

**Comparison the effect of paracetamol and ketorolac on pain relief after cesarean<sup>2</sup>  
section**

**Abstract:**

**Summary**

**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 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

## 34 **Introduction**

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

49 Non-steroidal anti-inflammatory drugs reduce pain by inhibiting cyclooxygenase. One of these drugs is  
50 ketorolac from the pyro lactic family that inhibits prostaglandin synthetase. It has not affected the central  
51 nervous system or the autonomic and cardiovascular nervous system (8). In a clinical trial study, 'Comparing  
52 the efficacy of parecoxib versus ketorolac with morphine in controlling patient pain after cesarean section'  
53 performed by Wong JO et al (2010) on 66 pregnant women, results showed that there was no significant  
54 difference in sedation, mood, sleep quality and patient satisfaction between the two groups. However,  
55 patients in the parecoxib group had less pain than the ketorolac group within the first 24 hours (9). In  
56 another study aimed at comparing the analgesic effect of intravenous paracetamol and meperidine with  
57 meperidine alone by Attarzadeh et al. (2013), the results showed that intravenous paracetamol had a  
58 significant analgesic effect on post-cesarean pain and reduces the overall dose of meperidine dramatically  
59 (10).

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

## Method

66

This is a double-blind clinical trial. The study population included pregnant women who referred to Albin  
Abi Talib 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. 70

Inclusion criteria in this study was 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. 75

### 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 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.

### 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.  $\alpha$  was  
considered significant at 0.05 level.

### Ethical considerations

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

## 105 Results

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

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

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

111  
112 There was no complication in any of the study groups in this study. The results of this study showed that  
113 according to independent t-test, there was no significant difference between the mean time of request for  
114 first analgesic ( $P = 0.839$ , Table 2).

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

Treatment	Mean $\pm$ SD	P value
Paracetamol	$2.7 \pm 1.2$	0.839
ketorolac	$2.8 \pm 1.7$	

120  
121 The results of the rates of request for additional drug are presented in Table 3. In this study, the frequency of  
122 requesting additional analgesics was significantly lower in the ketorolac group than in the paracetamol group  
123 ( $P = 0.023$ , Table 2).

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

124

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

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126

127 **Discussion**

128 In this study, 140 people who underwent cesarean section were studied. Mean age of patients was 28±7  
 129 years. In this study, mean pain scores at different hours (0, 6, 12 and 24 hours) were significantly lower in  
 130 the ketorolac group than in the paracetamol group. Frequency of additional opioid demand for pain control  
 131 was significantly lower in the ketorolac group than in the paracetamol group, but the mean duration of first  
 132 additional drug request was not significantly different between the two groups.

133 In a double-blind clinical trial, 'Use of ketorolac for postoperative cesarean pain', conducted by Karl E et al  
 134 (2004) patients were randomly divided into two groups. Immediately after surgery and then every 6 hours,  
 135 the experimental group received ketorolac and the control group received placebo. Pain was assessed every  
 136 hour for the first four hours postoperatively and then assessed at 6, 12, and 24 hours later using a visual  
 137 analogue scale (VAS). During this period, patients received morphine if pain persisted. The results of this  
 138 study showed that those treated with ketorolac showed a significant improvement in VAS scores at 2,3, 4, 6,  
 139 12 and 24 hours (P = 0.008). Patients in the placebo group also consumed approximately 50% more  
 140 morphine than the experimental group. They found that using ketorolac was effective in reducing  
 141 postoperative pain (11). In a double-blind clinical trial study, 'The effect of intravenous ketorolac on the  
 142 need for opioid medications and post-cesarean pain' performed by Pavy TJ et al. (2001) in Australia, 50  
 143 pregnant women were randomly assigned. They were divided into two groups. Group K received ketorolac  
 144 and group C received normal saline. Patients were given meperidine during the period of pain. The results of  
 145 the study showed that in the first 24 hours group K needed less meperidine than group C (P = 0.004). Also,  
 146 group K had less pain during the 12 hours postoperatively. There was no statistically significant difference  
 147 between the two groups in terms of postoperative pain in rest or motion as well as patient satisfaction. They  
 148 found that intravenous administration of ketorolac as an epidural analgesic adjuvant (PCEA) reduced the  
 149 need for meperidine by up to 30% (12).

150 In another double-blind clinical trial study, 'Investigating the effect of paracetamol versus meperidine on  
 151 post-cesarean pain' performed by Jarnishin et al. (2016) in Bandar Abbas, 70 pregnant women were

152 randomly selected and divided into two groups. Paracetamol group received 1 g paracetamol in 100 ml  
153 normal saline and meperidine group received 25 mg meperidine in 100 ml normal saline. Nausea and pain  
154 intensity were assessed by visual acuity scale (VAS). The results of the study showed that the two groups  
155 showed no significant difference in pain score based on VAS during the 30 minutes after surgery in the  
156 recovery room, however, the pain score after 30 minutes was higher in the paracetamol group than the  
157 meperidine group. Pain scores after 6 hours were significantly lower in the meperidine group than in the  
158 paracetamol group. VAS-based nausea and vomiting score was significantly higher in the meperidine group  
159 during the 24 hours than in the paracetamol group. The analgesic use in the meperidine group during the 24  
160 hours postoperatively was significantly lower than in the paracetamol group (13). In another study,  
161 "Assessing the analgesic effect of ketorolac or pethidine after cesarean section" by Gin T et al. (1994) in  
162 China, 100 pregnant women were randomly selected. One group received 30 mg of ketorolac  
163 intramuscularly and the other group received 75 mg of pethidine intramuscularly. Patients' pain was  
164 measured every 6 hours by VAS and verbal scale. Results showed that 26 patients in ketorolac group and 17  
165 patients in pethidine group needed more analgesic after 90 minutes. VAS criteria were similar in both  
166 groups but side effects were higher in the pethidine group (14).

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

## 184 **Conclusion**

185 According to the results of this study, the rate of pain reduction after cesarean section with ketorolac was  
186 significantly higher than paracetamol. In general, since ketorolac was more effective than paracetamol, it is  
187 recommended to use ketorolac under the conditions of this experiment to control post-cesarean pain.

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