

# A randomised controlled trial of opioid only versus combined opioid and non-steroidal anti inflammatory analgesics for pain relief in the first 48 hours after Caesarean section

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## ABSTRACT

**Background:** Post-Caesarean section pain is complex in nature, requiring a combination of pharmacological and non-pharmacological methods. Effective management of postoperative pain will reduce postoperative morbidity, hospital stay and cost. The objective of this study was to compare the clinical effectiveness and adverse effects of a combination of non-selective cyclooxygenase (COX) inhibitor (Diclofenac sodium 50 mg) and opioid (Pentazocine 60 mg) to opioid only (Pentazocine 60 mg) for pain management after Caesarean section (CS) at Aminu Kano Teaching Hospital (AKTH). **Materials and Methods:** This was a randomised double-blind controlled study conducted at AKTH, Kano, Nigeria. A total of 166 patients scheduled to undergo either emergency or elective Caesarean section were studied. Group I received a combination of COX inhibitor and opioid while Group II received opioid only for pain management after CS. **Results:** The average age of the patients was 28.35 years (SD  $\pm$  6.426) in the group I and 26.9(SD  $\pm$  6.133) in group II. The mean parity was 3.27(SD  $\pm$  2.67) and 2.75(SD  $\pm$  2.14) while the mean gestational age at admission was 37.68(SD  $\pm$  2.69) and 38.18(SD  $\pm$  2.63) weeks in the first and second groups, respectively. Comparison of the level of pain experienced and patients satisfaction during the first 48 hours postoperatively revealed that the level of pain was statistically significantly less and patient's satisfaction significantly better in group I compared to group II (*P*-value 0.00001). **Conclusion:** The use of combined compared to single agent analgesia is safe, significantly reduced pain and improved patient satisfaction after a caesarian section (CS).

**Key words:** Analgesia, caesarean section, pain, patient satisfaction

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## INTRODUCTION

Caesarean section (CS) is one of the most common operations undertaken worldwide. The global rate of CS is 10%.<sup>1</sup> It is estimated that 13 million Caesarean sections are performed each year which is equivalent to 24 procedures each minute.<sup>1</sup>

Patients worldwide are vulnerable to pain in the postoperative period. A study from Nigeria reported that 95% of patients experienced some degree of pain in the immediate postoperative period following CS.<sup>2</sup> The pain was severe in 79.6% of cases.<sup>2</sup> In South Africa, it was

reported that only 38.7% of patients were pain free.<sup>3</sup> Reducing the pain after CS is very important as it has been coupled with more positive emotional status and greater patient satisfaction with postoperative experience.<sup>4</sup> Effective management of postoperative pain also reduces postoperative morbidity, hospital stay and cost.

Post-CS pain is complex in nature, requiring a combination of pharmacological and non-pharmacological methods.<sup>5</sup> The non-pharmacological methods include processes such as explanation of the procedure to reduce anxiety and psychotherapy.<sup>6</sup> The pharmacological methods on the other hand include use of medications such as opioids, non-steroidal anti-inflammatory drugs (NSAIDs), epidural or patient controlled analgesia (PCA), and use of local anaesthetics for infiltration into peritoneal cavity and wound infiltration. Pethidine is usually prescribed alone by 51.6% of practitioners.<sup>3</sup> Doctors derived their analgesic regimes from current hospital protocols (48.6%), journals (19.45%) or experience (9.7%).<sup>3</sup> Only 6.5% of doctors used a pain score in the management of postoperative

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pain.<sup>3</sup> The most common dose interval is either eight or six hourly, which leaves a “window” during which patients may experience pain. Addition of other formulations, particularly non-steroid anti-inflammatory drugs, will help to reduce breakthrough pain.

Opioids act at various sites in the nervous system, inhibiting nociceptive impulses, while NSAIDs’ act by inhibiting cyclooxygenase, reducing release of cytokines and hence reducing postoperative inflammation, given additional benefit of visceral pain relief and achieving optimal analgesia.<sup>7,8</sup> Patients given a combination of diclofenac and paracetamol were found to need 38% less morphine compared to patients given paracetamol alone in the first 24 hours after CS.<sup>9</sup> The combination of tramadol and diclofenac resulted in more prolonged and pronounced postoperative analgesia with no increase in side effects.<sup>10</sup>

There is currently no “gold standard” for post-CS pain management. The choice of the method of pain relief is guided by factors such as departmental protocol, surgeon’s preference, drug availability, financial considerations, patient preference and history of drugs allergy. In many centres around the world, pain relief after major surgical procedures is achieved through a multimodal approach, which involves administering a combination of opioid and non-opioid analgesics.<sup>11</sup> In AKTH, only opioid analgesics were used in the departmental protocol for the postoperative management of CS. This study was designed to compare the effectiveness of a combination of agents (pentazocine and diclofenac) compared to a single agent (pentazocine) for pain management following CS.

## MATERIALS AND METHODS

This was a study randomised double-blind controlled trial of pain relief conducted at Aminu Kano Teaching Hospital (AKTH), Nigeria, from 1<sup>st</sup> April to 31<sup>st</sup> May 2012, after approval by the ethical committee of the hospital.

All women scheduled to undergo either emergency or elective CS during the period of the study were included in this study. Those excluded from the study included patients who had history of allergy to diclofenac sodium or pentazocine, those who did not consent to participate in the study, mentally disabled and unconscious patients, those who required the use of intra-abdominal drains, those on long-term analgesia, patients diagnosed to have sickle cell haemoglobinopathy, peptic ulcer disease or asthma and mothers aged less than 18 years.

Patients were assigned to the two groups using simple randomisation. Allocation was done by balloting pre-operatively.

Group 1 was given diclofenac and pentazocine while group 2 was given pentazocine only postoperatively. After the

operation, patients in the first group were administered pentazocine and diclofenac sodium 1 mg/kg body weight intramuscularly in the first group. The pentazocine was administered 6-hourly while the diclofenac was administered 12-hourly all for 48 hours. Those in the second group were administered intramuscular pentazocine 1 mg/kg body weight every 6 hours for 48 hours. The choice of anaesthesia, either general or regional was determined by the anaesthesiologist. Both groups received drugs made by the same pharmaceutical company and standard postoperative care. Patients were monitored by the nurses for side effects. Pain severity was assessed using pain rating scale (visual analogue scale) was used at the end of the first 12, 24 and 48 hours after the procedure<sup>12,13</sup> and patient satisfaction using Likert<sup>14</sup> scale 48 hours after the procedure. Patients in both groups were discharged from the hospital after return of bowel function, tolerance of meals, adequate pain control and healing of the operation site.

All data were analysed using computer-based EPI Info version 3.4.1 software. Quantitative variables were described using mean and standard deviation. Qualitative variables were presented as percentages. The Student *t*-test was used to analyze for significant differences between means, and chi-square and Mann-Whitney U-test were used for assessing the significance of associations between categorical groups. A *P*-value of <0.05 was considered statistically significant.

## RESULTS

A total number of 166 patients were enrolled in the study. Of these 166 participants, six were excluded because of incomplete data represented in the questionnaire. Eighty patients were allocated to each of the two groups.

Table 1 represents the baseline characteristics of the two groups. Overall, these groups were similar in age, parity and mean gestational age on admission. Also, the mean infant weights, first and fifth minute Apgar score as well as the mean duration of the surgery were similar in the two groups.

**Table 1: Baseline characteristics of the study population**

Variable	Group I	Group II	P-value
Mean maternal age	28.35(SD±6.426)	26.9(SD±6.133)	0.146
Mean parity	3.27(SD±2.67)	2.75(SD±2.14)	0.17
Mean gestational age	37.68(SD±2.69)	37.18(SD±2.63)	0.23
Mean infants weight	3.03(SD±704.49)	3.05(SD±687.26)	0.8
Mean 1 <sup>st</sup> minute Apgar score	7.0(SD±1.9)	7.02(SD±1.99)	0.9
Mean 5 <sup>th</sup> minute Apgar score	8.62(SD±1.02)	8.62(SD±1.24)	0.9
Mean duration of procedure	60.15(SD±21.11)	58.51(SD±24.48)	0.652

The commonest indication for CS was cephalo-pelvic disproportion (CPD) in both groups. However the indications were similar in both groups as shown in Table 2.

The majority of procedures were emergency procedures 127 (79.4%). Elective procedures were done only for 33 (20.6%) patient's giving a 1: 3.8 ratio for elective to emergency procedures.

The most common anesthesia was regional used for 140 (87.5%) patients. General anaesthesia was administered for 20 (12.5%) patients. There were no cases of maternal and perinatal death.

Table 3 showed the distribution of pain using pain score during the first 12, 24 and 48 hours of assessment in the ward, comparison of the level of pain experienced during 48 hours postoperatively revealed statistically significant difference in the level of pain reported among the groups ( $P$ -value = 0.00001). However, pain score progressively declined with each day in both groups.

Patients satisfaction (assessed using Likert scale) was better in the group I 68(85.0%), compared to group II 41(51.2%). Women in group II had higher dissatisfaction 11(13.8%) compared to women in group I, 3(3.8%). A comparison of the level of participant's satisfaction experienced during the first 48 hours postoperatively revealed statistically significant difference between the groups, as displayed on Table 4.

Patients of group I commenced oral sips, began mobilisation, initiated breastfeeding and returned bowel function earlier as found in 22(SD ± 6.38), 22.65(SD ± 5.72), 22.20 (SD ± 6.910) and 23.1(SD ± 6.824) hours, respectively, compared to participants of group II as found in 30(SD ± 10.84), 27(SD ± 10.48), 27.27(SD ± 9.09) and

**Table 2: Indications for Caesarean section in the study groups**

Indication	Group I (%)	Group II (%)
CPD	23 (28.8)	21 (26.2)
Previous C/S	17 (21.2)	15 (18.7)
Preeclampsia	16 (20.0)	14 (17.5)
Fetal distress	6 (7.5)	11 (13.8)
Others	18 (22.5)	19 (23.8)
Total	80 (100)	80 (100)

Df = 4;  $\chi^2 = 1.85$ ;  $P$ -value = 0.764

**Table 3: Median level of pain by treatment type in the study groups**

Median level of pain	Group I	Group II	Mann-Whitney	$P$ -value
	U-test			
12 hours	4.0 (range 1-8)	8.0 (range 4-10)	79.11	0.00001
24 hours	2.0 (range 1-6)	6.0 (range 1-8)	72.52	0.00001
48 hours	1.0 (range 1-4)	2.5 (range 1-6)	91.57	0.00001

30.6(SD±10.61) hours, respectively. These findings were statistically significant ( $P$ -value 0.00001). The mean pain scores were also lower for elective compared to emergency CS being 4.68(SD ± 2.3) compared to 5.9(SD ± 2.5) 12 hours post-operatively and 2.93(SD ± 1.92) compared to 3.8(SD ± 2.12) 24 hours postoperatively, respectively. These findings were statistically significant ( $P$ -value less than 0.05). At 48 hours postoperatively, the scores were still lower for elective compared to emergency CS being 1.75(SD ± 1.02) compared to 2.11(SD ± 1.2) but they were not statistically significant ( $P$ -value more than 0.05).

Majority of patients in group I, 48(60.0%) and 37(46.2%) in group II reported no side effects. Comparison of the side effects did not reveal statistically significant difference between the groups ( $P$ -value 0.135) as shown in Table 5.

Comparison of the infant's side effects also did not reveal statistically significant difference between the groups, as shown on Table 6 ( $P$ -value 0.46).

## DISCUSSION

Pain relief after CS is an important and relevant issue for reducing postoperative stress, providing subjective comfort and facilitating postoperative rehabilitation.<sup>15</sup>

This study showed a statistically significant difference in pain level between group I (pentazocine plus diclofenac) and group II (pentazocine only) within first 12, 24 and

**Table 4: Patients satisfaction by treatment type**

Level of pain	Group I (%)	Group II (%)
Neither satisfied or dissatisfied	3 (3.8)	11 (13.8)
Dissatisfied	9 (11.2)	28 (35.0)
Satisfied	68 (85.0)	41 (51.2)
Total	80 (100)	80 (100)

Df = 2;  $\chi^2 = 21.02$ ;  $P$ -value = 0.000027

**Table 5: Mother's side effects by treatment type**

Side effect	Group I (%)	Group II (%)
Dizziness	10 (12.5)	7 (8.8)
Nausea/vomiting	10 (12.5)	14 (17.5)
Excessive sleep	12 (15)	22 (27.5)
None	48 (60.0)	37 (46.2)
Total	80 (100)	80 (100)

Df = 3;  $\chi^2 = 5.56$ ;  $P$ -value = 0.135

**Table 6: Infant's side effects by treatment type**

Side effect	Group I (%)	Group II (%)
Excessive sleep	5 (6.2)	3 (3.8)
Poor sucking	6 (7.5)	10 (12.5)
None	69 (86.3)	67 (83.7)
Total	80 (100)	80 (100)

Df = 2;  $\chi^2 = 1.53$ ;  $P$ -value = 0.46

48 hours post-Caesarean section. The result showed that pain score was lower than what was found in the studies by Rahmanpoort *et al.*,<sup>15</sup> and Ziba *et al.*,<sup>4</sup> who compared use of single agents pethidine and diclofenac in post-CS pain relief, meaning that the use of combined analgesia provided more pain relief than the use of single-agent analgesia. This could be explained by the documented effect of combining action of two different analgesics that interrupt nociceptive transmission at different levels: opioid acts at the central nervous system, while NSAID's inhibit prostaglandin synthesis from arachidonic acid by inhibiting cyclooxygenase, thus reducing inflammation.<sup>7</sup> In addition, pentazocine is a mixed agonist and antagonist opioid, which produces sedation in addition to analgesia and reduces level of anxiety, compared to Meperidine(Pethidine), which is pure agonist opioid with the opposite effect.<sup>7</sup> The median pain score during first 12, 24 and 48 hours after Caesarean section was consistently decreasing in both groups, but more in group I (Pentazocine and Diclofenac combination) than group II. This could be due to longer half-life of Diclofenac,<sup>7</sup> which covered the pain relief between Pentazocine injections and the healing process. However, higher median pain score was observed even in group I in the first 12 hrs post-Caesarean section which could be due to the fixed time interval of the drugs administration and both drugs were given at the same time. Also in this study only 19(23.8%) in group I and 24(30.0%) in group II received post-operative analgesia within first 30 minutes. This is probably due to higher percentage [140(87.5%)] of regional anaesthesia given to the patients, which has become the most common technique for CS in the department, leading to some degree of pain relief in the few hours post-operatively. It might have had influence on personnel's judgment of the patients' pain experience thus underestimating it, which might have delayed post-operative drug administration. The high number of patients [71(60.7%)] who experienced moderate to severe pain during first 12 hours post-operatively and had delay in post operative analgesia over 30 minutes showed anaesthetic block is inadequate to provide post-operative comfort. This was also highlighted in a study by Kolawole *et al.*, in Ilorin, Nigeria.<sup>2</sup> Another reason for delayed post-operative drugs administration may be due to the belief that opioids induce sedation and may interfere with patient ability to nurse their babies due to sedation and poor sucking of the infants. However, this study did not show significant side effect affecting either mother or babies following analgesic administration in both groups. It rather showed earlier patient rehabilitation (mobilisation and return of bowel function) and earlier onset of breastfeeding.

There was no statistically significant difference among the groups in term of age. The mean age of group I being 28.35 (SD  $\pm$  6.426), that of group II being 26.9 (SD  $\pm$  6.13) and  $P = 0.146$ . This was slightly lower than the mean age

(32.72  $\pm$  8.40) found in a similar study conducted in Ilorin.<sup>2</sup> The explanation could be due to lower age of marriage among females in Northwestern Nigeria.<sup>16</sup>

## CONCLUSIONS

The present study shows that the use of combined analgesia compared to single-agent analgesia is safe, significantly reduced pain and improved patient satisfaction during post-operative period following Caesarean section.

## Recommendations

1. Introduction of the use of combined analgesia (Pentazocine plus Diclofenac) is an opportunity to improve post-CS pain management and quality of care in Obstetrics and Gynaecology department of AKTH and other similar departments across Nigeria.
2. Effective pain management should be given to all our patients regardless of age, tribe and education.
3. Introduction of pain rating scale to assess the degree of pain may help to individualise postoperative analgesia.
4. A prospective multi-centered, double blind controlled trial comparing the effectiveness and adverse side effects of the agents used in this study is recommended for stronger evidence and generalisation.

## Limitations

This study did not represent all women of Kano state undergoing Caesarean section, especially low-income women who tend to utilise the free maternity care available at the state government run hospitals.

There were a larger number of surgeons involved in the study. Post-operative pain might be affected by certain actions of individual surgeons such as surgical technique, tissue handling, suturing technique and post-operative counselling including explanation of the surgical procedure to the patient.

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