

Original Research Article

Comparison of the effect of pregabalin and diclofenac suppository on pain relief after elective cesarean section

Comment [B1]: Check Spelling.....???

Abstract:

Summary

Comment [B2]: Abstract or Summary.....??

Introduction: Cesarean section is one of the most common major surgeries performed worldwide. Considering the importance of post-cesarean pain, finding a drug that can provide the patient with the least amount of complications can make the patient feel the least pain and most relaxation. The aim of this study was to compare the effect of pregabalin and diclofenac suppository on pain relief after elective cesarean section with spinal anesthesia.

Comment [B3]: Rephrase it

Comment [B4]: Should be at the end.

Method: This study was performed in 2016 on 100 women admitted to Ali Ibn Abi Talib Hospital due to elective cesarean section. Patients were divided into two groups of 100mg rectal diclofenac half an hour before surgery and 300mg pre-gabalin group. Data were analyzed using SPSS software. Probability level lower than 0.05 was considered significant.

Comment [B5]: Need Space

Comment [B6]: Space.....??
Methodology is not clear.....????

Results: The mean score of after surgery pain at 6 and 12 hours after surgery in the diclofenac group was significantly lower than in the pregabalin group, but at 18 and 24 hours, the difference between the two groups was not statistically significant. The mean dose of pethidine used in the diclofenac group was significantly lower than the pregabalin group. Maternal satisfaction was significantly higher in the diclofenac group.

Comment [B7]: Not clear.....???

Comment [B8]: Why Pethidine.....???

Conclusion: According to the results of this study, diclofenac has a stronger antinociceptive effect than pregabalin.

Comment [B9]: Rephrase the sentence

Keywords: Cesarean section, Diclofenac, Pregabalin

Introduction

Cesarean delivery is referred to as the birth of a fetus by cutting the abdominal wall and the uterine wall (1). This is one of the most commonly used surgeries worldwide (2). Acute pain after surgery is a complex physiological response to tissue damage, visceral dilatation or disease and has various physiological effects on various organs. Pain that restricts the patient's after surgery gait, along with increased stress-coagulation capacity, can contribute to the development of deep vein thrombosis (3). Considering the importance of post-cesarean pain, finding a drug that can provide the patient with the least side effects and most pain relief is one of the most important issues after cesarean section. Currently, systemic opioids are used to control pain, providing high satisfaction in patients, but these drugs have side effects such as nausea, respiratory

36 depression, and drowsiness (4, 5). In general, antinociceptive therapies can affect the central mechanism of
37 pain (such as opioids), or block the activity of pain receptors (such as lidocaine), or such as non-steroidal
38 anti-inflammatory drugs used to reduce topical hormonal responses to injury, directly reduce pain receptor
39 activity (6, 7). Non-steroidal anti-inflammatory drugs, or NSAIDs, reduce pain by inhibiting
40 cyclooxygenase. One of these NSAIDs is diclofenac sodium, a derivative of phenylacetic acid. This drug
41 exerts its antinociceptive and anti-inflammatory effects by inhibiting the synthesis of prostaglandins and is
42 largely excreted by the kidney and small amounts by the bile. A study by Rahmanpour et al. (2007) showed
43 that the use of diclofenac suppository was more effective than other forms of pain medication and could
44 reduce post-cesarean pain and significantly reduce the need for opiate use (8).

45 Pregabalin is a new synthetic molecule and a synthetic derivative of the gamma aminobutyric acid inhibitor.
46 It is an α -2 α -ligand that has anesthetic, anticonvulsant, antisense and sleep-modulating effects. In cases of
47 Acute pain after surgery, pregabalin plays a role in treatment by reducing the excitability of posterior horn
48 neurons caused by tissue damage (9). Based on the results of the study by Essam et al. (2015), it was found
49 that the use of pregabalin or ketamine significantly reduces the need for morphine use after surgery (10).

50 According to a review of the literature, no study performed about comparing the effects of pregabalin and
51 diclofenac on post-cesarean pain control. Therefore, considering the importance of pain control after
52 cesarean section and the important side effects (11) of NSAIDs (Cardiovascular thrombotic events,
53 increased risk of gastrointestinal bleeding, kidney damage), on the other hand the lack of a study on
54 comparing concomitant Pregabalin and Diclofenac, a study was done in Ali Ibn Abi Talib Hospital aimed at
55 comparing the effect of Pregabalin and Diclofenac suppository on post-cesarean pain relief in gynecological
56 patients.

58 **method**

59 This study is a double-blind randomized clinical trial. The study population consisted of all women
60 hospitalized in the labor ward of Ali Ibn Abi Talib Hospital in Zahedan, Iran, who underwent cesarean
61 section in 2017. Data were collected through a questionnaire and then the study conditions were explained to
62 the patients. They were included in the study if they wanted and completed the informed consent form and
63 having the study criteria.

64 Inclusion criteria was; be their first child, age between 20 and 45 years, weight between 60 and 80 kg, term
65 embryo, elective cesarean section, class of anesthesiologist's association 1 and 2 and spinal anesthesia
66 method. Exclusion criteria in this study was: sensitivity to NSAIDs and pregabalin, History of asthma,
67 previous abdominal surgery, having hemorrhoids, proctitis, pregnancy blood pressure, preeclampsia,
68 coagulopathy, gastrointestinal wounds, kidney and liver diseases, severe visual impairments, addiction to
69 drugs or any other psychoactive substance, spinal anesthesia failure and general anesthesia, patient
70 dissatisfaction, having diabetes and use of anticonvulsant drugs.

Comment [B10]: Please rephrase the whole Introduction section. Update the references. Typographical mistakes were found in whole manuscript.

Comment [B11]: It should be Methods..... Please rephrase the Methodolgy section. Should be written precisely and clearly.....Not clearly discussed.

71 **Sample Size and Sampling Method;**

72 Based on the formula and considering the 95% confidence level and the values below, the sample size was
73 calculated to be 50 in each group (100 in total).

76 Alpha 0.05 = beta = 0.2 S1 = 1.16 X1 = 2.89 S2 = 0.90 X2 = 2.25 N = 48

$$n = \frac{(s_1^2 + s_2^2)^2 (z_{1-\frac{\alpha}{2}} + z_{1-\beta})^2}{(\bar{x}_1 - \bar{x}_2)^2}$$

Comment [B13]: Please justify it with proper references.

82 Finally, 50 patients were studied in each group.

84 **Method of Study;**

85 Patients' unwillingness to participate in the study had no effect on the normal course of treatment. Patients
86 were randomly divided into two groups of 50 each. Sampling was done by randomized block design. Thus,
87 according to the sample size [100 (50 patients in the pre-gabaline group and 50 patients in the diclofenac
88 group)], 10 blocks were identified.

89 Before surgery, the visual analogue scale (VAS) was trained and the corresponding number was recorded in
90 her information form and then under spinal anesthesia, cesarean section was performed. Patients were
91 randomly assigned to receive 300 mg of pre-gabaline capsule orally and diclofenac 100 mg rectally, half an
92 hour before surgery, respectively.

93 Patients were then assessed for vital signs and VAS, up to 24 hours, every 6 hours from entry to recovery (6,
94 12, 18, 24 hours), as well as pethidine requirement and patient satisfaction (= 1 excellent, = 2 Good, = 3
95 Moderate, = 4 Dissatisfaction) were recorded in each patient's information form. In VAS above score 3, 25
96 mg of pethidine was slowly injected for the patient. By the end of the study, neither the patient nor the
97 person responsible for collecting and evaluating the patients were not known of allocation of patients to the
98 study groups.

Comment [B14]: The format is not followed properly.

99 data analysis method

100 The data were entered into SPSS software version 22. Then, descriptive statistics (mean, standard deviation,
101 frequency and percentage) were analyzed. Significance level was set at 0.05.

Comment [B15]:??????

103 **Results**

104 In this study, 100 women undergoing cesarean section were studied. Table 1 compares the mean age of
105 patients and weight of patients in the two groups based on independent t-test. As can be seen in Table 1,
106 there was no significant difference between the study groups.

Comment [B16]: Repeation.....

Results seems to be not upto the standard.
There is no proper discussion about Pethidine and
its use pre or post surgical procedures.....Please
justify your results with proper references and
mention it professionally.

107
108 **Table 1. Comparison of patients' age and weight in the two study groups**

Parameter	Diclofenac	Pregabalin	Value P
Age	29.54 ± 5.48	30.30 ± 5.82	0.504
Weight	71.18 ± 6.26	70.92 ± 5.96	0.832

109
110 Also, according to Chi-Square test, patients' gravida did not differ significantly between the two groups. The
111 majority of patients in both groups were Gravid 1 or 2 (Table 2).

112
113 **Table 2. Comparison of the gravid of patients in the two groups**

Gravid	Diclofenac	Pregabalin	Value P
1	23 (46 %)	21 (42 %)	
2	19 (38 %)	20 (40 %)	0.098
3	7 (14 %)	8 (16 %)	
4	1 (2 %)	1 (2 %)	

114
115 According to the independent t-test, the mean score of after surgery pain at 6 and 12 hours after surgery was
116 significantly lower in the diclofenac group (P value: 0.029 and 0.023, respectively). But at 18 and 24 hours,
117 the difference between the two groups was not statistically significant (P values: 0.127 and 0.175,
118 respectively, Table 3).

119
120
121 **Table 3. Comparison of mean pain scores in the diclofenac and pregabalin groups**

Time (h)	Diclofenac	Pregabalin	Value P
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6	4.76 ± 1.58	5.56 ± 1.99	0.029
12	3.02 ± 1.05	3.62 ± 1.49	0.023
18	1.84 ± 1.26	2.26 ± 1.45	0.127
24	0.50 ± 0.88	0.78 ± 1.14	0.175

The mean of pethidine intake during the 24 hours after surgery in the studied patients was 51 ± 28 and 39 ± 22 mg respectively for the pregabalin and diclofenac groups. Comparison of mean pethidine consumption during the 24 hours after surgery showed that this amount was significantly lower in the diclofenac group (P = 0.04, Table 4).

Table 4. Mean dose of pethidine consumed in the diclofenac and pregabalin groups

Treatment	Mean ± SD	Value P
Diclofenac	39 ± 22	0.04
Pregabalin	51 ± 28	

The results of maternal satisfaction are presented in Table 5. In this study, the highest percentage of patients in the pregabalin group had moderate satisfaction (30%). Most of the patients in the diclofenac group had excellent satisfaction (44%). According to the Chi-Square test, mothers' satisfaction in the pregabalin group was significantly lower than the diclofenac group (P = 0.028, Table 5).

Table 5. Comparison of maternal satisfaction in pregabalin group with diclofenac

Satisfaction	Diclofenac	Pregabalin	P value
Excellent	22 (44 %)	13 (26 %)	0.028
Good	12 (24 %)	9 (18 %)	
Medium	13 (26 %)	15 (30 %)	
Dissatisfaction	3 (6 %)	13 (26 %)	

The results of this study showed that the median time to first analgesic application in the diclofenac group was 5.6 ± 1.9 hours and this index was 4.6 ± 1.5 hours in the pregabalin group. Median time to first analgesic application for pregabalin recipient group was significantly lower than diclofenac recipient group (P = 0.028, Table 6).

139 **Table 6. Comparison of mean time to first analgesic application in the diclofenac and pregabalin**
 140 **group**

Treatment	Mean \pm SD	Value P
Diclofenac	5.6 \pm 1.9	0.009
Pregabalin	4.6 \pm 1.5	

142 **Discussion**

143 In this study, 100 patients undergoing cesarean section were studied. The mean pain score at the 6th and
 144 12th hours after surgery in the diclofenac group was significantly lower than that of the pregabalin group,
 145 but at 18 and 24 hours, the difference between the two groups was not statistically significant. Also, the
 146 mean dose of pethidine used in the diclofenac group was significantly lower than in the pregabalin group.
 147 Maternal satisfaction was significantly lower in the pregabalin group than in the diclofenac group. In the
 148 diclofenac group, 44% of patients were satisfied and only 6% were dissatisfied, but in the pregabalin group,
 149 26% were dissatisfied and 26% were satisfied. The mean time of first analgesic application in the
 150 pregabalin group was significantly less than that of the diclofenac group. This means that patients in the
 151 pregabalin group needed additional pain relief shortly after surgery.

152 In a study evaluating the analgesic effect of rectal diclofenac on reducing after surgery opiate use on 80
 153 women, Rabie et al. (2006) reported that the number of pethidine's received in the diclofenac recipient
 154 group was significantly lower than the control group. Mean pain score in the receiving group was not
 155 significantly different from the control group (13). In another study by Joshi Vyankatesh S et al (2013), they
 156 compared the analgesic effect of rectal tramadol and diclofenac suppositories in patients undergoing
 157 cesarean section and studied 60 patients. In that study, it was reported that mean pain scores at 2, 4, 6, 8 and
 158 10 hours were significantly lower in the diclofenac group than in the tramadol group (14).

159 Also, in another study by Somboon Thienthong et al (2012) investigating the effect of intravenous
 160 diclofenac on pain relief after cesarean section using 30 patients showed that the mean pain score in
 161 diclofenac recipient group was significantly lower than the placebo group in the 24th h after surgery.
 162 Tramadol intake was not significantly different between the two groups (15). In another study conducted by
 163 Akhavan Akbari and colleagues in Ardabil in 2013, they evaluated the effect of indomethacin, diclofenac
 164 and acetaminophen on pain and opioid use in patients undergoing cesarean section, using 120 women. The
 165 pain intensity in the control group was significantly higher than the other groups. Pain intensity was
 166 significantly lower in the acetaminophen group than in the indomethacin and diclofenac groups. Duration of
 167 first analgesic application in the three intervention groups was significantly longer than the control group
 168 (16).

Comment [B18]: Repeation.....????

169 In another study conducted by Sumesh et al. In 2013 on 66 patients undergoing head and neck surgery, the
170 effect of diclofenac (75 mg orally) compared to pregabalin (150 mg orally) on severity Postoperative pain
171 and need for analgesics were assessed. The results of this study showed that patients in the pregabalin
172 group showed less pain intensity at 12 and 24 hours postoperatively and fewer patients required analgesia
173 after surgery (17). In another study conducted by Mohsen Mohamed El-guoshi and colleagues in Egypt in
174 2018, they investigated the effect of pregabalin on the reduction of the frequency of post-cesarean headache
175 using spinal anesthesia and studied 400 patients. The frequency of shivering, nausea, vomiting, headache
176 frequency, and the need for additional analgesics were significantly lower in the pregabalin group than in
177 the control group (18).

178 In a study by Darwish et al. (2014), 120 women undergoing cesarean section under spinal anesthesia were
179 selected to evaluate the analgesic effect of diclofenac and paracetamol compared to meperidine in cesarean
180 section. In this study, women were randomly divided into two groups. In the first group, subjects received
181 diclofenac suppository at the end of surgery and then 1 g bolus of paracetamol and in the second group
182 received 20 mg bolus of meperidine to control postoperative pain after transfer to the recovery room. The
183 results of this study showed that combination of paracetamol and diclofenac had better efficacy in
184 controlling postoperative pain compared to meperidine and reduced the need for analgesia (19).

186 Conclusion

187 According to the results of this study, the rate of pain reduction after cesarean section with diclofenac was
188 significantly higher than that of pregabalin. In general, since diclofenac is more effective than pregabalin
189 and patients are more satisfied with the less need for additional analgesics, it is recommended to use
190 diclofenac to control post-cesarean pain.

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Comment [B19]: Please rephrase .
Discuss your results with other relevant studies and
justify it with updated references.

Comment [B20]: Change the conclusion part

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