PENTAZOCINE VERSUS PENTAZOCINE WITH RECTAL DICLOFENAC FOR POSTOPERATIVE PAIN RELIEF AFTER CESAREAN SECTION - A DOUBLE BLIND RANDOMIZED PLACEBO CONTROLLED TRIAL IN A LOW RESOURCE AREA

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Abstract

Background: The unimodal approach of using pentazocine as post-cesarean section pain relief is inadequate, hence the need for a safer, easily available and more effective multimodal approach.

Aim: To evaluate the effectiveness of rectal diclofenac combined with intramuscular pentazocine for postoperative pain following cesarean section.

Methods: In this double blind clinical trial, 130 pregnant women scheduled for cesarean section under spinal anesthesia were randomly assigned to two groups. Group A received 100mg diclofenac suppository and group B received placebo suppository immediately following surgery, 12 and 24h later. Both groups also received intramuscular pentazocine 30mg immediately following surgery and 6 hourly postoperatively in the first 24 h. Postoperative pain was assessed by visual analogue scale at end of surgery and 2, 12 and 24 h after surgery. Patient satisfaction scores were also assessed.

Results: One hundred and sixteen patients completed the study. Combining diclofenac and pentazocine had statistically significant reduction in pain intensity at 2, 12, and 24 hours postoperatively compared to pentazocine alone (p <0.05). No significant side effects were noted in both groups. The combined group also had significantly better patient satisfaction scores.

Conclusion: The addition of diclofenac suppository to intramuscular pentazocine provides better pain relief after cesarean section and increased patient satisfaction.

Keywords: Pentazocine, diclofenac suppository, cesarean section, postoperative, analgesia

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Introduction

Postoperative pain management is a common problem following cesarean section\(^1^,\)\(^2\). Effective pain relief promotes early mobilization and good mother-child interactions\(^1\). Established methods of postoperative pain relief include infiltration of surgical wound with local anesthetic agent, continuous epidural, oral, intramuscular, intravenous and rectal analgesia. Intramuscular pentazocine, a partial agonist opioid is widely used in low resources countries for postoperative analgesia with limited effect\(^3\). A multimodal approach has been proposed to be more effective\(^2\).

Non-steroidal anti-inflammatory drugs (NSAIDs) have beneficial effect on postoperative analgesia and are devoid of adverse effects associated with opioids such as sedation, respiratory depression, nausea and vomiting\(^4\). NSAIDs also reduce pain of uterine contraction by inhibiting prostaglandin synthesis. Diclofenac sodium, a NSAID, is readily available as an oral, intramuscular or rectal medication. Intramuscular diclofenac is painful and oral absorption unpredictable in the perioperative period\(^5\). The rectal route offers rapid absorption of low molecular weight drugs, partial avoidance of first pass metabolism leading to improvement in rate controlled drug delivery and absorption\(^6\). Rectal diclofenac also avoids rare but hazardous complications of intramuscular diclofenac which include necrotizing fasciitis\(^7\), upper limb gangrene\(^8\), and anaphylactic shock\(^9\). Although awareness and use of rectal diclofenac among Nigerian physician anesthetists is limited, its role in post caesarean section pain relief is recognized elsewhere\(^10\).

We explored multimodal approach to pain relief after cesarean section using two different drugs with different routes of administration and mechanisms of action. We therefore compared the analgesic and side effect profile of intramuscular pentazocine alone or in combination with rectal diclofenac.

Materials and Methods

This study was a prospective, hospital-based, double-blind randomized placebo controlled trial approved by the hospital ethics and research committee. One hundred and thirty patients of ASA (American Society of Anesthesiologists’ Classification) I and II status undergoing elective or emergency caesarean section were recruited and written informed consent obtained. Exclusion criteria included refusal to participate in the study, epigastic pain, known peptic ulcer, bleeding complications, excessive intraoperative blood loss (>1000mls), and previous history of hypersensitivity reaction to NSAIDS, pentazocine, or tramadol. Intravenous metochlopramide 10mg and ranitidine 50mg were given to all patients preoperatively. All patients had cesarean section under spinal anesthesia. The spinal was performed using a 25-gauge Quincke needle with hyperbaric bupivacaine 5mg/ml to reach the appropriate level of analgesia (T8 to T6). No other intraoperative analgesia was given. Time of spinal needle insertion, operation time and intraoperative blood loss were recorded. The patients were randomly allocated with envelope concealment to two groups A and B. Group A (diclofenac) received 100mg diclofenac suppository (Lofnac\(^\text{®}\), Green Pharmaceuticals) and group B (placebo) were given an identical-looking suppository containing the main vehicle in which diclofenac is normally dissolved named polyethylene glycol. The study drug was administered immediately after surgery on the operating table by the attending obstetrician and repeated 12 and 24 hours postoperatively by the ward nurse. Also, all patients received 30mg intramuscular pentazocine immediately after surgery and 6 hourly for 24 hours. The attending anesthetist, obstetrician, nurses and patients were blinded to the trial drugs received by both groups.

Pain at rest and movement estimated by a visual analogue scale (VAS, 0cm = no pain to 10cm = worst imaginable pain), the need for rescue analgesics (intramuscular tramadol) and side effects such as nausea alone, nausea and vomiting, epigastric pain, respiratory depression, dizziness, anal discomfort and diarrhea, were recorded. Pain assessment was done by an anesthetist blinded at 0, 2, 12, and 24 hours after surgery. Intramuscular tramadol(50 mg) was given as rescue analgesia if the VAS pain score was greater than 30mm. Likert scales for level of satisfaction with pain relief ranging from very satisfied to very dissatisfied and preferred route of drug administration (i.m or rectal) were also assessed.
Data obtained were entered into a predesigned sheet and analyzed using SPSS version 16 (SPSS Inc., Chicago, IL). Categorical data were analyzed using Chi-square test with Fisher’s exact test. Means and standard deviation (SD) were calculated for quantitative variables and the differences between two independent groups were compared using student’s t-test. The level of statistical significance was considered at p < 0.05.

Results

One hundred and sixteen patients completed the study (completion ratio 89.2%) out of 130. Six subjects were excluded because of postpartum hemorrhage. There were no significant differences between the two groups with reference to patients’ demographic and obstetric characteristics as shown in Tables 1 and 2.

Table 1
Patients’ baseline characteristics and duration of surgery in the two groups

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number</td>
<td>64</td>
<td>52</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>31.4 ± 4.5</td>
<td>29.8 ± 5.1</td>
<td>0.078</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>74.5 ± 15.9</td>
<td>72.3 ± 14.1</td>
<td>0.423</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.6 ± 0.1</td>
<td>1.6 ± 0.1</td>
<td>0.905</td>
</tr>
<tr>
<td>Body Mass Index (BMI) Kg/m²</td>
<td>28.8 ± 5.9</td>
<td>27.8 ± 4.3</td>
<td>0.335</td>
</tr>
<tr>
<td>Duration of surgery (mins)</td>
<td>61.98 ± 12.28</td>
<td>59.98 ± 15.41</td>
<td>0.437</td>
</tr>
</tbody>
</table>

Data is presented as mean ± standard deviation.

The pain score in the two groups was similar at zero minutes (while on the operating table) in the immediate postoperative period but there was a statistical significant difference in VAS scores between the two groups at 2, 12, and 24 h after surgery both at rest and with movement (Figure 2). Fifteen (28.8%) patients in placebo group compared to six in diclofenac group (9.4%) (p = 0.0001) required intramuscular tramadol as a rescue analgesia.

Only one case of nausea and vomiting was seen in both group A (1.6%) and group B (1.9%). There were two cases of epigastric pain in group B (3.8%) and none in group A. There were no melena stool,
respiratory depression, dizziness, anal discomfort and diarrhea in either group. There was statistical significant difference between the two groups in level of satisfaction as shown in Table 3. Comparison between preference for route of drug administration in diclofenac group and placebo group.

**Discussion**

In this study, the average level of postoperative pain as estimated by VAS was lower in the diclofenac suppository group than in the placebo group. A study done by Akhanakbari et al compared the effects of indomethacin, diclofenac, and acetyaminophen suppositories following cesarean section. Patient in the diclofenac group had the least pain intensity at 12 hour and 24 hour. In their study, 50mg diclofenac suppository was administered 6 hourly over 24h which was equivalent to 12 hourly 100mg diclofenac suppository used in our study. A maximum mean VAS pain score of 1.4 in our study was comparable to 2.0 in diclofenac group by Akhavanakbari et al where unimodal approach to pain relief was used. The American Society of Anesthesiologists Task Force on Acute Pain Management however recommends the use of multimodal analgesia. The addition of diclofenac suppository to parenteral pentazocine in our study accounted for a lower VAS and fewer patients required rescue analgesia compared to the placebo group.

Studies by Dahl et al and Munishankar et al using 200mg of diclofenac daily also demonstrated less rescue analgesia required. In another study, combination of diclofenac and tramadol or diclofenac with acetyaminophen provided satisfactory postoperative pain control in parturients undergoing cesarean section. The addition of piroxicam to pentazocine as a multimodal approach showed good effect at 12 hour post cesarean section. The challenge however, was the intramuscular administration of both drugs. Intramuscular injection is painful and may predispose to adverse effects. Alternative routes are desirable other than oral. Oral diclofenac is one of most frequently implicated NSAIDs in upper gastrointestinal bleeding or ulceration. In Akhavanakbari et al’s study, rectal diclofenac did not cause gastrointestinal bleeding complications. Other previous studies also showed that diclofenac suppositories had been used successfully as postoperative pain relief after cholecystectomy and herniorrhaphy with no significant side effects.

Samimi et al compared combination of rectal diclofenac with paracetamol and rectal diclofenac alone for postoperative pain relief for hysterectomy and found significant lower pain scale in the first 24 hours in the combination group. Despite the use of rectal suppositories in our study, patients still experienced mild pain based on their VAS pain scores. It is possible that a more varied multimodal approach adding a mild analgesic such as acetyaminophen, may further add to improved pain relief.
Inadequate analgesia has been found to reduce patients’ satisfaction\(^2\) and may cause unwanted physiologic and psychological effects\(^3\). In a preliminary study by Pinto Pereira et al\(^4\), patients in the diclofenac suppository group were discharged earlier than the patients in the intramuscular diclofenac group. There was a correlation between time of discharge and level of satisfaction in a study done by Marinsek et al\(^5\) where 60% of patients were satisfied at discharge with their postoperative analgesia\(^6\). Time of discharge was not measured in our study because financial constraint on the part of mother and neonatal admission for sick babies were important factors that affect discharge in our hospital. Nonetheless, level of satisfaction was statistically significant in the diclofenac group which was similar to a separate study done by Soroori et al\(^7\).

Ortiz et al did a study on preoperative patient education and found a significant improvement in related questions about satisfaction with reference to options for pain management\(^8\). Patient satisfaction is improved after adequate information is provided to patients about the perioperative process especially when unfamiliar technique or route of drug administration is being introduced. The addition of diclofenac suppository increased the significant level of satisfaction in the diclofenac group.

There may be a link between level of satisfaction and preference for a particular route of administration of drug for postoperative analgesia. Our study demonstrated a significant preference for suppository form than intramuscular route of administration. Suppository form was effective and well tolerated in the Vyvan and Hanafial study but patients wanted to be informed preoperatively\(^9\). Our explanation to patients preoperatively may have contributed to improved acceptance.

**Conclusion**

In conclusion, the addition of diclofenac suppository to intramuscular pentazocine was found to be safe and efficacious, and increased patient satisfaction following cesarean section. The combination may be an ideal alternative in poor resource settings where more potent opioids and regional techniques are not routinely available.

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The drugs (lofnac suppository and placebo) used for this study were provided by Greenlife Pharmaceutical Company but there were no financial gains attached to it.
References


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- 97% of BRIDION patients recovered to a TOF* ratio of 0.9 from 1 to 2 PTCs within 5 minutes

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- BRIDION rapidly reversed patients from 1 to 2 PTCs in 2.7 minutes

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