

Original Article

## The comparison between suppository diclofenac and pethidine in post-cesarean section pain relief: a randomized controlled clinical trial

Ziba Zahiri Soroori\*, Seyedeh Hajar Sharami\*\*,  
Abtin Heidarzadeh\*\*\*, Leila Shokri\*\*\*\*

### Abstract

**BACKGROUND:** Narcotic drugs are usually used for postoperative pain control which could cause several complications such as respiratory depression and apnea. Therefore, replacement of these drugs with safer analgesics is recommended. The aim of this study was to compare the analgesic effects of suppository diclofenac and pethidine in post-cesarean section (C/S) patients.

**METHODS:** In this clinical trial, pregnant women who were admitted to Alzahrah Hospital, Isfahan, Iran, between August and February 2004 and met the inclusion criteria were recruited. After obtaining informed consent, the patients were randomly assigned (block randomization) to two groups. In group A, 100 mg rectal suppository diclofenac was used after operation at four time points: at the end of operation and 8, 16 and 24 hours after the operation. Group B received pethidine 1 mg/kg intramuscularly at similar time points. The pain scores were assessed at 2, 10, 18 and 26 hours after C/S using the Visual Analogue Scale (VAS). Age, gestational age, parity, history of previous abortion, C/S and abdominal surgery, level of education, pain score, side effects and satisfaction level were assessed. Analysis was carried out with ANCOVA model and  $\chi^2$  Mantel Haenszel tests by SPSS.10 software.  $P < 0.05$  was considered significant.

**RESULTS:** Two hundred forty patients met inclusion criteria. Age, parity, history of previous abortion, history of previous C/S and abdominal surgery, level of education and satisfaction level were similar in the two groups ( $P > 0.05$ ). There was no significant difference between side effects in the two groups except for dizziness in 11 cases in group B. There were significant statistical difference between pain intensity in 10, 18 and 26 hours after C/S in group A and group B ( $2.05 \pm 2.07$ ,  $1.4 \pm 1.6$  and  $0.5 \pm 1.1$  vs.  $2.6 \pm 2.2$ ,  $2.3 \pm 2.2$  and  $1.3 \pm 1.9$ ) respectively.

**CONCLUSIONS:** The results of the present study showed that the use of suppository diclofenac is an appropriate replacement therapy for pain relief after C/S.

**KEY WORDS:** Diclofenac, pethidine, cesarean section, pain relief.

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Pain in the postoperative period is an important impediment to recovery from surgery and anesthesia. Hence, reducing the pain after cesarean section (C/S) or any other surgery is very important<sup>1</sup>. However, managing the pain after C/S is more complicated because the patients are always young, healthy and active women who are eager to care for their infants<sup>2</sup>. Since the first postpar-

tum hours and days are important for interaction between mother and newborn, pain should not interfere with the mother's ability to nurse the baby<sup>3</sup>. However, opioid analgesic drugs were commonly used for pain relief<sup>4</sup>, but none of these drugs is the ideal one for analgesia after C/S<sup>2</sup>. Pethidine in high doses can suppress the central nervous system and cause adverse effects such as hypotension, nausea,

\*Assistant Professor, Department of Obstetric and Gynecology, Gilan University of Medical Sciences, Gilan, Iran.

\*\*Associate Professor, Department of Obstetric and Gynecology, Gilan University of Medical Sciences, Gilan, Iran.

\*\*\*Assistant professor, Department of Epidemiology, Gilan University of Medical Sciences, Gilan, Iran.

\*\*\*\*Resident of Obstetric and Gynecology, Gilan University of Medical Sciences, Gilan, Iran.

Correspondence to: Dr Ziba Zahiri Soroori, Department of Obstetric and Gynecology, Gilan University of Medical Sciences, Gilan, Iran.  
e-mail: drzibazahiri@yahoo.com

vomiting, drowsiness, itching, respiratory depression, and tachycardia<sup>5,6</sup>. High cost and difficult availability are other reasons of avoiding the use of these drugs as routine analgesic medications after surgery<sup>7</sup>. Some analgesics such as nonsteroidal anti-inflammatory drugs (NSAIDs) have been more applied because they reduce pain of uterine contraction by inhibiting prostaglandin synthesis<sup>8,9</sup>. Apart from direct anti-inflammatory and analgesic effects, these drugs have an indirect effect on pain relief by reducing chemical mediators of pain that make painful impulses. Moreover, NSAIDs have been found to neither cause respiratory depression, nor other opioids side effects such as drowsiness, nausea and ileus. NSAIDs have some gastrointestinal (GI) effects and there is a theoretical risk of post-partum hemorrhage with the use of NSAIDs as they prolong bleeding time and reduce platelet aggregation. However, NSAID-induced post-operative hemorrhage is infrequent in clinical practice<sup>10,11</sup>. It has also been stated that using NSAIDs increases the efficacy of opioids and consequently reduces their consumption<sup>1,7,12-14</sup>. Several studies showed that sodium diclofenac is one of the best analgesics and has a wide application in postoperative pain relief. In addition to its analgesic effect, this drug is more available than opioids and its usage is easier<sup>14-18</sup>. We chose the suppository form of diclofenac because the parenteral form was unavailable and using the oral form was not possible. Many studies have been conducted to compare NSAIDs with opioids, but there have been no studies to determine the efficacy of suppository diclofenac and pethidine after C/S. This study was designed to evaluate this idea in post C/S pain relief in women presenting to Alzahra Hospital of Gilan Medical University.

## Methods

This was a randomized controlled trial. All women who were scheduled for C/S with a gestational age more than 28 weeks and no history of convulsion, drug sensitivity, opioid addiction, epigastric pain and gastrointestinal bleeding were recruited. They were given spi-

nal anesthesia with injection of hyperbaric lidocaine at L4-L5 space, to reach the appropriate level of analgesia (T4 to T6). The dose of lidocaine was adjusted for the patients' heights (<150 cm: 60-70 mg, 150-170 cm: 80 mg and >170 cm: 100 mg). Women were excluded if their operation time was more than 90 minutes, had any complication during the surgery that needed another operation, or if they had postoperative ileus or any other state which required administration of other analgesics. Written informed consent was obtained from all patients. Using block randomization method, the patients were randomly allocated to two groups to receive either suppository diclofenac (group A) or intramuscular pethidine (group B). Pethidine has an onset of action of 10 minutes, peak effect of 1 to 2 hours and duration of action of 2-4 hours. Diclofenac has an onset of action of 30 minutes, peak effect of 2 hours and is gradually excreted<sup>19</sup>. Group A received 100 mg diclofenac suppository immediately after operation followed by 3 other identical doses at 8-hour intervals<sup>15,20</sup>. Group B received 1 mg/kg intramuscular pethidine after the operation and then 3 other doses at 8-hour intervals. Pain assessment considering the severity and pain scores was based on Visual Analogue Scales (VAS) that is a graded ruler ranging from zero to ten showing the minimum and maximum pain scores, respectively. After giving information about the pain assessment process to the patients, pain assessments by VAS was made by 2 trained midwives 2 hours after the surgery and 10, 18 and 26 hours after surgery. If patients needed further analgesia, pethidine 1 mg/kg was injected after evaluation of pain scores. During the process, vital signs and side effects such as nausea, vomiting, headache, dizziness, heartburn and dyspepsia were also assessed. If the patients had nausea or vomiting metoclopramide was administered parenterally.

At the end of the process, patients were asked by the standby gynecologist in the ward to subjectively rank their satisfaction with pain relief after C/S as good, moderate and poor. Other information including age, gestational

age, parity, history of C/S and abdominal surgery, educational level, pain scores and side effects was also collected. Data were analyzed by SPSS 10, with ANCOVA model,  $\chi^2$ Mantel-Haenzel.  $P < 0.05$  was considered significant.

## Results

Two hundred forty women were enrolled in this study. Mean age of group A subjects (who took diclofenac) was  $27.2 \pm 6.5$  years and that of group B (who received pethidine) was  $26.4 \pm 5.6$  years ( $P > 0.05$ ). Mean gestational age in groups A and B was  $38.8 \pm 1.7$  weeks and  $39.1 \pm 1.4$  weeks, respectively ( $P > 0.05$ ). The Baseline characteristics were similar in the two study groups (table 1). Only one case of headache (0.8%) was seen in group A and there were two cases (1.6%) in group B ( $P > 0.05$ ). There were 11 cases of dizziness (9.1%) in group B and none in group A ( $P < 0.05$ ). Nausea and vomiting occurred at similar rates in both groups ( $P > 0.05$ ). There were no cases of GI bleeding in either group. Statistically significant differences between two groups in term of pain scores were seen at 10, 18 and 26 hours after surgery (table 2). There was no statistical significant difference between the two groups in pain scores at

2 hours after surgery and patient satisfaction with pain relief (table 3).

**Table 1.** Baseline characteristics in two study groups.\*

Variable name	Diclofenac suppository n (%)	Pethidine IM n (%)
Age (year)		
$\leq 24$	45 (37.5)	55 (45.8)
25-34	56 (46.7)	54 (45)
$\geq 35$	19 (15.8)	11 (9.2)
Gestational Age (wk)		
$\leq 37$	11 (9.2)	16 (13.3)
$> 38$	109 (90.8)	104 (86.7)
Parity		
1	99 (82.5)	109 (90.8)
$\geq 2$	21 (17.5)	11 (9.2)
History of previous abortion		
0	105 (87.5)	104 (86.7)
1-2	13 (10.8)	16 (13.3)
$> 3$	2 (1.7)	-
History of previous C/S		
Yes	29 (24.2)	25 (20.8)
No	91 (75.8)	95 (79.2)
Educational level		
Illiterate	43 (35.8)	42 (35)
High school	48 (40)	35 (29.2)
College	23 (19.2)	36 (30)
Postgraduated	6 (5)	7 (5.8)

\*P values weren't statistically significant

**Table 2.** Mean pain scores based on VAS criteria in two study groups.

Mean pain scores	Diclofenac suppository Mean $\pm$ SD	Pethidine IM Mean $\pm$ SD	ANCOVA test
2 hr	$6.8 \pm 2.3$	$7.3 \pm 2.4$	$P > 0.05$
10 hr	$2.05 \pm 2.07$	$2.6 \pm 2.2$	$P < 0.05$
18 hr	$1.4 \pm 1.6$	$2.3 \pm 2.2$	$P < 0.05$
26 hr	$0.5 \pm 1.1$	$1.3 \pm 1.9$	$P < 0.05$

**Table 3.** Patient satisfaction of pain relief after CS.

Satisfaction level	Diclofenac suppository n (%)	Pethidine IM n (%)	$\chi^2$ Mantel-Hanzel test
Good	85 (70.8)	73 (60)	$P > 0.05$
Moderate	31 (25.8)	36 (30)	
Poor	4 (3.3)	11 (9.2)	

## Discussion

Owing to the wide range of side effects and dependency associated with opioids, their replacement with other analgesics has always

been considered<sup>12,21</sup>. The application of NSAIDs in various operations has increased. NSAIDs inhibit prostaglandin biosynthesis by blocking the cyclooxygenase enzyme, which

catalyzes the conversion of arachidonic acid to prostaglandin. By reducing the production of these agents, the feeling of pain may decrease in the peripheral nervous system. In other words, these drugs remove chemical agents of pain while opioids cannot remove them and by using opioids, the patients still have an ambiguous feeling of pain<sup>22</sup>. On the other hand, NSAIDs have no effect on CNS or cause no drowsiness. Then, the patients wake up early from the deep rest which promotes wound recovery and prevents postoperative side effects. There is also a decrease in using opioids by administering NSAIDs so the adverse effects of systemic opioids would be avoided<sup>7,23</sup>.

Abdollahi et al compared pethidine (0.5 mg/kg intrathecal every 8 hours) and diclofenac suppository (100 mg every 8 hours) for pain relief after inguinal herniation surgery and found no difference of mean pain score between the two groups at the first 8 hours, but at the second and third 8 hours, the feeling of pain was statistically lower in the diclofenac group<sup>12</sup>. In the present study, absence of difference between the two groups in the feeling of pain 2 hours after C/S could be due to increased intensity of pain immediately after removal of the analgesic effect of spinal anesthesia that may take about 2 hours to start and neither diclofenac nor pethidine was able to relieve pain appropriately. The mean pain scores at 10, 18 and 26 hours after surgery in the diclofenac group were lower than those in the pethidine group, however, the reported pain severity had decreased more with the passage of time after surgery. This difference between the two groups could be due to the longer effects of diclofenac and blockage of pain receptors and inhibition of prostaglandin release. Abedinzadeh et al found that sodium

diclofenac is a better analgesic than pethidine after appendectomy<sup>7</sup>. Olofsson and colleagues reported that in women receiving diclofenac rectally, the consumption of ketobemidone was reduced by 39% compared to the placebo group<sup>23</sup>. Rashid and colleagues evaluated the efficacy of 100 mg rectal diclofenac immediately after C/S followed by 50 mg at 12 hours and 100 mg at 39 hours after the surgery. Their results showed that VAS of pain in the study group was significantly less at 12, 14 and 24 hours after surgery compared to the control group who did not receive any drugs. Moreover, the amount of pethidine consumed and the incidence of sedation and constipation were significantly lower in the study group than in the control group<sup>16</sup>. In a study comparing 100 mg diclofenac suppository plus 1.5 mg/kg intravenous morphine, with intravenous morphine alone after C/S, the wound pain and uterine contraction pain in the group receiving diclofenac plus morphine was lower than in the other group. Nausea and vomiting occurred at similar rates in the two groups<sup>9</sup>. Lower incidence of side effects in both study groups can be the result of their separate consumption and lower doses of opioids. Paying attention to pain relief quality is directly related to patient satisfaction which is related to the kind of analgesic. However, we found a significant difference in pain relief between the two groups, while there was no statistically significant difference in patient satisfaction.

**Conclusion:** Pethidine is one of the most effective opioids for pain relief after C/S, but general concerns have been raised for its wide side effects, high cost, and legal issues. It seems that diclofenac suppository is a suitable replacement for this drug because it has shown better analgesic effects on postoperative pain.

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