



## **Comparison the Effect of Paracetamol and Ketorolac on Pain Relief after Cesarean Section**

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### **Authors' contributions**

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

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### **ABSTRACT**

**Introduction:** Cesarean section is one of the most common surgical procedures in women. Effective pain control is an important component of post-operative care, as calming the mother increases her ability to take care of herself, reduce nosocomial infections, and hospitalization costs. The aim of this study was to compare the effect of paracetamol and ketorolac on the relief of post-cesarean pain in order to find a drug with minimal complications.

**Methods:** This study was performed on 140 women admitted to Ali Ibn Abi Talib Hospital due to cesarean section. Patients were divided into two groups of 500 mg paracetamol after cord clamp and 30 mg intravenous ketorolac group. Pain score, need for additional analgesia and visual analogue scale (VAS) were measured and compared in two groups. Data were analyzed using SPSS software.

**Results:** In this study, mean pain scores at 0, 6, 12 and 24 hours were significantly lower in the ketorolac group than in the paracetamol group. There was no complication in any of the experimental groups in this study. There was no significant difference between the mean time of

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first request for the additional analgesic of two groups. Frequency of additional analgesic request in the ketorolac group was significantly lower than in the paracetamol group.

**Conclusion:** Overall, the results of this study showed that the rate of pain reduction after cesarean section with ketorolac was significantly higher than paracetamol.

*Keywords: Cesarean section; ketorolac; paracetamol.*

## 1. INTRODUCTION

Cesarean section is one of the most common surgical procedures in women. Cesarean delivery is referred to as the birth of a fetus by cutting the abdominal wall and the uterine wall [1]. The rate of cesarean delivery around the world has steadily increased over the past two decades [2-4]. Cesarean section is characterized by a complex physiological response in response to intraoperative tissue damage, visceral dilatation and acute uterine contractions [5]. Cesarean section is in the range of moderate to severe in terms of the severity of postoperative pain and requires an appropriate treatment protocol for pain management. This pain can have undesirable effects on various body systems if not properly managed and controlled, such as inability to discharge respiratory secretions, hypertension and heart rate, sweating, staining and prolonged hospitalization. As a result, it increases the risk of deep vein thrombosis and delayed breastfeeding [6]. One of the effective strategies to relieve post-cesarean pain is to use different medications. Different types of analgesics are used to achieve the most analgesic effect and the least side effects. Opioids are widely used for postoperative pain management, which are not very satisfactory due to side effects and inadequate response to opioids [7]. Ancillary drugs such as paracetamol (acetaminophen) and non-steroidal anti-inflammatory drugs (NSAIDs) are used in combination with opioids.

Non-steroidal anti-inflammatory drugs reduce pain by inhibiting cyclooxygenase. One of these drugs is ketorolac from the pyro lactic family that inhibits prostaglandin synthetase. It has not affected the central nervous system or the autonomic and cardiovascular nervous system [8]. In a clinical trial study, 'Comparing the efficacy of parecoxib versus ketorolac with morphine in controlling patient pain after cesarean section' performed by Wong JO et al. (2010) on 66 pregnant women, results showed that there was no significant difference in sedation, mood, sleep quality and patient satisfaction between the two groups. However,

patients in the parecoxib group had less pain than the ketorolac group within the first 24 hours [9]. In another study aimed at comparing the analgesic effect of intravenous paracetamol and meperidine with meperidine alone by Attarzadeh et al. (2013), the results showed that intravenous paracetamol had a significant analgesic effect on post-cesarean pain and reduces the overall dose of meperidine dramatically [10].

According to a review of literature, pain management is always a professional challenge. Therefore, prevention and treatment of postoperative pain is one of the main issues in surgical care that has an important role in accelerating and improving the general condition of patients admitted to the surgical ward. Therefore, a study was conducted to compare the effect of paracetamol and ketorolac on pain relief after cesarean section.

## 2. MATERIALS AND METHODS

This is a double-blind clinical trial. The study population included pregnant women who referred to Ali ebne Abitaleb Hospital in Zahedan, Iran for elective cesarean section. The data collection tool is the information form. Sampling was completely randomized and patients who met the inclusion and exclusion criteria were enrolled in the study.

Inclusion criteria in this study were all term pregnant women, between the ages of 20 and 45 years and weight between 60 and 80 kg. Exclusion criteria in this study included early onset of labor pains, premature rupture of the fetal membrane, preeclampsia intrauterine fetal death, emergency cesarean section and chronic maternal diseases such as lupus endocrinopathy.

### 2.1 Procedure

In this study, homogenization was performed in terms of variables such as maternal age and gestational age and patients were divided into two groups of 70 people, A and B. In the next step, these patients, their families and the nurses

participating in this study were instructed on how to complete the questionnaire and how to report pain. All patients underwent spinal anesthesia. At the end of anesthesia and wake up, the patient was recorded by VAS system on a score of 0 for complete analgesia and a score of 10 for severe and unbearable pain in the questionnaire at 0, 6, 12, 24 hours. In group A, paracetamol was injected at a dose of 500 mg at time zero (cord clamp). Each ampule of paracetamol (6.7 ml) contained 1000 mg of acetaminophen, which dissolved half of each ampoule in 100 ml of normal saline and was infused over 15 minutes by intravenous infusion. Pain score was recorded at 0, 6, 12, 24 h and 500 mg every 8 hours was injected until the 24-hour period.

Group B was received 30 mg ketorolac intravenously (every 8 hours to 3 days) for at least 15 seconds and then pain score was recorded at 0, 6, 12, 24 injection. At the end, each patient was examined for vital signs and visual acuity criteria at 0, 6, 12 and 24 hours after drug administration, and was evaluated and compared using VAS form. Ethically and respecting patients' rights, if the patient still had pain despite paracetamol and ketorolac and had a VAS greater than 3, 25 mg of intravenous Pethidine was administered to the patient and the time of first request of Pethidine and total amount of received Pethidine was recorded. In case of any problems and complications (nausea, vomiting, hypotension), immediate treatment was performed for the patient. Then the results of each patient's evaluation were recorded in the information form.

**2.2 Data Analysis Method**

The data were entered into SPSS software version 22 and the results were analyzed using T-test student and K2 statistical tests for demographic variables and Mann-Whitney test for nonparametric variables. P value was considered significant at 0.05 level.

**3. RESULTS**

In this study, 140 people who underwent cesarean section were studied. Mean age of patients was 28 ± 7 years. In this study, mean pain scores at 0, 6, 12 and 24 hours were significantly lower in the ketorolac group than in the paracetamol group (Table 1).

There was no complication in any of the study groups in this study. The results of this study

showed that according to independent t-test, there was no significant difference between the mean time of request for first analgesic (P = 0.839, Table 2).

**Table 1. Comparison of mean pain scores in paracetamol and ketorolac groups**

Hour	Paracetamol	Ketorolac	P value
0	6.5 ± 1.6	5.6 ± 1.1	0.002
6	3.5 ± 1.7	2.6 ± 1.1	0.001
12	2.0 ± 1.1	1.3 ± 0.9	0.001
24	0.7 ± 0.7	0.2 ± 0.4	<0.0001

**Table 2. Comparison of mean time to first analgesic request in paracetamol and ketorolac groups**

Treatment	Mean±SD	P value
Paracetamol	2.7 ± 1.2	0.839
ketorolac	2.8 ± 1.7	

The results of the rates of request for additional drug are presented in Table 3. In this study, the frequency of requesting additional analgesics was significantly lower in the ketorolac group than in the paracetamol group (P = 0.023, Table 2).

**Table 3. Comparison of frequency of excess drug requirement in the two study groups**

Treatment	Extra drug request		P value
	Yes	No	
Paracetamol	24	46	0/023
ketorolac	34%	66%	
	10	60	
	14%	86%	

**4. DISCUSSION**

In this study, we observed the rate of pain decrease after cesarean ward with ketorolac was notably higher than paracetamol. Frequency of additional opioid demand for pain control was significantly lower in the ketorolac group than in the paracetamol group, but the mean duration of first additional drug request was not significantly different between the two groups.

In a double-blind clinical trial, 'Use of ketorolac for postoperative cesarean pain', conducted by Karl E et al. (2004) patients were randomly divided into two groups. Immediately after surgery and then every 6 hours, the experimental group received ketorolac and the control group received placebo. Pain was assessed every hour

for the first four hours postoperatively and then assessed at 6, 12, and 24 hours later using a visual analogue scale (VAS). During this period, patients received morphine if pain persisted. The results of this study showed that those treated with ketorolac showed a significant improvement in VAS scores at 2,3, 4, 6, 12 and 24 hours ( $P = 0.008$ ). Patients in the placebo group also consumed approximately 50% more morphine than the experimental group. They found that using ketorolac was effective in reducing postoperative pain [11]. In a double-blind clinical trial study, 'The effect of intravenous ketorolac on the need for opioid medications and post-cesarean pain' performed by Pavy TJ et al. (2001) in Australia, 50 pregnant women were randomly assigned. They were divided into two groups. Group K received ketorolac and group C received normal saline. Patients were given meperidine during the period of pain. The results of the study showed that in the first 24 hours group K needed less meperidine than group C ( $P = 0.004$ ). Also, group K had less pain during the 12 hours postoperatively. There was no statistically significant difference between the two groups in terms of postoperative pain in rest or motion as well as patient satisfaction. They found that intravenous administration of ketorolac as an epidural analgesic adjuvant (PCEA) reduced the need for meperidine by up to 30% [12].

In another double-blind clinical trial study, 'Investigating the effect of paracetamol versus meperidine on post-cesarean pain' performed by Jarnishin et al. (2016) in Bandar Abbas, 70 pregnant women were randomly selected and divided into two groups. Paracetamol group received 1 g paracetamol in 100 ml normal saline and meperidine group received 25 mg meperidine in 100 ml normal saline. Nausea and pain intensity were assessed by visual acuity scale (VAS). The results of the study showed that the two groups showed no significant difference in pain score based on VAS during the 30 minutes after surgery in the recovery room, however, the pain score after 30 minutes was higher in the paracetamol group than the meperidine group. Pain scores after 6 hours were significantly lower in the meperidine group than in the paracetamol group. VAS-based nausea and vomiting score was significantly higher in the meperidine group during the 24 hours than in the paracetamol group. The analgesic use in the meperidine group during the 24 hours postoperatively was significantly lower than in the paracetamol group [13]. In another

study, "Assessing the analgesic effect of ketorolac or pethidine after cesarean section" by Gin T et al. (1994) in China, 100 pregnant women were randomly selected. One group received 30 mg of ketorolac intramuscularly and the other group received 75 mg of pethidine intramuscularly. Patients' pain was measured every 6 hours by VAS and verbal scale. Results showed that 26 patients in ketorolac group and 17 patients in pethidine group needed more analgesic after 90 minutes. VAS criteria were similar in both groups but side effects were higher in the pethidine group [14].

In a study by Darwish et al. (2014), 120 women undergoing cesarean section under spinal anesthesia were selected to evaluate the analgesic effect of diclofenac and paracetamol compared to meperidine in cesarean section. In this study, women were randomly divided into two groups. In the first group, subjects received diclofenac suppository at the end of surgery and then 1 g bolus of paracetamol and in the second group received 20 mg bolus of meperidine to control postoperative pain after transfer to the recovery room. The results of this study showed that combination of paracetamol and diclofenac had better efficacy in controlling postoperative pain compared to meperidine and reduced the need for analgesia [15]. In another study comparing the analgesic effect of oral ketorolac and intramuscular tramadol showed that 10 mg oral ketorolac had a better analgesic effect than 50 mg tramadol [16]. In a study comparing the effect of paracetamol and ketorolac on post-thyroidectomy pain control, it was reported that paracetamol may be an alternative to ketorolac for pain prevention in cases where NSAIDs are inappropriate [17]. In another study investigating the effect of intravenous diclofenac and acetaminophen suppositories and their combination on the severity of postoperative pain in patients undergoing spinal anesthesia during cesarean section, reported concomitant use of intravenous acetaminophen and diclofenac supplementation on pain relief and reduction the need for repeated doses of drugs and prolonged postoperative analgesia have a significant effect [18].

## 5. CONCLUSION

According to the results of this study, the rate of pain reduction after cesarean section with ketorolac was significantly higher than paracetamol. In general, since ketorolac was more effective than paracetamol, it is

recommended to use ketorolac under the conditions of this experiment to control post-cesarean pain.

### CONSENT AND ETHICAL APPROVAL

Authorization was obtained from the Ethics Committee of Zahedan University of Medical Sciences and registered in IRCT system. Pregnant women received informed consent form and all stages and goals of the study were described to patients and their relatives and the patient was informed that his or her dissatisfaction had no effect on the treatment process. Approval completed.

### COMPETING INTERESTS

Authors have declared that no competing interests exist.

### REFERENCES

1. Bakhsha F, Niaki AS, Jafari SY, Yousefi Z, Aryaie M. The effects of diclofenac suppository and intravenous acetaminophen and their combination on the severity of postoperative pain in patients undergoing spinal anaesthesia during cesarean section. *Journal of Clinical and Diagnostic Research: JCDR*. 2016;10(7): UC09.
2. Merrikhihaghi S, Farshchi A, Farshchi B, Farshchi S, Abedin-Dorkoosh F. Tramadol versus diclofenac in pain management after cesarean section: A cost analysis study. *Journal of Pharmacoeconomics and Pharmaceutical Management*. 2015;1(1): 22-4.
3. Miller KE. Use of ketorolac for pain control after cesarean section. *American Family Physician*. 2004;70(1):191-2.
4. Ramashwar S. In Asia, cesarean section associated with increased risk of neonatal mortality. *International Perspectives on Sexual and Reproductive Health*. 2010;36(2):116-118.
5. Miller RD, Ward TA, Shiboski SC, Cohen NH. A comparison of three methods of hemoglobin monitoring in patients undergoing spine surgery. *Anesthesia & Analgesia*. 2011;112(4):858-63.
6. Bamigboye AA, Hofmeyr GJ. Non-closure of peritoneal surfaces at caesarean section-a systematic review. *South African Medical Journal*. 2005;95(2):123-6.
7. Zangeneh M, Veisi F, Ebrahimi B, Ghadami MR. Comparing the Effects of Indomethacin-acetaminophen Suppository and Indomethacin Suppository alone on Post Cesarean Section Pain. *Journal of Mazandaran University of Medical Sciences*. 2014;24(117):157-64.
8. Lowder JL, Shackelford DP, Holbert D, Beste TM. A randomized, controlled trial to compare ketorolac tromethamine versus placebo after cesarean section to reduce pain and narcotic usage. *American Journal of Obstetrics and Gynecology*. 2003; 189(6):1559-62.
9. Wong JON, Tan TDM, Cheu NW, Wang YR, Liao CH, Chuang FH, et al. Comparison of the efficacy of parecoxib versus ketorolac combined with morphine on patient-controlled analgesia for post-cesarean delivery pain management. *Acta Anaesthesiologica Taiwanica*. 2010;48(4): 174-7.
10. Amiryamale P, Alijanpour A, Zabihi, A, Atarzade S. H, Shirkhani Z, Rezaei B. Comparison of analgesic effect of intravenous paracetamol and meperidine with meperidine alone on pain after caesarean section elective. *Anesthesiology and Pain Journal*. 1392;4(1).
11. Miller KE. Use of ketorolac for pain control after cesarean section. *American Family Physician*. 2004;70(1):191-2.
12. Pavy TJ, Paech MJ, Evans SF. The effect of intravenous ketorolac on opioid requirement and pain after cesarean delivery. *Anesthesia & Analgesia*. 2001;92(4):1010-4.
13. Jarineshin H, Fekrat F, Kashani S. The effect of paracetamol versus meperidine on postoperative pain of cesarean section. *Anesthesia, essays and researches*. 2017;11(1):165.
14. Gin T, Kan A, Lam K, O'Meara M. Analgesia after caesarean section with intramuscular ketorolac or pethidine. *Anaesthesia and intensive care*. 1993;21(4):420-3.
15. Darvish H, Memar Ardestani B, Mohammadkhani Shali S, Tajik A. Analgesic efficacy of diclofenac and paracetamol vs. meperidine in cesarean section. *Anesth Pain Med*. 2013;4(1): e9997. DOI: 10.5812/aapm.9997. eCollection 2014
16. Isiordia-Espinoza MA, Pozos-Guillen A, Martinez-Rider R, Perez-Urizar J.

- Comparison of the analgesic efficacy of oral ketorolac versus intramuscular tramadol after third molar surgery: A parallel, double-blind, randomized, placebo-controlled clinical trial. *Med Oral Patol Oral Cir Bucal*. 2016;21(5):e637–e643.  
[Published 2016 Sep 1]  
DOI: 10.4317/medoral.21077
17. Lee SY, Lee WH, Lee EH, Han KC, Ko YK. The effects of paracetamol, ketorolac and paracetamol plus morphine on pain control after thyroidectomy. *Korean J Pain*. 2010;23(2):124–30.
18. Bakhsha F, Niaki AS, Jafari SY, Yousefi Z, Aryaie M. The effects of diclofenac suppository and intravenous acetaminophen and their combination on the severity of postoperative pain in patients undergoing spinal anaesthesia during cesarean section. *J Clin Diagn Res*. 2016;10(7):UC09–UC12.  
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