Med. J. Cairo Univ., Vol. 93, No. 1, Accepted 19/1/2025
DOI: 10.22608/MJCU. 399-404, March 2025
www.medicaljournalofcairouniversity.net

Small-Dose Ketamine's Impact on Morphine Consumption in Surgical Intensive Care Unit Patients after Major Abdominal Surgery

KHALID A. KARAM, M.D.[1]; ZAKARIA M. ABDELBASET, M.D.[2];
DALYA A. ISKANDARANI, M.Sc.[3] and YARA A. ISKANDARANI, M.Sc.[4]

The Department of Radiology, Faculty of Medicine, Al-Azhar University[1], Department of Neuropsychiatric, Psychatric, Faculty of Medicine, Al-Azhar University[2], Department of Internal Medicine, Bahçeşehir University, Turkey, Istanbul[3] and Medical Doctor, King Fahad Hospital, Department of Internal Medicine, Saudi Arabia, Madinah (Medical Resident)[4]

Abstract

Background: Surgical intensive care unit (SICU) cases require persistent and efficient pain relief with insignificant adverse reactions, and intravenous morphine alone isn't always effective in this situation. Adverse reactions to opioids, such as nausea, vomiting, and drowsiness, frequently restrict the pain treatment following surgery.

Aim of Study: To investigate the analgesic impact of ketamine in pain treatment following surgery as well as its effect on morphine consumption and adverse events.

Patients and Methods: This prospective, randomized research has been performed on 100 cases scheduled to have major abdominal surgery and divided randomly into 2 groups: Group I: 50 cases received Morphine + Ketamine, and Group II: 50 patients received Morphine in Al-Azhar University from Jan. 2022 to Feb. 2023.

Results: A statistically significant variance was observed among both groups according to morphine consumption and regarding visual analogue score (VAS) at rest at 6, 12, 18, and 24 hours, while a statistically insignificant variance was observed among both groups according to side effects incidence, type of operation carried out, intraoperative dosage of sufentanil, as well as SAPS II.

Conclusion: It is obvious that low-dose ketamine is safe for administration and improves analgesia following surgery. Ketamine is a drug that has the potential to decrease postoperative opioid consumption, pain score, and adverse effects when administered at low dosages.

Key Words: Ketamine – Morphine – Abdominal surgery – VAS.

Correspondence to: Dr. Khalid A. Karam, The Department of Radiology, Faculty of Medicine, Al-Azhar University

Introduction

SICU cases require persistent and efficient pain relief with no significant adverse reactions, and intravenous morphine alone isn't always effective in this situation **[1].**

Actually, the nociceptive inputs of cases in the Surgical intensive care unit have sources and severity levels that exceed those generated by tissue damage. Hyperalgesia and allodynia are the primary pathologic pain states that may be produced. Consequently, morphine might be less efficient regardless of its increased consumption **[2].** This morphine tolerance is an early process that is facilitated by paradoxical nociceptive stimulus. 2 studies have indicated N-methyl-d-aspartate (NMDA) receptors in these phenomena **[3].**

Ketamine is the most extensively investigated general anesthetic in the quest for strategies to regulate the systemic perioperative cytokine reaction. Ketamine is an anesthetic as well as an analgesic that is considered to be highly potent. Ketamine that was administered intravenously throughout anesthesia in adults resulted in a reduction in pain severity following surgery for a period of up to 48 hours, a delay in the initial demand for analgesia, and a reduction in the total 24-hour morphine consumption **[4].**

According to the most recent ketamine recommendations, there is evidence of a level I opioid-sparing benefit, in addition to evidence of level II anti-hyperalgesia and opioid tolerance safety impacts, in addition to a decrease in persistent pain following surgery **[5].**

The influence of ketamine on perioperative inflammatory reactions was investigated in cases who were undergoing cardiac operations with cardiopulmonary bypass (CPB), off-pump heart surgery, hysterectomy, and abdominal operation. Dosages varied from a single additional small dosage to full narcotic dosages of ketamine with racemic drug or S- (+), the most pharmacologically active ketamine. Immune-modulating properties were identified in ketamine. Ketamine is also purported to be a distinctive anti-inflammatory drug that prevents a systemic response with no affecting local healing processes **[6].**

The research aimed to assess the ketamine analgesic effect in postoperative pain management and its effect on morphine consumption and adverse events.

Patients and Methods

This prospective, randomized research has been performed on 100 cases scheduled to have major abdominal surgery and divided randomly into 2 groups: Group I: 50 cases received Morphine + Ketamine, and Group II: 50 patients received Morphine in Al-Azhar University from Jan. 2022 to Feb. 2023.

Inclusion criteria:

Adult patients older than 18 years who have been scheduled to have a major abdominal operation.

Exclusion criteria:

Cases with severe cardiovascular conditions (ejection fraction less than thirty%), impaired kidney function (creatinine clearance less than thirty mL/min), or that were incapable of comprehending the utilize of patient-controlled analgesia (PCA).

Sample size:

This investigation depends on the research conducted by Guillou et al. **[7]**. The following assumptions were taken into account when calculating the sample size using Epi Info STATCALC: - A power of 80% and a two-sided confidence level of 95%. At 48 hours, the mean morphine consumption for the morphine group was 80±37, with an α error of 5% and the mean consumption at 48 hours of morphine for the morphine and ketamine groups was 58±35. The final maximum sample size obtained from the Epi-Info output was 89. Therefore, the sample size was raised to 100 participants to assume any drop out cases through follow-up: Morphine group: 50 patients and morphine and ketamine group: 50 patients.

Methods:

Pre-operative: Before the operation, cases have been advised regarding the use of the VAS and PCA. Oral midazolam was administered to each patient 90 minutes prior to the operation.

During surgery: Propofol (two mg/kg) or thiopental (ten mg/kg) were administered to induce general anesthesia. Isoflurane, Nitrous oxide, atracurium, as well as sufentanil were utilized to sustain anesthesia. Both an arterial radial catheter and a central venous catheter were inserted. Blood pressure, capnography, pulse oximetry, electrocardiograms, and central venous pressure were continuously monitored. If the central venous pressure dropped below 3cm H_2O during the surgical procedure, crystalloids were given, and if the case's level of hemoglobin dropped below 7.0g/dL, packed red blood cells were administered. No antagonists were utilized at the end of the operation.

Following the operation: Cases received treatment in the Surgical intensive care unit for a minimum of forty-eight hours. Upon admission, the nurse responsible for the case's care reported the visual analogue score for pain while the patient was conscious. The nurse shifted the cursor of the 100-millimeter horizontal line from the point "no pain" to the point "worst pain imaginable," as the case indicated with their head or hand, if feasible, where the nurse must stop. The distance in mm among the patient's designated point and "no pain" was recorded. Then, subjects were randomly assigned to take morphine PCA with either ketamine or a placebo. Morphine was present in the patient-controlled analgesia device at a concentration of one mg/ml. Each case was administered initial loading dosages of two milligrams of morphine until their visual analogue score was below thirty. Subsequently, they were permitted to receive bolus dosages of morphine (1mg every seven minutes) without any restrictions. During the first 24 hours, the ketamine group received an initial bolus of 0.5mg/kg, then a perfusion of 2μg. kg^{-1}. min^{-1}, as well as a perfusion of 1μg · kg^{-1}. min^{-1} in the subsequent 24 hours. Ketamine was given separately. Ketamine was substituted with saline serum in the morphine group and administered under similar situations. A placebo or Ketamine has been given concurrently with morphinetitration. The syringes of placebo or ketamine were prepared by a nurse who wasn't involved in the patients' care. During their stay in the SICU, patients weren't administered any further analgesia or sedation.

Statistical analysis of the data: The IBM SPSS software package version 20.0 was utilized for analyzing the data that was inputted into the computer. (Armonk, NY: IBM Corp.) Numbers and percentages were utilized for describing qualitative data. The normality of the distribution was confirmed utilizing the Kolmogorov-Smirnov test. Range (minimum & maximum), mean, standard deviation, median, and interquartile range (IQR) were utilized for describing quantitative data. The outcomes were assessed at the 5% level of significance. The following tests were conducted: The chi-square test is utilized for assessing categorical variables among

various groups. When a predicted count over twenty percent of the cells is lower than five, the chi-square test is corrected using Fisher's Exact or Monte Carlo. The student *t*-test is a statistical test utilized for comparing 2 groups of normally distributed quantitative variables. Paired *t*-test: A statistical test that is utilized for comparing 2 periods of normally distributed quantitative variables. Mann-Whitney test: A statistical test that is utilized for comparing 2 groups of quantitative variables that are abnormally distributed. The Wilcoxon signed rank test is utilizedfor comparing 2 periods of abnormally distributed quantitative variables.

Results

According to demographic data, Table (1) shows a statistically insignificant variance among both groups according to sex and age.

Table (2) shows a statistically insignificant variance among both groups according tooperation type carried out, intraoperative dosage of sufentanil and SAPS II.

Table (3) shows a statistically insignificant variance among both groups according to VAS at rest at 0 hours and 6 hours, while a statistically significant variance was observed among the examined patients according to VAS at rest at 12, 18, and 24 hours.

Table (4) demonstrates a statistically insignificant variance was observed among both groups according to VAS at rest at 0 hour, while a statistically significant variance was observed among the examined patients according to VAS at rest at 6, 12, 18, and 24 hours.

Table (5) demonstratesa statistically significant variancea mong both groups according to morphine consumption.

According to side effects, Table (6) demonstrates a statistically insignificant variance among both groups according to side effects incidence.

Table (1): Distribution of general characteristics among both groups.

	Morphine + Ketamine group N=50	Morphine group N=50	*p*-value
Age (years):			
Mean ± SD	57±18.5	56±17.5	0.78
Sex:			
Male	32 (64%)	37 (74%)	0.27
Female	18 (36%)	13 (26%)	

p-value >0.05: Insignificant.
p-value <0.05 is statistically significant.
p<0.001 is greatly significant.
SD: Standard deviation.

Table (2): Distribution of type of surgery carried outand intraoperative dosage of sufentanil among both groups.

	Morphine + Ketamine group N=50	Morphine group N=50	*p*-value
Type of Surgery Performed:			
Hepatectomy	27 (54%)	22 (44%)	0.51
Esophageal surgery	10 (20%)	10 (20%)	
Others	13 (26%)	18 (36%)	
Intraoperative sufentanil dose (mcg):			
Mean ± SD	147±66	142±60	0.69
SAPS II:			
Mean ± SD	28±8	29±9	0.55

SAPS: Simplified Acute Physiology Score.

Table (3): Distribution of visual analog scale score at rest through the 24 hours among both groups.

	Morphine + Ketamine group N=50	Morphine group N=50	*p*-value
VAS at rest:			
0 hour	37.6±2.3	38.2±1.2	0.1
6 hours	26.9±1.4	27.3±1.4	0.15
12 hours	20±1.1	24.2±1.2	<0.001
18 hours	22.4±1.25	25.1±1.36	<0.001
24 hours	24.7±1.32	26.5±1.36	<0.001

Table (4): Distribution of visual analog scale score at mobilization through the 24 hours among both groups.

	Morphine + Ketamine group N=50	Morphine group N=50	*p*-value
VAS at mobilzation:			
0 hour	39.7±1.4	40.2±1.3	0.06
6 hours	44.6±1.7	42.3±1.36	<0.001
12 hours	38.4±1.62	39.3±1.63	0.006
18 hours	37.6±1.5	40.3±1.44	<0.001
24 hours	37.9±1.7	40.1±1.8	<0.001

Table (5): Distribution of morphine consumption at 48h among both groups.

	Morphine + Ketamine group N=50	Morphine group N=50	*p*-value
Morphine consumption mg:			
Mean ± SD	56.7±34.2	82.3±36.5	<0.001

Table (6): Distribution of side effects incidence among both groups.

	Morphine + Ketamine group N=50	Morphine group N=50	P-value
Side Effects:			
Nausea	3 (6%)	5 (10%)	0.4
Confusion	3 (6%)	3 (6%)	1
Hallucinations	2 (4%)	2 (4%)	1
Hypoventilation	2 (4%)	4 (%)	0.39
Pruritus	2 (4%)	2 (4%)	1

Discussion

PCA with IV opioids is a well-known method for managing pain following major surgery. This method improves patient satisfaction and cooperation, in addition to adjusting the degree of pain control more effectively compared to IV bolus dosages **[8].**

Adverse reactions to opioids, such as nausea, vomiting, and drowsiness, frequently restrict the management of pain after surgery. When opioids are administered in large quantities for an extended period, they can induce acute tolerance, that exacerbates pain control and, more seriously, respiratory and hemodynamic depression **[9].**

The stimulation of NMDA receptor through nociceptive stimulation results in hyperexcitability, a process that plays a role in the pathophysiology of acute pain. Ketamine, a non-competitive NMDA antagonist, provides an anti-hyperalgesic impact by modulating central sensitization & causing a specific NMDA blockade at sub-anesthetic dosages **[10,11].**

Regarding demographic findings, this study revealed that a statistically insignificant variance was observed among the examined cases according to sex and age.

Similarly, our outcomesagreed with those of Guillou et al., **[7]**, who assessed the analgesic efficacy of ketamine in the pain treatment in a SICU following a major abdominal operation. Cases were administered morphine PCA in conjunction with either ketamine (Group K) or a placebo (Group M). They revealed insignificant variance among both groups according to age and sex.

Also, this study was consistent with AbdelRady et al., **[12]**, who assessed the preventive impacts of low dosages of ketamine given before the skin incision in abdominal operation to evaluate the analgesic effectiveness and intra-operative and post-operative adverse reactions. They reported insignificant variance among the ketamine and control groups according to age and sex.

As well, our outcomes are in agreement with those of Atif et al., **[13]** who evaluated the impact of a subanesthetic dosage of ketamine on narcotic consumption as well as the postoperative pain scores of cases having abdominal surgery under general anesthesia. They revealed insignificant variance among the ketamine and control groups according to age & sex.

Recent research reported that a statistically insignificant variance was observed among the examined patients according to the surgery type carried out, the intraoperative dosage of sufentanil, as well as SAPS II.

According to our outcomes, Guillou et al., **[7]** demonstrated that a statistically insignificant variance was observed among both studied groups regarding type of surgery carried out, dosage of sufentanil utilized throughout the surgery and SAPS II (Simplified Acute Physiology Score).

Also, Abdel Rady et al., **[12]** reported a statistically insignificant variance among the ketamine and control groups according to the type of surgery performed.

Our findings demonstrated a statistically insignificant variance among the examined patients according to VAS at rest at 0 hours and 6 hours, while a statistically significant variance was observed among the examined patients according to VAS at rest at 12, 18, and 24 hours.

Similarly, our outcomes agreed with those of AbdelRady et al., **[12],** who demonstrated that visual analogue score scores at rest and movement were significantly reduced in the ketamine group. The ketamine group showed reduced visual analogue score scores at nearly all-time intervals, and the variance in VAS scores among both groups became statistically significant at nearly all-time intervals prior to thirty-six hours.

Also, this study was consistent with Atif et al., **[13]** who documented a statistically significant variance among the ketamine group and controls regarding VAS pain scores at 1-, 3-, 6-, and 12-hour intervals. Nevertheless, the variance of the pain score at twenty-four hours among both groups was insignificant.

The recent research demonstrated a statistically significant variance among the examined patients according to morphine consumption at 48 hours. Conversely, we observed a statistically insignificant variance among the examined patients based on the incidence of side effects.

Also, our outcomes agreed with Guillou et al., **[7],** who demonstrated that it was observed that the

decrease in morphine consumption was more significant in Group K throughout the initial hours following admission to the SICU, and the cumulative consumption of morphine was significantly lower. They found that the incidence of adverse reactions was comparable in both groups.

Similarly, our research agreed with Abdel Rady et al., *[12]*, reported that the ketamine and control groups demonstrated a significant variance in the total quantity of postoperative morphine consumption. However, we observed a statistically insignificant variance in side effects between both groups.

As well, Atif et al., *[13]* established that intraoperative low-dosage ketamine produced effective analgesia within the initial 12 hours following surgery, as evidenced by the significantly declined total morphine consumption and lower pain scores.

In 2015, a review of the of the literature conducted by Jouguelet-Lacoste et al., *[14]* who aimed to investigate the evidence that supports the utilization of low-dosage intravenous infusions of ketamine for the treatment of perioperative pain. Their investigation involved thirty-nine clinical trials that evaluated the efficacy of a continuous infusion or a bolus of low-dosage ketamine for analgesia following surgery. The primary endpoint was a decline in pain scores or a decrease in opioid consumption. The theory that ketamine's advantages are primarily derived from a decrease in opioid burden rather than a decline in pain scores was generally supported by their review.

The analgesic efficiency of ketamine administered perioperatively throughout the acute postoperative period has been shown in numerous studies *[15,16]*. A systematic study established the analgesic advantages of ketamine, particularly in surgeries with a high degree of pain following surgery *[16]* and when combined with morphine to reduce morphine consumption *[17]*.

Conclusion:

It is obvious that low-dose ketamine is safe for administration and improves analgesia following surgery. Ketamine is a drug that has the potential to decrease postoperative opioid consumption, pain score, and adverse effects when administered at low dosages.

References

1- DOWELL D.: CDC clinical practice guideline for prescribing opioids for Pain United States, 2022. MMWR Recomm reports, 71, 2022.

2- LIU S. and KELLIHER L.: Physiology of pain a narrative review on the pain pathway and its application in the pain management. Dig. Med. Res., 5, 2022.

3- DEDEK A. and HILDEBRAND M.E.: Advances and barriers in understanding presynaptic N-methyl-D-aspartate receptors in spinal pain processing. Front Mol. Neurosci., 15: 864502, 2022.

4- LII T.R., SMITH A.E., FLOHR J.R., OKADA R.L., NYONGESA C.A., CIANFICHI L.J., et al.: Trial of Ketamine Masked by Surgical Anesthesia in Depressed Patients. Medrxiv Prepr Serv Heal Sci., 2023.

5- Cheung C.K., Adeola J.O., Beutler S.S. and Urman R.D.: Postoperative pain management in enhanced recovery pathways. J. Pain Res., 123–35, 2022.

6- LI M., LI X., WU Y., ZHANG T., LI M. and CHEN Y.: The Effects of Different Doses of Sufentanil on Intraoperative Cardiovascular Response and Postoperative Recovery in Patients Undergoing Cardiac Surgery: A Retrospective Cohort Study. Drug Des Devel Ther., 535–47, 2024.

7- GUILLOU N., TANGUY M., SEGUIN P., BRANGER B., CAMPION J.P. and MALLÉDANT Y.: The effects of small-dose ketamine on morphine consumption in surgical intensive care unit patients after major abdominal surgery. Anesthesia & Analgesia., Sep 1; 97 (3): 843-7, 2003.

8- BIALKA S., COPIK M., DASZKIEWICZ A., RIVAS E., RUETZLER K., SZARPAK L., et al.: Comparison of different methods of postoperative analgesia after thoracotomy a randomized controlled trial. J. Thorac. Dis., 10 (8): 4874, 2018.

9- CARSTENSEN M. and MØLLER A.M.: Adding ketamine to morphine for intravenous patient-controlled analgesia for acute postoperative pain: A qualitative review of randomized trials. Br. J. Anaesth., 104 (4): 401–6, 2010.

10- MA X., YAN J. and JIANG H.: Application of ketamine in pain management and the underlying mechanism. Pain Res Manag., 2023 (1): 1928969, 2023.

11- EIDE P.K., STUBHAUG A. and ØYE I.: 8 The NMDA-antagonist ketamine for prevention and treatment of acute and chronic post-operative pain. Baillière's clinical anaesthesiology, Sep 1; 9 (3): 539-54, 1995.

12- ABDELRADY M.M., ABOELFADL G.M., OTHMAN MOHAMED E.A., ABDEL-REHIM M.G., ALI A.H., SAAD IMBABY A.S., et al.: Effect of small dose ketamine on morphine requirement after intestinal surgery: A randomized controlled trial. Egypt J. Anaesth., 37 (1): 302–9, 2021.

13- ATIF M., KHURSHID T., HAQUE I.U., YOUSAF M.J. and SYED F.T.: Effect of intraoperative low dose ketamine infusion on postoperative analgesia: A randomized controlled trial. Isra Med. J., 11 (3): 154–8, 2019.

14- JOUGUELET-LACOSTE J., LA COLLA L., SCHILLING D. and CHELLY J.E.: The use of intravenous infusion or single dose of low-dose ketamine for postoperative analgesia: A review of the current literature. Pain Med., 16 (2): 383–403, 2015.

15- HADI B.A., DAAS R. and ZELKO R.: A randomized, controlled trial of a clinical pharmacist intervention in

microdiscectomy surgery–low dose intravenous ketamine as an adjunct to standard therapy. Saudi Pharm J., 21 (2): 169–75, 2013.

16- DING X., JIN S., NIU X., WANG T., ZHAO X., REN H., et al.: Morphine with adjuvant ketamine versus higher dose of morphine alone for acute pain: A meta-analysis. Int. J. Clin. Exp. Med., 7 (9): 2504, 2014.

17- HIMMELSEHER S., DURIEUX M.E. and WEISKOPF R.B.: Ketamine for perioperative pain management. J. Am. Soc. Anesthesiol., 102 (1): 211–20, 2005.

تأثير جرعة صغيرة من الكيتامين على استهلاك المورفين لدى مرضى وحدة العناية المركزة الجراحية بعد جراحة البطن الكبرى

تتطلب حالات وحدة العناية المركزة الجراحية تخفيف ألم مستمر وفعال دون حدوث آثار جانبية كبيرة، والمورفين الوريدى وحده ليس دائمًا فعالًا فى هذه الحالات.

فى الواقع، المدخلات المؤلمة فى حالات وحدة العناية المركزة الجراحية تأتى من مصادر ومستويات شدة تتجاوز تلك الناتجة عن تلف الأنسجة. ويُعد فرط التحسس والآلام المحورية هما حالتى الألم المرضى الرئيسيتين التى قد يتم إنتاجها. وبناءً على ذلك، قد يكون المورفين أقل فعالية بغض النظر عن زيادته فى الاستهلاك.

إن تحمل المورفين هو عملية مبكرة يتم تسهيلها بواسطة التحفيز المؤلم المتناقض. وقد أشارت دراستان إلى دور مستقبلات N-methyl-d-aspartate فى هذه الظواهر.

يُعتبر الكيتامين من أوسع المخدرات العامة التى تم التحقيق فيها في محاولة للبحث عن استراتيجيات لتنظيم الاستجابة السيتوكينية الجهازية فى فترة ما حول الجراحة. الكيتامين هو مخدر ومسكّن قوى يعتبر شديد الفعالية. أظهرت الدراسات أن إعطاء الكيتامين عن طريق الوريد أثناء التخدير فى البالغين أدى إلى تقليل شدة الألم بعد الجراحة لفترة تصل إلى ٤٨ ساعة، وتأخير الطلب الأولى على المسكنات، وتقليل الاستهلاك الكلى للمورفين خلال ٢٤ ساعة.

وفقًا لأحدث توصيات الكيتامين، هناك دليل على فائدة من المستوى الأول في تقليل استهلاك الأفيونيات، بالإضافة إلى دليل على تأثيرات من المستوى الثانى فى تقليل فرط الألم وتحمل الأفيونيات، إلى جانب تقليل الألم المستمر بعد الجراحة.

تم التحقيق فى تأثير الكيتامين على التفاعلات الالتهابية ما حول الجراحة في حالات خضعت لعمليات قلبية مع التحويلة الرئوية القلبيةوعمليات القلب بدون مضاعفات، واستئصال الرحم، والعمليات البطنية. تراوحت الجرعات من جرعة إضافية صغيرة واحدة إلى جرعات كاملة من الكيتامين باستخدام الدواء الراسيمى أو S- (+)، وهو الكيتامين الأكثر تأثيرًا من الناحية الصيدلانية. وتم تحديد خصائص تعديل المناعة فى الكيتامين. كما يُعتقد أن الكيتامين هو دواء مضاد للالتهاب مميز يمنع الاستجابة الجهازية دون التأثير على عمليات الشفاء المحلية .

هدف البحث كان تقييم تأثير الكيتامين المسكن في إدارة الألم بعد الجراحة وتأثيره على استهلاك المورفين والآثار الجانبية. تم إجراء هذا البحث الاستباقى العشوائى على ١٠٠ حالة مجدولة لإجراء جراحة بطنية كبرى، تم تقسيمها عشوائيًا إلى مجموعتين: المجموعة الأولى: ٥٠ حالة تلقت مورفين + كيتامين، والمجموعة الثانية: ٥٠ مريضًا تلقوا مورفين فى جامعة الأزهر من يناير ٢٠٢٢ إلى فبراير ٢٠٢٣.

الاستنتاج: من الواضح أن الكيتامين بجرعات منخفضة آمن للإعطاء ويُحسن التسكين بعد الجراحة. يُعتبر الكيتامين دواءً لديه القدرة على تقليل استهلاك الأفيونيات بعد الجراحة، وتقليل درجات الألم، والآثار الجانبية عند إعطائه بجرعات منخفضة.