Original Article

Intravenous Paracetamol (Perfalgan) for analgesia after cesarean section: A double-blind randomized controlled study.

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ABSTRACT

Objective
To evaluate the analgesic efficacy of intravenous paracetamol (Perfalgan) for pain control after cesarean delivery.

Patients and Methods
This prospective, double-blind, randomized, placebo-controlled study was performed on eighty ASA I-II women who had elective cesarean sections under spinal anesthesia with spinal morphine. Patients were randomly divided into two equal groups by a table of randomization. Forty patients received (1g/100ml) intravenous paracetamol (group I) at the end of surgery and every 6 hours for 24 hours and 40 patients received 100ml normal saline as placebo (group II) at the stated time. Standard analgesia meperidine (pethidine) was available as a rescue drug to both groups. The number of patients who required rescue analgesic drug, pain scores and satisfaction of patients were evaluated for 24 hours postoperatively.
Results

In the group I, no patients required rescue drug compared to 25% in the group II (P<0.05). Median pain scores were less in the group I at 6 hours [1(range 1-6) vs. 3 (range 1-8), p = 0.002] at 12 hours [2 (range 0-5) vs. 3 (range 0-7), p = 0.031] and at 24 hours [1.5 (range 0-4) vs. 3 (range 1-8), p< 0.0001], respectively. Satisfaction was comparable in both groups.

Conclusion

We conclude that Intravenous paracetamol is an effective treatment option and can be used to reduce the requirement of rescue opioid drugs for pain control after cesarean section. (Rawal Med J 2011;36:269-273).

Key words

Paracetamol, cesarean section, postoperative pain.

INTRODUCTION

Delivery by cesarean section is one of the commonest major operative procedure in obstetrics worldwide. Management of postoperative pain relieves suffering and leads to earlier mobilization, shortened hospital stay, reduced hospital costs, and increased patient satisfaction. Perioperative analgesia has traditionally been provided by opioid analgesics. However, extensive use of opioid is associated with a variety of perioperative side effects, such as respiratory depression, drowsiness and sedation, postoperative nausea and vomiting, pruritus, urinary retention, ileus, and constipation, which can delay hospital discharge. Therefore, anesthesiologists and surgeons are increasingly turning to non-opioid analgesic techniques for managing pain during the perioperative period.
Meperidine is a synthetic opioid agonist with a slightly more rapid onset of action and shorter duration of action than morphine which is frequently used for postoperative pain.\(^5\) Non-opioid analgesics, such as paracetamol and non steroidal anti-inflammatory drugs (NSAIDS) are commonly used alone or in combination with opioid-base analgesics to treat moderate to severe pain.\(^4\) Perfalgan is an injectable paracetamol (1g/100ml) in a unite-dose form, ready for infusion. Various clinical studies show that paracetamol is an effective analgesic drug in the treatment of postoperative pain\(^6,7\) and has few contraindications and lacks significant drug interactions.\(^8\) Its precise mechanism of action is not fully understood, however, it is found in significant concentration in the cerebrospinal fluid (CSF) after infusion.\(^9\) It may also work through central cyclooxygenase (COX2) inhibition, with a reduction in central nervous system prostaglandin E2 production and activation of descending serotonergic pathway.\(^10,11\) The analgesic effect of intravenous (IV) Paracetamol starts within 5 minutes, peaks at one hour and lasts 4-6 hours which is consistent with a plasma half-life of 2.7 hours.\(^10\) The purpose of this study was to evaluate the analgesic efficacy of intravenous paracetamol (Perfalgan) for pain control after cesarean delivery.

**PATIENTS AND METHODS**

After approval by our institutional ethics committee and a written informed consent, 80 healthy parturient who had American Society of Anesthesiologists Physical status I or II and were scheduled to undergo elective cesarean delivery at Prince Zaid Ben Al-Hussein Hospital-Jordan between January and May 2010 were enrolled for the study. Patients with known contraindication to paracetamol or meperidine, a history of severe allergic, hepatic, renal, cardiovascular, pulmonary disease, preeclampsia or eclampsia, diabetes
and emergency cesarean sections were excluded from the study. Patients who had intraoperative complications, history of chronic abdominal pain or treated with analgesics also were excluded from the study. Standard anesthetic and surgical techniques were used. In all patients 8-10 mg hyperbaric bupivacaine with 0.2 mg morphine were injected through a 25 gauge spinal needle placed at L3-L4 interspace. Thereafter, they were placed in supine position with a 10-15 degree left lateral tilt. A T4 sensory deficit was ensured before the onset of surgery. If failed or inadequate sensory block occurred, general anesthesia was given and patient excluded from the study.

Patients were randomly divided into two equal groups by table of randomization. Forty patients received (1g/100ml) IV paracetamol (group I) at the end of surgery and every 6 hours for 24 hours and 40 patients received 100ml normal saline as a placebo (group II) at the stated time points. Investigators, surgeon and recovery personnel were blinded to the identity of study treatment and substances administered were labeled as an analgesic drug. Only the senior resident knew what substance (paracetamol or normal saline) was given. Standard analgesia with meperidine was available as a rescue drug to both groups. The number of patients who required rescue analgesic drug, pain scores and satisfaction of patients were evaluated for 24 hours postoperatively.

The postoperative order protocols were inserted in the sealed envelope and opened by the surgeons when the patients met the inclusion criteria. Visual analog score (VAS) was used to evaluate pain level (0= no pain to 10= worst pain) at 6, 12 and 24 hours postoperatively by a resident and nurse who did not know about the treatment protocols. After 24 hours, the investigator collected the number of patients who required rescue drugs and defined patients in placebo group or paracetamol group from administration
records. Satisfaction was evaluated at 12 and 24 hours postoperatively (1 = very unsatisfied to 5 = very satisfied). SPSS version 15 was used to analyze the data. Student t–test, Chi-square test, and Mann-Whitney U-Test were used where appropriate for statistical analysis. P-value of < 0.05 was considered statistically significant.

RESULTS

There was no significant difference between groups (Table 1). In the paracetamol group, no patient required a rescue drug while in the placebo group 25 % of patients required a rescue drug (P<0.05).

Table 1. Patients characteristics and obstetric data.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Paracetamol group n = 40</th>
<th>Placebo group n = 40</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years) (mean ± SD)</td>
<td>30.80 ± 4.79</td>
<td>29.60 ± 5.20</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Gest. Age (days) (mean ± SD)</td>
<td>269.86 ± 5.89</td>
<td>271.97 ± 6.59</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Repeat cesarean section (n) %</td>
<td>32 (80)</td>
<td>29 (72.5)</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Nulliparity (n) (%)</td>
<td>8 (20)</td>
<td>11 (27.5)</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Multiparity (n) (%)</td>
<td>32 (80)</td>
<td>29 (72.5)</td>
<td>&gt; 0.05</td>
</tr>
</tbody>
</table>

P-value > 0.05 = statistically not significant.

Median pain scores were less in the paracetamol group at 6, 12, and 24 hours respectively compared to Placebo group (Table 2). All patients who required rescue drugs required them within the first 24 hours postoperatively (2-20 hours) and four patients required multiple doses of rescue drug.
Table 2. Rescue drugs requirement, pain scores and patient satisfaction.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Placebo group n = 40</th>
<th>Paracetamol group n = 40</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rescue drugs used (n) (%)</td>
<td>8 (20)</td>
<td>0 (0)</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Pain score at 6 h (median, range)</td>
<td>4, (0-6)</td>
<td>1, (0-6)</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Pain score at 12 h (median, range)</td>
<td>3, (0-7)</td>
<td>2, (0-5)</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Pain score at 24 h (median, range)</td>
<td>3 (1-8)</td>
<td>1.5, (0-4)</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>P S after 12 h</td>
<td>4.05 ± 0.59</td>
<td>4.33 ± 0.52</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>P S after 24 h</td>
<td>4.00 ± 0.50</td>
<td>4.25 ± 0.54</td>
<td>&lt; 0.05</td>
</tr>
</tbody>
</table>

P-value < 0.05 = statistically significant.

In the paracetamol group, patients had more satisfaction at 24 hours than in placebo group, but the difference between the groups was not statistically significant.

Table 3. Pain score analysis in subgroups.

<table>
<thead>
<tr>
<th>Group</th>
<th>Placebo</th>
<th>Paracetamol</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>M</td>
</tr>
<tr>
<td>Parity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain score at 6 hours (Median, range)</td>
<td>5, (0-5)</td>
<td>3, (0-6)</td>
</tr>
<tr>
<td>Pain score at 12 hours (Median, range)</td>
<td>4, (0-7)</td>
<td>3, (0-5)</td>
</tr>
<tr>
<td>Pain score at 24 hours (Median, range)</td>
<td>4.5, (3-4)</td>
<td>3, (1-8)</td>
</tr>
</tbody>
</table>

NS = Not significant N=nulliparity M=parity.

From subgroup analysis of pain scores in relation to parity, no statistically significant difference was observed between nulliparity and multiparity (Table 3).
DISCUSSION

Cesarean delivery is associated with substantial postoperative discomfort and pain. Continuous epidural analgesia or patient-controlled analgesia are being replaced by more traditional approach of on-demand parenteral administration of opioids. Women after cesarean section are reluctant to feel sleepy, drowsy or restricted by equipment that does not allow them free access to attend their babies and these are the most common side effects of opioid analgesics. In our study, IV paracetamol gave adequate pain relief and significantly reduced the requirement of rescue opioid drugs (P=0.003). Meperidine was less effectiveness than IV paracetamol because in placebo group, four out of ten patients who required rescue drug required multiple doses of meperidine to control pain. However, this study could not directly demonstrate the effectiveness of meperidine compared to paracetamol. Many patients in the paracetamol group described less periodic uterine cramping after pain. Two patients in the paracetamol group had adequate pain control and did not require more than one dose of paracetamol. However, further studies are required to establish this effect.

Studies regarding the analgesic effectiveness of IV Paracetamol in obstetric population are few and have reported conflicting results. Alhashemi et al compared IV paracetamol with oral ibuprofen in post cesarean patients and found no difference in 48-hour morphine consumption. Siddik et al found a significant morphine-sparing effect with rectal diclofenac but not IV paracetamol and no additional benefit when both were combined. In contrast, Munushankar et al and Cliff et al demonstrated that combination of paracetamol and diclofenac resulted in significantly less morphine requirement than paracetamol alone. Sammour et al compared the efficacy of oral
naproxen and oral tramadol for pain relief after cesarean delivery and found that both drugs were similar in terms of pain scores, but naproxen had a better adverse effect profile. In one study performed after surgery for breast cancer, IV paracetamol administered in repeated doses had a significant analgesic effect indistinguishable from that of IV dipyridone but with an improved side effects profile. IV paracetamol has been shown to provide good quality postoperative analgesia, with decreased consumption of morphine and minimal side effects after total abdominal hysterectomy. Mustafaeva and Mizikov compared the analgesic efficacy of paracetamol and tramadol and found that despite the high efficacy of tramadol, the quality of analgesia using IV paracetamol was almost five times better with fewer adverse effects.

In our study, the median pain scores in paracetamol group were significantly lower compared with placebo group (Table 2). These results are in agreement with other studies. The maximal pain score in the placebo group was higher than in paracetamol group (8 vs. 4). In the paracetamol group, the minimal pain score reached 0 at all periods of evaluation, but in the placebo group, no patients had a pain score of 0. From subgroup analysis of parity, no statistically significant difference of pain scores was observed between nulliparity and multiparity. Limitation of the study include small number of patients and, therefore, larger and multi-center studies comparing IV paracetamol to other analgesic drugs for control of post-cesarean section pain are required.
Conclusion

In our study, IV paracetamol (Perfalgan) was an effective option for post-cesarean section pain control and it can be used to reduce the requirement of rescue opioid drugs to avoid their side effects.

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REFERENCES


6. Atef AD, Fawaz AA. Intravenous Paracetamol is highly effective in pain treatment after tonsillectomy in adults. Eur Arch Otorhinolaryngol 2008;565:351-


