

## Postoperative ketamine infusion in comparison with tramadol infusion for postoperative pain relief

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### الخلاصة:

من المعلوم أن الأدوية المخدرة الوريديّة- الناركوتكس - التي تستخدم لعلاج ألم ما بعد العملية الجراحية تكون مصحوبه بالعادة بأعراض جانبية مهمة رغم فعالية تلك الادوية. لذلك فقد أجريت عدة دراسات خلال العقدين الماضيين للوصول الى أفضل أسلوب يكون فعالا لعلاج الالم بأقل أعراض جانبية. في هذه الدراسة تم أخضاع 120 مريضة مهياة لأجراء عملية قيصرية باردة تحت التخدير العام. جميع المريضات هن تحت تصنيف الدرجة الاولى او الثانية من تصنيف الرابطة الأميركية لأطباء التخدير و أعمارهن بين 20 – 40 سنة. تم تقسيم المريضات بعد إجراء العملية الى مجموعتين في كل مجموعة 60 مريضة. تم إعطاء مريضات المجموعة الأولى عقار الكيتامين بجرعة 0.3ملغ -كغم وريديا يعقبها إعطائه بالمغذي بجرعة 0.1ملغ-كغم – ساعة. أما المجموعة الثانية فتم إعطائهم عقار الترامادول بجرعة وريديّة 2 ملغ – كغم يعقبها إعطائه بالمغذي بجرعة 0.2 ملغ – كغم – ساعة. و تم إعطاء تحاميل الديكلوفيناك للمريضات بعد العملية حسب طلبهن عند شعورهن بالألم . تم دراسة فترة التسكين في كلا المجموعتين قبل إعطاء عقار الديكلوفيناك و عدد المرات التي تم فيها إعطاء تحاميل الديكلوفيناك خلال أول 24 ساعة كذلك تم تحديد درجة التهدئة و عدد مرات الشعور بالغثيان أو حدوث التقيؤ . أثبتت الدراسة أن عقار الكيتامين أكثر فعالية بتسكين الألم من عقار الترامادول. الفروقات بنسب حدوث الأعراض الجانبية في كلا المجموعتين كانت غير مهمة. توصي هذه الدراسة بأستعمال عقار الكيتامين بالطريقة المذكورة بعد العملية و خصوصا للمرضى الذين لديهم فرط حساسية من أدوية الناركوتكس المخدرة

### Abstract

Background: Systemic narcotics commonly used for postoperative analgesia are associated with many side effects.

Many studies regarding the best postoperative analgesic regimen with minimum side effects have been done over the last 20 years. In this study we compare between the postoperative intravenous infusion of tramadol with the postoperative intravenous infusion of ketamine

Method : This study was carried out on 120 parturients prepared for an elective caesarian section under general anaesthesia . All patients subjects according to American Society Of Anaesthesiologist ( ASA) classification were grade 1 & 2 between 20 – 40 of age. Subject were allocated into two groups ( 60 patients in each group ):

Group A ( Ketamine group ) ( n = 60 ) patients received a bolus dose of ketamine ( 0.3 mg/kg ) followed by an intravenous infusion at 0.1 mg • kg<sup>-1</sup> • h<sup>-1</sup> postoperatively .

Group B ( Control group ) ( n = 60 ) patients received a bolus dose of tramadol ( 2 mg/kg ) followed by an intravenous infusion ( 0.2 mg • kg<sup>-1</sup> • h<sup>-1</sup> ) postoperatively

Diclofenac suppositories were given to both groups postoperatively.

Results: The ketamine group had less pain at rest and with movement , required less diclofenac suppositories throughout the 24 h study period. Ketamine, improved subjective analgesic efficacy . Hallucinations were more common in ketamine patients, but other side effects were similar .

Conclusion: Small doses of postoperative intravenous infusion of ketamine is a better choice for postoperative analgesia than an intravenous infusion of tramadol.

## Introduction :

Acute pain is an integrated process that is mediated by activation of numerous biochemical and anatomical pathways. (1)Therefore, administration of analgesics acting on different targets is a rational postoperative analgesic strategy. Among the receptors implicated in the nociceptive transmission, the N-methyl-D-aspartate (NMDA) receptor play a critical role in neuronal plasticity leading to central sensitization and, therefore, in the intensity of perceived postoperative pain (2).

There is a growing body of evidence that ketamine, a non-competitive antagonist at NMDA receptors (3), can facilitate postoperative pain management (4). Ketamine also alleviates provoked pain by preventing postoperative hyperalgesia (5).Narcotics when used for postoperative analgesia may release histamine and cause bronchospasm in asthmatic patients (6).Therefore, Ketamine in subanaesthetic doses is an effective analgesic (7).

Tramadol hydrochloride , On the other hand is a synthetic opioid agonist

analgesic acting at the  $\mu$  receptor ( $OP_3$ ) (8). Its analgesic potency has been described as 5–10 times less than that of morphine, equal to that of meperidine (9) and to 0.001 that of fentanyl (10). Its analgesic efficacy lies between that of codeine and morphine. Tramadol is a racemic mixture of two enantiomers with a structure similar to that of other opioid analgesics (11). However, only 30% of its effect can be antagonized by naloxone (9), and a significant portion of its action is mediated through non-opioid mechanisms( 10,12).

Postoperative bolus of tramadol, followed by an infusion, shows a good risk/benefit ratio as an analgesic regimen for postoperative pain relief and is at least as effective as epidural morphine ( 13 ). The analgesic action of tramadol is based on a multimodal mechanism of action, which may also have advantages over conventional opioids in terms of side effects (14). Intraoperative tramadol was as effective as morphine for postoperative analgesia (15)

controlled ventilation with oxygen supplemented with halothane 1-1.5%. Tidal volume was maintained at about 10 mL-kg<sup>-1</sup> at a frequency of 12 breaths/mint . Fentanyl ( 0.001 mg- kg IV )after the clamping of the umbilical cord was administered . At the end of the anesthetic, reversal of neuromuscular block was achieved with 2.5 mg of neostigmine with atropine 1.2 mg IV. All patients were retained in the recovery room and monitored with ECG , blood pressure and oxygen saturation . Patients were transferred to the surgical ward with full recovery criteria.

Postoperatively , patients were allocated into two groups ( 60 patients in each group ) :

## Materials and Methods :

We studied 120 healthy term parturients from 38 – 42 weeks gestation with ASA physical status I-II patients. All were scheduled to undergo elective caesarian section with general anesthesia. Exclusion criteria included the use of any analgesic medication during the 36 h before surgery and the contraindications to the use of ketamine or tramadol. Without any preanesthetic medication,preoxygenation for 3 minutes and anesthesia was induced by administration of Sodium thiopentone (5 mg- kg IV) and pancuronium (0.1 mg-kg IV).Tracheal intubation was followed by

Group A ( Ketamine group ) ( n = 60 ) patients received a bolus dose of ketamine( 0.3 mg/kg) followed by an intravenous infusion at  $0.1 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ ) postoperatively.

Group B (Control group) ( n = 60 ) patients received a bolus dose of tramadol ( 2 mg/kg ) followed by an

intravenous infusion ( $0.2 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ ) postoperatively.

Diclofenac suppositories were given to both groups postoperatively according to the patient's request.

### **Data collected :**

1 – Patient age , weight , height and surgery time .

2 – All patients were assessed for 24 hours postoperatively.

3 – Haemodynamic recording ( heart rate and mean arterial blood pressure monitoring ) and oxygen saturation at fixed intervals ( 3 , 6 , 9 , 12 , 24 hours ) were recorded.

4 – Degree of recorded at fixed intervals ( 3 , 6 , 9 hours ) postoperatively ( Ramsey sedation score ) (16).

Score 0 = Alert or drowsy.

Score 1 = Sleepy but arousable by verbal command.

Score 2 = Sleepy but arousable by tactile command.

Score 3 = Sleepy but not arousable by tactile command.

5 - For postoperative pain relief , diclofenac suppository given in increments of 50 mg on patient demand . The time from the end of surgery to first request , and the number of times diclofenac was requested in the first 24 hours after surgery , were recorded.

6 – Number of postoperative nausea and vomiting were recorded. Postoperative nausea and vomiting were treated with 10 mg I.V.metoclopramide on patient demand.

### **Results :**

- 1- No significant difference in the demographic data of the patients as regarding age , weight and surgery time between the two groups ( table 1 ).
- 2- No significant difference in the haemodynamic data between the two groups ( table 1 ).
- 3- The postoperative analgesic duration ( as expressed as the time of first rescue analgesic supplementation of diclofenac suppository given ), was significantly longer in group A than group B ( table 2 )

- 4- The number of time diclofenac was required during the first 24 hours after surgery were significantly lower in group A than group B. ( table 2 ).
- 5- No significant difference between the two groups as regarding the sedative effects ( table 3 ) ( figure 1 ).
- 6- There was no significant difference between the two groups as regarding postoperative nausea and vomiting ( table 4 ). Most of them occur during the first 6 hours postoperatively.
- 7- Hallucination is more common in group A than group B

Variable	GROUP A		GROUP B	
	Mean	S.D	Mean	S.D
Age(yrs)	29.1	4.8	28.6	4.7
Weight(Kg)	75.1	9.3	80.3	8.9
Surgery time(min)	49.5	6.2	52.2	5.8
Mean bl.pr	94.3	6.9	89.1	8.1
Heart rate	98.1	5.8	96.7	5.3
SPO2%	95.1	3.1	94.6	2.7

Table 1 : Demographic and haemodynamic data for both groups me of surgery , mean arterial blood pressure ( MAP) , heart rate and arterial oxygen saturation ( SPO2 ).

Variables	GROUP A	GROUP B
Average time to first diclofenac ( min )	135	90
Number of diclofenac	1 ( 1 – 2 )	3 ( 2 – 4 )

Table 2 : Analgesic duration expressed in minutes , in both groups calculated from the time of intravenous administration of postoperative ketamine ( group A) or tramadol ( group B ) to the time of first diclofenac administration and the number of times diclofenac was requested during the first 24 hours after surgery.

	GROUP A		GROUP B	
	Score		Score	
3 hours postoperatively	0	9 ( 15% )	0	10 ( 16.6% )
	1	20(33.3 %)	1	25 ( 41.6%)
	2	20(33.3 %)	2	14 ( 23.3% )
	3	11 ( 18.3% )	3	11 ( 18.3% )
6 hours postoperatively	0	18 ( 30% )	0	15 ( 25% )
	1	24 ( 40% )	1	28 ( 64.6% )
	2	13 ( 21.6% )	2	9 ( 15% )
	3	5 ( 8.3% )	3	8 ( 13.3% )
9 hours postoperatively	0	28 ( 64.6% )	0	23 ( 38.3% )
	1	24 ( 40% )	1	28 ( 64.6% )
	2	5 ( 8.3% )	2	5 ( 8.3% )
	3	3 ( 5% )	3	4 ( 6.6% )

Table 3 : No significant difference between the two groups as regarding the sedative effects

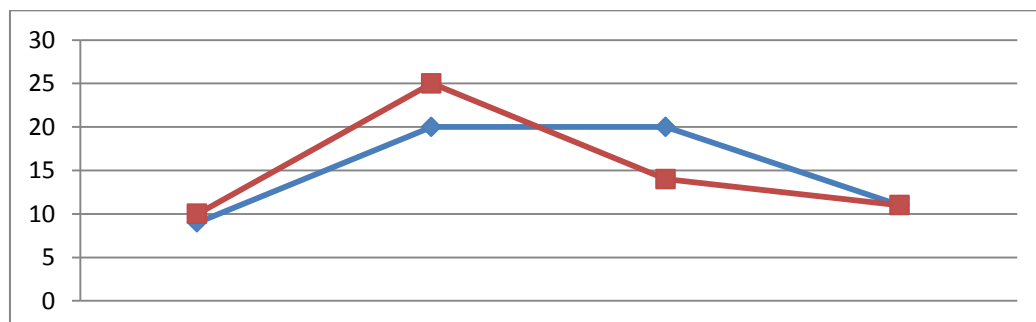


Figure 1 :Sedative effect 3 hours postoperatively. blue line = group A , red line = group B

	GROUP A	GROUP B
	Number of patients & %	
Postoperative nausea & vomiting	6 ( 10 % )	8 ( 13.3 % )
Hallucination	5 ( 8.33% )	0 ( 0 % )

Table 5 : there was no significant difference between the two groups as regarding postoperative nausea and vomiting . Hallucination is significantly more common in group A than group B.

## Discussion

Post-operative pain management is usually limited by adverse effects such as nausea and vomiting. Adjuvant treatment with an inexpensive opioid-sparing drug such as ketamine may be of value in giving better analgesia with fewer adverse effects in comparison with opioids . postoperative ketamine may also be useful for patients who traditionally require larger doses of opioids, such as cancer patients on long-term opioid therapy or the drug-dependent patient population. Patients who are especially sensitive to the adverse effects of opioids, such as the elderly, may also be a target group for this treatment ( 17 ) .

Frédéric Adam and his students find that the activation of NMDA receptors by opiates mediates tolerance to opioids and that tolerance is thus attenuated by NMDA receptor antagonists including ketamine. the reduction of morphine requirements in patient receiving ketamine may thus have resulted from attenuation of acute tolerance to opioids ( 18)

Mark B.Bloch and his students ( 13 ) find that the analgesic action of tramadol is

## Recommendation

Tramadol and ketamine( small bolus dose followed by intravenous infusion postoperatively ) are a better to be selected by anaesthesiologists and surgeons for

based on a multimodal mechanism of action, which may also have advantages over conventional opioids in terms of side effects .In a study of 40 patients undergoing abdominal hysterectomy, it was concluded that tramadol was as effective as morphine for postoperative analgesia.

The objective of this study was to assess the effectiveness and adverse effects of postoperative ketamine in the treatment of acute postoperative pain and compare it with tramadol.

This study reveals that postoperative small bolus dose of ketamine( 0.3 mg/kg) followed by an intravenous infusion at  $0.1 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$  is a good selection for postoperative analgesia ( more potent and longer analgesic duration ) than tramadol (tramadol 2 mg/kg followed by an intravenous infusion  $0.2 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$  postoperatively). There is no obvious superiority of ketamine over tramadol regarding side effects. There is no significant difference between the two groups as regarding the sedative effects , postoperative nausea & vomiting. Hallucination is more common in group A ( ketamine group ) than group B ( tramadol group ).

the treatment of postoperative pain than the use of morphine or other opioids .Therefore , try restrict the use of opioids which is associated with many adverse effects. Ketamine is better than tramadol when a

greater degree of analgesia are desirable for longer period of time with no significant or important

difference between both regarding adverse effects.

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