Original Article

The Efficacy of Pentazocine + Diclofenac versus Paracetamol + Diclofenac for Post- Caesarean Section Analgesia

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Abstract

Background: The most common major obstetric procedure is caesarean section (CS) and one of the greatest concerns for women after CS is to have optimal pain relief. **Aim:** This study aims to compare the efficacy of pentazocine + diclofenac and paracetamol + diclofenac on post-operative analgesia after CS. **Methodology:** This was a single-blind, randomised trial. Pregnant women that had CS were randomized into two groups. Group A received intramuscular pentazocine + rectal diclofenac postoperatively. Group B received intramuscular paracetamol + rectal diclofenac postoperatively. Post-operative pain was assessed by numeric rating scale at 1 h after the surgery, at 6 h, 12 h and 24 h. The result obtained was analysed using SPSS Version 22 and $P < 0.05$ was considered statistically significant. **Results:** The median pain scores in both groups ranged from 2 to 3 across all periods of assessment. The pain relief was slightly better in the pentazocine + diclofenac group with no significant difference in the pain score between the two groups at all periods of assessment. The satisfaction level was good in 66.3% and 69.5% of the participants in the pentazocine + diclofenac and paracetamol + diclofenac group respectively but the difference was not statistically significant ($\chi^2 = 4.14$, $P = 0.12$). Nausea, vomiting and drowsiness were significantly more in the pentazocine + diclofenac combination ($P < 0.001$). **Conclusion:** Both combination of analgesics provided adequate analgesia but pentazocine + diclofenac combination had better pain relief but was more associated with side effects.

Keywords: Caesarean section, diclofenac, post-operative pain relief, pentazocine, paracetamol

Introduction

Caesarean section (CS) is the most significant obstetric operative intervention and one of the most common obstetric operations performed worldwide with a global rise in excess of 30% in some regions.[1] Post-operative pain is a major concern because it involves a number of systems and affects the physiological, psychological and immunological changes in the body.[2] Women who had CS have unique challenges than other surgical patients. They have higher risk for thromboembolism which may be precipitated by immobilisation due to pain or sedative effect of opioids.[3] In addition, effective post-operative analgesia after CS is important because the mother has to recover from a major surgery and also take care of her baby.

An ideal post-operative analgesic after CS would be one that is simple to administer, with effective pain relief, cost-effective, with minimal side-effects and complications.[4] It should not interfere with the establishment of breastfeeding and maternal care of the newborn.[4] Perioperative pain management has traditionally been based on opiates.[3] However, due to their side effects such as respiratory depression, nausea and vomiting; new drugs with opiate-sparing side effects were introduced. A multimodal approach has been introduced to improve post-operative analgesia, to decrease the opioid-related side

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effects and also to improve quality of care.[3,5] Pain relief after CS can be achieved using safe and effective analgesic combinations.[6] There is presently no agreed gold standard for postoperative pain relief after CS and the therapeutic superiority of the best combination remains controversial. There are many options and the choices are determined by institutional protocols, drug availability, available resources, individual preferences and financial considerations.[7] However, the key challenge is finding the right combination which is well tolerated and has minimal side effects.

Some studies have compared pentazocine alone versus pentazocine and diclofenac and all have shown that combination of pentazocine and diclofenac was more effective than pentazocine alone in providing postoperative pain relief after CS.[8-11] Another group of studies have compared the efficacy of paracetamol alone and its combination with diclofenac and found that combination of paracetamol and diclofenac was more effective.[12,13]

The combination of parenteral opioid-like pentazocine or tramadol with nonsteroidal anti-inflammatory drugs (NSAIDs) like diclofenac provides a form of multimodal analgesia, with the benefits of both pain relief and additive anti-inflammatory actions has been well accepted.[6] It has also been suggested by Schyns-van den Berg *et al*. that more research is needed in order to develop well tolerated and effective alternatives to opioids.[14] The combination commonly used in our hospital for postoperative pain relief after CS is pentazocine and diclofenac which is considered effective. However, there is still concern about the opioid side effects of pentazocine on the mother who is encouraged to ambulate early and commence early breastfeeding. In addition, injectable paracetamol is cheaper and devoid of opioid side effects. Hence, there is need to compare the efficacy and side effects of other combinations like paracetamol-diclofenac in our center which could guide in setting a local protocol to improve on the care rendered. The combination of paracetamol + diclofenac which is a nonopioid multimodal analgesic combination could be used as substitute if found to be effective and more tolerated than the currently practiced regimen in our hospital.

The aim of this study was to compare the efficacy of pentazocine + diclofenac versus paracetamol + diclofenac for postoperative pain relief among women that had CS at Usmanu Danfodiyo University Teaching Hospital (UDUTH), Sokoto.

Methodology

This was a single-blind randomised study among women that had CS. Women that had CS for various indications during the study were randomised into two groups using computer-generated random numbers. Group A received intramuscular pentazocine and rectal diclofenac while Group B received intramuscular paracetamol and rectal diclofenac.

Inclusion criteria were women that had elective or emergency CS under spinal anaesthesia and had consented to participate in the study. Those who had intraoperative complications and those with allergy to non-steroidal anti-inflammatory drugs or opioids were excluded from the study. Convenience sampling method was used to recruit the participants into the study and 200 participants were recruited.

All pregnant women scheduled for elective CS were informed about the study a day prior to surgery and informed consent obtained. Those for emergency CS were informed of the study as soon as the decision for the CS was taken. An informed consent was obtained from them. The use of numeric rating scale (NRS) for pain assessment with score of 0 as "no pain" to 10 as "worst imaginable pain" was explained to them. They were randomly allocated into two groups using computer generated random numbers. Group A received intramuscular pentazocine 60 mg 6 hourly for 24 h and rectal diclofenac 100 mg 12 hourly for 24 h. Group B received intramuscular paracetamol 600 mg 6 hourly for 24 h and rectal diclofenac 100 mg 12 hourly for 24 h. Each analgesic agent was commenced within 30 min after surgery. Women who requested for additional analgesia were given rescue analgesia in form of intramuscular piroxicam 20 mg stat.

During the study, vital signs, side effects such as nausea, vomiting, dizziness, headache, heartburn and dyspepsia were also assessed. Women that developed any side effect were managed appropriately. At the end of 24 h, the women were asked to subjectively rank their satisfaction with pain relief after CS using 5-point Likert scale as very dissatisfied, dissatisfied, neither satisfied nor dissatisfied, satisfied, or very satisfied.

The primary outcome was pain score. It was assessed by NRS at 1 h, 6 h, 12 h and 24 h postoperative. Score of 1–4 were considered as mild pain, score of 5-7 as moderate pain while score of 8 and above were considered as severe pain. Effective pain relief was defined as NRS ≤ 4. Secondary outcome were patient's satisfaction, maternal side effects, request for additional analgesia and desire for the same treatment next surgery.

This study was conducted in line with Helsinki Declaration on human subject experiment. Ethical approval was obtained from UDUTH Ethics and health research committee (UDUTH/HREC/2018/679). Informed consent was also obtained from the participants before data collection.

Data analysis was done with Statistical Package for Social Sciences version 22 (IBM SPSS statistics for windows version 22.0. Armonk, NY: IBM Corp.). Data entry, data transformation and exploratory data analysis were carried out. The mean and median of pain score at all periods of assessment was obtained. Mann–Whitney U test was used to compare the pain score between the two groups. The level of statistical significance was set at $P < 0.05$.

Results

There were 200 participants recruited for this study and 7 participants did not complete the study. Hence, 193 participants

completed the study and were thus used in the analysis. There were 98 participants in the pentazocine + diclofenac group and 95 participants in the paracetamol + diclofenac group. This is shown in the consort flow chart below.

The mean age of the participants was 29.8 ± 5.9. The youngest was 16 years while the eldest was 45 years. Most of the participants in both groups were between the ages of 20 and 34 years. Most of the participants were Muslims and Hausa/Fulani. Majority of the participants in both the groups had at least secondary school certificate. There was no significant difference in the sociodemographic characteristics of the participants in both groups. This is shown in Table 1.

Both groups had mean pain score of <4 over the first 24 h postoperatively at all points of assessment and the pain score was lower in the pentazocine group. This is shown in Figure 1. The median pain scores in both groups ranged from 2 to 3 across all periods of assessment. The upper limit of the interquartile range was 4 and 5 which indicates significant pain relief in both groups. The pain relief is slightly better in the pentazocine + diclofenac group especially at 12 h post-operative. However, there was no significant difference in the pain score between the two groups. This is shown in Table 2.

In terms of request for additional analgesia, 28.4% of the participants in the paracetamol + diclofenac group requested for additional analgesia against 18.4% in the pentazocine + diclofenac group. However, the difference was not statistically significant ($\chi^2 = 2.727$, $P = 0.099$). The satisfaction level of the participants was 66.3% and 69.5% in the pentazocine + diclofenac and paracetamol + diclofenac groups, respectively. The difference in satisfaction between the two groups was not statistically significant ($\chi^2 = 4.14$, $P = 0.12$). Majority of the participants in both groups desired similar analgesia in future and there was no significant difference in desire for similar analgesia between the 2 groups ($\chi^2 = 1.206$, $P = 0.272$). This is shown in Table 3.

The side effects encountered during the first 24 h postoperative were nausea, vomiting, headache and drowsiness. None of the participants had epigastric pain, dark stool and other side effects. A higher percentage of the participants in the pentazocine group had nausea and there was significant association between nausea and the combination of analgesic

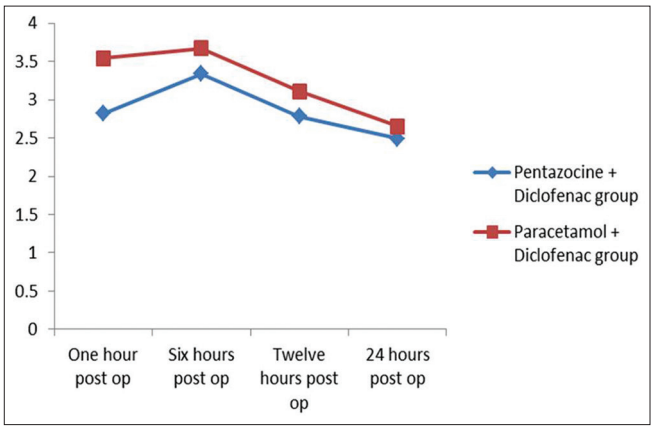

Figure 1: Mean pain score btw the 2 groups at 1, 6, 12 and 24 h post-operative

Table 1: Sociodemography, indications for caesarean section and biological characteristics of the participants

Characteristics	Pentazocine + diclofenac group, *n* (%)	Paracetamol + Diclofenac group, *n* (%)	χ^2	*P*
Age (years) 2013				
<20	4 (4.1)	5 (5.3)	1.310	0.86
20-24	11 (11.2)	15 (15.8)		
25-29	27 (27.6)	27 (28.4)		
30-34	31 (31.6)	26 (27.4)		
35 and above	25 (25.5)	22 (23.2)		
Ethnicity				
Hausa	64 (65.3)	64 (67.4)	3.14	0.370
Ibo	12 (12.2)	11 (11.6)		
Yoruba	10 (10.2)	4 (4.2)		
Others	12 (12.2)	16 (16.8)		
Religion				
Islam	79 (80.6)	74 (77.9)	0.217	0.641
Christianity	19 (19.4)	21 (22.1)		
Educational status				
No formal education	10 (10.2)	18 (18.9)	6.711	0.082
Primary	2 (2.0)	7 (7.4)		
Secondary	31 (31.6)	24 (25.3)		
Tertiary	55 (56.1)	46 (48.4)		
Parity				
Nullipara	27 (27.6)	24 (25.3)	1.117	0.572
Multipara	52 (53.1)	57 (60.0)		
Grandmultipara	19 (19.4)	14 (14.7)		

received (χ^2 = 14.415, $P \leq 0.001$). Similarly, there was significant association between vomiting and the combination of analgesic received (χ^2 = 13.734, $P \leq 0.001$). Drowsiness occurred in about 41% of the participants in the pentazocine group compared with 14% of the participants in the paracetamol group. There was significant association between drowsiness and the combination of analgesics received (χ^2 = 17.827, $P \leq 0.001$). This is shown in Table 4.

Discussion

The mean pain score of less than 4 and nonsignificant difference in the pain score between the two groups of analgesics implies that both combinations of analgesics could provide adequate pain relief in the first 24 h postoperative. The mean pain score in the group that had pentazocine + diclofenac was lower at all points of assessment and this implies that pentazocine + diclofenac provided better analgesia than paracetamol + diclofenac in the first 24 h after CS. This could be due to difference in the mechanism of action between pentazocine and paracetamol. The analgesic effects of pentazocine are due to agonist effects on opioids receptors and interrupt pain pathways in the spinal cord.[15,16] On the other hand, paracetamol exert its analgesic effect by central mechanisms which include effects on prostaglandin production, and on serotonergic, nitric oxide and cannabinoid pathways.[17] The effect of paracetamol may not be as pronounced as that of opioids in providing analgesia. Pentazocine probably exerts more profound analgesic effect compared to paracetamol.

The findings of pentazocine + diclofenac as efficacious analgesic after CS have been reported in previous studies

Table 2: Comparison of pain score between the 2 groups

Time	Median (IQR)		Mann-Whitney U-test	*P*
	Pentazocine + Diclofenac group	Paracetamol + Diclofenac group		
1 h postoperative	3 (1-4)	3 (2-5)	3,921	0.056
6 h postoperative	3 (2-5)	3 (2-5)	4,251	0.292
12 h postoperative	2 (1-4)	3 (2-4)	4,183	0.217
24 h postoperative	2 (1-4)	2 (2-4)	4,403	0.510

IQR: Interquartile range

Table 3: Comparison of request of rescue analgesia, satisfaction and desire for similar analgesia between the 2 groups

Variable	Pentazocine + Diclofenac group, *n* (%)	Paracetamol + Diclofenac group, *n* (%)	χ^2/Fischer's exact	*P*
Request for additional analgesia				
No	80 (81.6)	68 (71.6)	2.727	0.099
Yes	18 (18.4)	27 (28.4)		
Satisfaction				
Dissatisfied	2 (2)	7 (7.4)	4.14	0.12
Neutral	31 (31.6)	22 (23.2)		
Satisfied	65 (66.3)	66 (69.5)		
Desire for similar analgesia				
No	12 (1.2)	17 (17.9)	1.206	0.272
Yes	86 (87.8)	78 (82.1)		

Table 4: Comparison of side effects between the two groups

Side effect	Pentazocine + Diclofenac group, *n* (%)	Paracetamol + Diclofenac group, *n* (%)	χ^2/Fisher's exact	*P*
Nausea				
No	64 (65.3)	84 (88.4)	14.415	<0.001
Yes	34 (34.7)	11 (11.6)		
Vomiting				
No	80 (81.6)	93 (97.9)	13.734	<0.001
Yes	18 (18.4)	2 (2.1)		
Headache				
No	86 (87.8)	88 (92.6)	1.292	0.256
Yes	12 (12.2)	7 (7.4)		
Drowsiness				
No	58 (59.2)	82 (86.3)	17.827	<0.001
Yes	40 (40.8)	13 (13.7)		

in Kano,[8] Rivers,[10] Abakaliki,[9] and Ile Ife.[11] These studies compared pentazocine alone versus pentazocine and diclofenac and all showed that combination of pentazocine and diclofenac was more efficacious than pentazocine alone in providing adequate postoperative pain relief after caesarian section. Similarly, studies that have assessed the efficacy of paracetamol + diclofenac have reported that combination of paracetamol and diclofenac provide analgesia and resulted in less morphine consumption for postoperative pain relief after CS.[12,13] The result from my study is similar to that reported by Mitra *et al*.[6] in India, that both combination of diclofenac + tramadol and diclofenac + paracetamol provide similar pain relief. The reason for the similarity was that we used similar drug combinations except that the opioid I used was pentazocine.

It is unethical to allow the participants to be in pain to assess the analgesic efficacy of the two drug combinations, hence, rescue analgesia was given for those who requested and also for those who had pain score of more than 4. Request for additional analgesics was also used to assess the analgesic efficacy of the two drug combinations. This was high for both groups and indicates that both groups of analgesics did not completely relieve post-operative pain. A higher percentage of request for additional analgesia of 43% was reported by Bakhsha *et al*.[12] in Iran. The findings in my study showed higher percentage of request for additional analgesia compared to 12% and 13% reported by Mitra *et al*., in India.[6] The possible reason for the low percentage of request of analgesia in the study by Mitra *et al*. could be because rectal diclofenac was given 8 hourly against the 12 hourly doses in my study.

The quality of pain management can be evaluated by patient's satisfaction. The satisfaction with overall analgesia in both groups (66.3% and 69.5%) did not reach the proposed target by Royal College of anesthesiologist for best practice in post-operative analgesia which states that >95% of women should be satisfied with analgesia on the 1st day post-CS.[18] The spikes of severe pain before administration of rescue analgesics and side effects would have been responsible for the poor satisfaction experienced by the participants. Even though the optimum satisfaction was not achieved, majority of the participants still desired to have similar analgesia in case of future CS. The satisfaction level in my study is lower than the range of 80%–87% that was reported from previous studies that compared pentazocine alone versus pentazocine + diclofenac.[9-11,18] The finding in satisfaction with pain relief in the paracetamol + diclofenac group in my study is also lower than that reported by Munishankar *et al*. in the UK who reported 100% satisfaction.[13] The difference in satisfaction between my study and the previous studies was most likely due to higher number of participants that developed side effects of the drugs in my study. In addition, patient's satisfaction is a subjective assessment and may depend on other factors like promptness in the treatment of acute pain and attitude of health-care professionals which I did not study.

Participants in the pentazocine + diclofenac group had more nausea, vomiting and drowsiness and the difference was statistically significant. This is not surprising considering that pentazocine is an opioid and these are known side effects of opioids. About 18% of the participants in pentazocine group had vomiting and this is higher than 12.5% reported to have vomiting in the study by Adamou *et al*.[8] The percentage of 40% that had drowsiness is also higher than 12.5% reported to have drowsiness in the study by Adamou *et al*.[8] The difference could be due to individual variation in developing these side effects.

The finding in my study is similar to that by Mitra *et al*. in India that reported fewer side effects in the paracetamol + diclofenac group compared to tramadol + diclofenac group.[6] This is not surprising since both tramadol and pentazocine are opioids and these are known side effects of opioids.

Conclusion

The mean pain score in both the groups was lower than the cut off of 4 that implies adequate pain relief. Hence, both combinations of analgesics could provide adequate pain relief in the first 24 h postoperative. Pentazocine + diclofenac provided better analgesia than paracetamol + diclofenac in the first 24 h after CS but more associated with side effects.

Strengths and limitations of the study

This was a single-blind study in which the patients were not aware of the treatment regimen they were given so as to allow an objective assessment of their pain. However, the researcher and other trained assistants knew the regimen each patient received so as to give necessary intervention in case of any side effect. The method of the assessment of pain is reliable and can be used for both literate and illiterate patients. Another alternative analgesic regimen was found which could improve in patient's management. The sample size was increased to 200 so as to increase the power of the study.

Some of the limitations of the study were that it was carried out only on the women who had CS at UDUTH. A large multi-centre study would be better for generalisation. A double-blind study would have been better to minimize bias. Pain perception is subjective and pain threshold among individuals varies. In addition, post-operative pain may also depend on some other factors such as suturing techniques, type of sutures and tissue handling which were not assessed in this study.

Recommendation

Paracetamol + diclofenac combination could be used as alternative for post-operative analgesia after CS. More research is needed to find more analgesics with better satisfaction. A large multicentre study is recommended to ascertain the efficacy of paracetamol + diclofenac for postoperative analgesia after CS and make the findings generalisable. Further research using 3 analgesic combinations or increasing the dose of paracetamol to 900 mg is recommended to assess if we can

improve on postoperative analgesia after CS and improve on patients' satisfaction.

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Conflicts of interest

There are no conflicts of interest.

References

1. Basket TF, Calder AA. Caesarean section. In: Basket TF, Calder AA, Arulkumaran S, editors. Munro Kerr's Operative Obstetrics. 12th ed. India: Saunders, Elsevier; 2014. p. 132-44.
2. Samimi Sede S, Davari Tanha F, Valadan M, Modaressi Z. Comparison between preoperative rectal diclofenac plus paracetamol and diclofenac alone for postoperativepain of hysterectomy. J Family Reprod Health 2014;8:91-5.
3. Pan PH. Post cesarean delivery pain management: Multimodal approach. Int J Obstet Anesth 2006;15:185-8.
4. McDonnell NJ, Keating ML, Muchatuta NA, Pavy TJ, Paech MJ. Analgesia after caesarean delivery. Anaesth Intensive Care 2009;37:539-51.
5. Jahr JS, Filocamo P, Singh S. Intravenous acetaminophen: A review of pharmacoeconomic science for perioperative use. Am J Ther 2013;20:189-99.
6. Mitra S, Khandelwal P, Sehgal A. Diclofenac-tramadol vs. diclofenac-acetaminophen combinations for pain relief after caesarean section. Acta Anaesthesiol Scand 2012;56:706-11.
7. Kuczkowski KM. Postoperative pain control in the parturient: New challenges in the new millennium. J Matern Fetal and Neonatal Med 2011;24:301-4.
8. Adamou N, Tukur J, Muhammad Z, Galadanci H. 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. Niger Med J 2014;55:369-73.
9. Egede JO, Ajah LO, Umeora OU, Ozumba BC, Onoh RC, Obuna JA, *et al*. Pentazocine alone versus pentazocine plus diclofenac for pain relief in the first 24 hours after caesarean section: A randomized controlled study. J Clin Diagn Res 2017;11:QC01-5.
10. Eleje GU, Egeonu RO, Obianika C, Mbachu KI, Okohue JE, Osuagwu I, *et al*. Diclofenac and pentazocine versus pentazocine alone for post operative analgesia in Caesarean section. Int J Med Health Dev 2015;20:2-11.
11. Olateju SO, Adenekan AT, Olufolabi AJ, Owojuyigbe AM, Adetoye AO, Ajenifuja KO, *et al*. Pentazocine versus pentazocine with rectal diclofenac for postoperative pain relief cesarean section-A double blind randomized placebo controlled trial in a low resource area. MEJ Anesth 2016;23:443-8.
12. Bakhsha F, Niaki AS, Jafari SY, Yousefi Z, Aryaie M. The effects of diclofenac suppository and intravenous acetaminophen and their combination on the severity of postoperative pain in patients undergoing spinal anaesthesia during cesarean section. J Clin Diagn Res 2016;10:9-12.
13. Munishankar B, Fettes P, Moore C, McLeod GA. A double-blind randomised controlled trial of paracetamol, diclofenac or the combination for pain relief after caesarean section. Int J Obstet Anesth 2008;17:9-14.
14. Schyns-van den Berg A, Huisjes A, Stolker R. Postcaesareansection analgesia: Are opioids still required? Curr Opin Anaesthesiol 2015;28:267-74.
15. Henderson K. Update in Anaesthesia-Pentazocine; 2008. Available from: http//www.worldanaesthesia.org. [Last accessed on 2017 Dec 26].
16. Yaksh TL, Wallace MS. Opioids, analgesia and pain management. In: Brunton LL, Chabner BA, Knollmannn BC, editors. Goodman and Gilman's the Pharmacological Basis of Therapeutics. 12th ed. New York: McGrow Hill; 2012. p. 481-526.
17. Sharma CV, Mehta V. Paracetamol: Mechanisms and updates. Contin Educ Anaesth Crit Care Pain 2013;14:153-8.
18. Lucas N, Pickering E, Plaat F. Pain relief after caesarean section. In: Section 8: Obstetrics, edited, Kinsella M. In: Royal College of Anaesthetists, Raising the Standard: a compendium of audit recipes, for continuous quality improvement in anaesthesia, 3rd edition 2012, Editors, Colvin JR and Peden CJ. Pages 205-30.