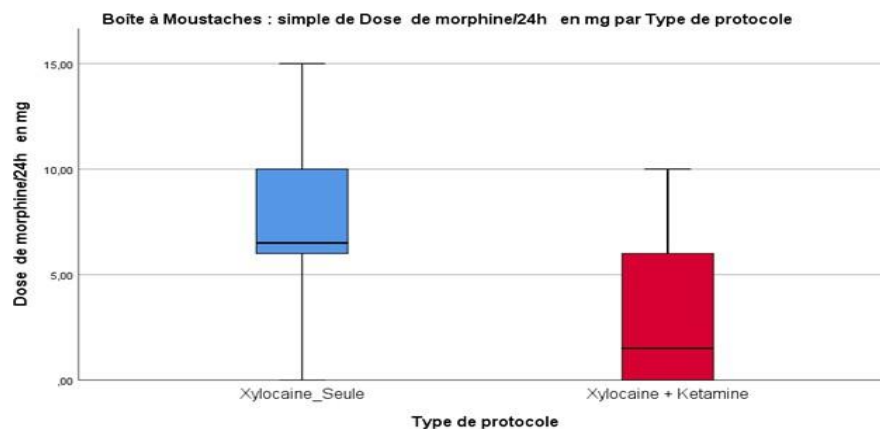


figure 2: Average total dose of morphine consumed 24 hours post-operatively according to protocol type

The average consumption of morphine during the first 24 hours was significantly lower in group P2 ($P < 0.001$) (Figure 2).

Mean resting DPO scores for SSPI at H48:

Table 02: Average DPO scores for both groups P1 and P2 at rest up to H48

Protocol type	Assessment time	The average	Standard error	P value (signification)
Group P1	SSPI	2,88	0,19	$P < 0.001$
	H 1	4,72	0,21	
	H2	3,09	0,14	
	H 4	2,81	0,12	
	H6	3,66	0,18	
	H12	2,97	0,12	
Group P 2	H24	2,72	0,18	
	H36	1,84	0,12	
	H48	1,62	0,14	
	SSPI	1,70	0,19	
	H1	2,91	0,21	
	H2	2,53	0,14	
	H4	2,85	0,12	
	H6	2,97	0,17	
	H12	2,67	0,12	
	H24	1,67	0,17	
	H36	1,91	0,12	
	H48	0,70	0,13	

DPO scores at mobilisation at H24

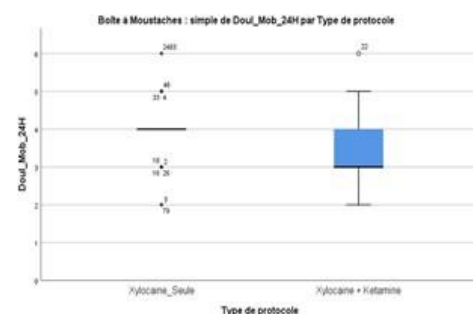


Figure 3: Average pain scores during mobilisation at 24 hours by type of protocol

DISCUSSION:

The results obtained in our study demonstrated that the addition of ketamine to systemic lidocaine during the perioperative period and up to 24 hours postoperatively provided superior analgesia compared to IV lidocaine alone. This superiority was confirmed by a considerable reduction in cumulative morphine consumption at 24 hours, with improved DPO scores at rest and during mobilisation at 24 hours, which were significantly lower in group P2 ($p < 0.001$).

intravenous administration of lidocaine during surgery has several analgesic and anti-hyperalgesic effects (at the peripheral level, it increases the excitability threshold of A delta and C fibres) [7]. It also has an anti-inflammatory action by modifying the ratio between pro-inflammatory cytokines (decreased release of

several pro-inflammatory cytokines (IL6, IL8) and anti-inflammatory cytokines) [8].

At the central level, it inhibits NMDA receptors at another site, clinically resulting in a reduction in DPO, which reflects a decrease in primary and secondary hyperalgesia[7] [9].

Ketamine administered at low doses during surgery blocks NMDA receptors in a non-competitive manner[14], attenuating the central sensitisation responsible for the neuronal plasticity that generates hyperalgesic and allodynic components, which could be the basis of DCPC[15]. This central sensitisation is induced not only by tissue damage (surgical incision) but also exacerbated by the high doses of opiates used during surgery, which led us to reduce the doses of analgesics (fentanyl) during anaesthetic induction and limit their reinjection during maintenance.

Ketamine has been extensively studied in the perioperative setting. To date, there are seven meta-analyses evaluating the benefits of ketamine in the perioperative period, five of which focus on immediate postoperative effects [20] and two on long-term efficacy [15]. Ketamine administered perioperatively reduces the average consumption of morphine by 15 mg at 24 hours across all types of surgery [21]. However, the reduction can be much greater, reaching up to 30 mg at 24 hours, particularly in thoracic and abdominal surgery above the umbilicus, which is consistent with the results of our study, where the reduction in morphine consumption at 24 hours reached more than 70% in the group receiving ketamine to achieve the predefined therapeutic goal of an EN<3

The administration of the combination of xylocaine and ketamine has become commonplace in multimodal analgesia strategies, particularly in ERAS (enhanced recovery after surgery) protocols; in several OFA (opioid-free anaesthesia) protocols, or anaesthesia without opioids, with the total exclusion of morphine mimetics during various types of surgery, particularly cardiac surgery [22] and abdominal surgery [23].

CONCLUSION:

Our work is a randomised comparative study of two multimodal analgesia protocols to prevent peripheral and central hyperalgesia in major abdominal surgery, which is associated with significant postoperative pain and chronic hyperalgesia. Our initial results confirm that ketamine combined with systemic xylocaine significantly reduces perioperative opioid consumption and provides optimal control of DPO at rest and during mobilisation at 24 hours.

Our work used the OSA (opioid-sparing anaesthesia) technique, whereby the intraoperative use of opioids was minimised with a view to excluding them from OFA (opioid-free anaesthesia) protocols, a technique currently undergoing innovation with other molecules such as dexmedetomidine and other combinations.

REFERENCES:

- O. Bernard, O, 'The pathways of pain: post-operative hyperalgesia', Jan. 06, 2012.
- M. Chauvin, 'Mechanisms of Postoperative Pain: Can It Be Prevented or Eliminated?', *Oleur et Analgésie, Ambroise Paré Hospital Anaesthesia and Intensive Care Department*, Oct. 2013.
- 'Opioid-induced hyperalgesia: pain hurts?', 2010.
- D.D, Fletcher and H. H, Harkouk, An update on hyperalgesia in adults and children. When, how and why to treat it?, *Sfar, Paris*, 2017.
- M. Chauvin, 'Perioperative hyperalgesia: mechanisms and prevention,' *Anaesthesia and Intensive Care Department, Ambroise Paré Hospital, 9 Avenue Charles de Gaulle*, 2011.
- P. Kranke et al., 'Continuous intravenous perioperative lidocaine infusion for postoperative pain and recovery,' *Cochrane Database Syst Rev*, no. 7, p. CD009642, July 2015, doi: 10.1002/14651858.CD009642.pub2.
- [7].H.O Wallace et al, 'Intravenous lidocaine inhibits visceral nociceptive reflexes and spinal neurons in the rat,' pp. 1685-1691., 2000.
- L. Weinberg, 'Pharmacokinetics and pharmacodynamics of lignocaine: A review,' *WJA*, vol. 4, no. 2, p. 17, 2015, doi: 10.5313/wja.v4.i2.17.
- G. Wallin et al. 'Effects of lidocaine infusion on the sympathetic response to abdominal surgery,' *Anesth. Analg.*, vol. 66, no. 10, pp. 1008–1013, Oct. 1987.
- J. Cassuto, G. Wallin, S. Högrström, A. Faxén, and G. Rimbäck, "Inhibition of postoperative pain by continuous
- G. L. Bryson, I. Charapov, G. Krolczyk, M. Taljaard, and D. Reid, 'Intravenous lidocaine does not reduce length of hospital stay following abdominal hysterectomy,' *Canadian Journal of Anaesthesia/Journal canadien d'anesthésie*, vol. 57, no. 8, pp. 759–766, August 2010, doi: 10.1007/s12630-010-9332-2.
- (12) N. T. Ventham et al., 'Efficacy of Intravenous Lidocaine for Postoperative Analgesia Following Laparoscopic Surgery: A Meta-Analysis,' *World J Surg*, vol. 39, no. 9, pp. 2220–2234, Sept. 2015, doi: 10.1007/s00268-015-3105-6.
- H. M. Paterson, 'Continuous intravenous lidocaine infusion for postoperative pain and recovery in adults,' *Tech Coloproctol*, vol. 23, no. 1, pp. 69–71, 2019, doi: 10.1007/s10151- 018-1890-2.
- E. C. Brinck, E. Tiippana, M. Heesen, R. F. Bell, S. Straube, and V. Kontinen, 'Perioperative intravenous ketamine for acute postoperative pain in adults,' in *Cochrane Database of Systematic Reviews*, The Cochrane Collaboration, Ed. Chichester, UK: John Wiley & Sons, Ltd, 2016.
- Chaparro, L.E., et al, 'Pharmacotherapy for the prevention of chronic pain after surgery in adults,' *Cochrane Database Syst Rev*, 2013.
- M. De Kock, S. Loix, and Lavand'homme, 'Ketamine and peripheral inflammation,' *CNS speculates on a potentialisation of effects Neurosci*, pp. 403-410, 2013.
- S. Loix, M. De Kock, and P. Henin, 'The anti-inflammatory effects of ketamine: state of the art,' *Anaesthesiol Belg*, pp. 47-58, 2011.
- R. F. Bell, C. Eccleston, and E. A. Kalso, 'Ketamine as an adjuvant to opioids for cancer

- pain,' in Cochrane Database of Systematic Reviews, The Cochrane Collaboration, Ed. Chichester, UK: John Wiley & Sons, Ltd, 2003.
19. R. F. Bell, J. B. Dahl, R. A. Moore, and E. Kalso, 'Perioperative ketamine for acute postoperative pain,' Cochrane Database Syst Rev, no. 1, p. CD004603, Jan. 2006, doi: 10.1002/14651858.CD004603.pub2.
 20. K. Laskowski, A. Stirling, W. P. McKay, and H. J. Lim, 'A systematic review of intravenous ketamine for postoperative analgesia,' Canadian Journal of Anaesthesia/Journal canadien d'anesthésie, vol. 58, no. 10, pp. 911-923, Oct. 2011, doi: 10.1007/s12630-011-9560-0.
 21. H. Bilgin et al., 'The influence of timing of systemic ketamine administration on postoperative morphine consumption,' Journal of Clinical Anaesthesia, vol. 17, no. 8, pp. 592- 597, Dec. 2005, doi: 10.1016/j.jclinane.2005.04.005.
 22. P.-G. Guinot et al., 'Effect of opioid-free anaesthesia on post-operative period in cardiac surgery: a retrospective matched case-control study,' BMC Anaesthesiol, vol. 19, no. 1, p. 136, 31 May 2019, doi: 10.1186/s12871-019-0802-y.
 23. M. Toleska and A. Dimitrovski, 'Is Opioid-Free General Anaesthesia More Superior for Postoperative Pain Versus Opioid General Anaesthesia in Laparoscopic Cholecystectomy?', PRILOZI, vol. 40, no. 2, pp. 81–87, Oct. 2019, doi: 10.2478/prilozi-2019-0018.