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Original Research Article

Comparative Study of Safety and Efficacy of Tramadol versus Paracetamol as Post-operative Analgesia after Caesarean Section

Saikat Kumar Sarkar[1], Ashis Kumar Mukhopadhyay[2], Sanjay Vashisth[3], Alpana Chhetri[4]

[1]3rd Year Post-graduate Trainee, Department of Obstetrics & Gynaecology, CSS College of Obstetrics Gynaecology & Child Health, Kolkata.
[2]Unit in Charge, Department of Obstetrics & Gynaecology, CSS College of Obstetrics Gynaecology & Child Health, Kolkata.
[3]Dept of Physiology, R.G Kar Medical College and Hospital, Kolkata, West-Bengal, India.
[4]Associate Professor, Department of Obstetrics & Gynaecology, CSS College of Obstetrics Gynaecology & Child Health, Kolkata, West-Bengal, India.

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Corresponding author: Dr. Alpana Chhetri
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Abstract

Aims: To compare the degree of safety, efficacy and acceptability of paracetamol & tramadol as postoperative analgesia after Caesarean Section.

Method: It is a comparative prospective observational study carried out between April 2021-October 2022 (18 months) in the post recovery ward of the department of Obstetrics & Gynaecology Chittaranjan Seva Sadan College of Obstetrics Gynaecology & Child Health, 200 patients undergoing caesarean section under spinal anesthesia, excluding the patients who fall under exclusion criteria were included in the study. Out of 200 patients, 100 patients were chosen randomly, Group 1 received intravenous paracetamol 1gm infusion over 10-15 minutes 6 hourly for 4 doses & Group 2 received 100 mg tramadol infusion over 10-15 minutes in 100 ml normal saline 8 hourly for 3 doses. The degree of pain relief was measured on a numerical rating scale (NRS) of 0-10 (0 indicates no pain, 1-3 indicates mild pain; 4-6 indicates moderate pain,7-10 indicates severe pain). The aim was assessed 2,6,12,24 hours after completion of surgery. Additional analgesia (rescue analgesia) before 8 hours, if required (NRS Score>=6) were managed by giving injection pethidine 50 mg. intramuscularly. Statistical Analysis was performed with help of Epi Info (TM) 7.2.2.2.

Results: t-test showed that the mean postoperative NRS of the patients administered with Tramadol was significantlyhigher than the patients treated with PCM ($p<0.0001$). Fisher exact test showed that a proportion of side effects was are available for control of pain but our study shows that efficacy, safety & acceptability of paracetamol infusion is better than intravenous tramadol and thus paracetamol infusion may be opted for better post-caesarean section pain management higher in Tramadol group (12.0%) as compared to PCM group (0.0%) ($p<0.0001$). There was no side effect in PCM group.

Conclusion: In the post-operative period innumerable analgesics are available for control of pain but our study shows that efficacy, safety & acceptability of paracetamol infusion is better than intravenous tramadol and thus paracetamol infusion may be opted for better post-caesarean section pain management.

Keywords: Postoperative, Pain, Analgesic, Caesarean Section, paracetamol, tramadol.

Introduction

Caesarean section is the most common surgical procedure performed worldwide. With a dramatic rise in the rate of caesarean delivery post-operative pain management of patients has become a major challenge but it is very important that the mother need to carry out her daily day-to-day work as well as to look after her newborn. Analgesia administered to post-caesarean women must be effective and reliable, while remaining safe for both the mother and her new-born and should not cause excess sedation which can hamper her child care.

Moreover, presence of uterine contraction in the involuting uterus may be an additive cause for the cramping pain. Inadequate pain relief can be mentally traumatic for the recuperating mother which may lead to adverse outcome hampering breast-feeding & care of the newborn.

Despite several analgesics for pain management, we have so far, there is no clear guideline regarding appropriate analgesia in the post operative pain management in caesarean section. Caesarean delivery patients should have optimal post-operative pain relief because they have a higher risk of thromboembolic events which may be precipitated by immobility from inadequate pain control.

There are many pain score assessors available to assess pain like, numerical rating scale, visual analogue scale, and categorical scale. We have chosen numerical rating scale (NRS) to assess pain score of patients. It is one of the most commonly used pain assessing scale in healthcare. In this scale 0 indicates no pain; 1-3 indicates mild pain; 4-6 indicates moderate pain, 7-10 indicates severe pain. Periodic assessment by NRS keeps post-operative pain in- check and also helps to give necessary analgesia whenever required.

Postoperative patients are given different opioids but most commonly used are tramadol or nalbuphine. Tramadol is a centrally acting, synthetic analgesic which is an opioid receptor agonist and serotonin nor-epinephrine reuptake inhibitor. It is approved for oral, intravenous and intramuscular administration and efficiently decreases moderate to severely moderate pain. The mean elimination half-life of tramadol following intravenous administration is 5-6 hours. Nausea & vomiting are common side effects of tramadol. Tramadol when injected in patients taking selective serotonin reuptake inhibitors (SSRI) may produce "serotonin syndrome", autonomic instability (e.g., tachycardia, hyperthermia), neuromuscular aberrations (hyperreflexia, incoordination) and gastrointestinal symptoms (e.g. nausea, vomiting, diarrhea).

Paracetamol is generally considered to be a weak inhibitor of the synthesis of the prostaglandin. However, the in vivo effect of the paracetamol of similar to those of selective cyclooxygenase-2(COX-2) inhibitors. There is considerable evidence that the analgesic effects of paracetamol are central & is due to activation of descending serotonergic pathways, but its primary site of actions may still be inhibition of prostaglandin synthesis.

Though its primary site action is debatable which may be inhibition of prostaglandin synthesis or through an active metabolite influencing cannabinoid receptors.

The metabolites of paracetamol are mainly excreted in the urine, 90% of the dose

administered is excreted in 24 hours, mainly as glucuronide (60% to 80%) and sulphate (20% to 30%) conjugates. Less than 5% is eliminated unchanged. Plasma half-life is 2.7 hours. It is metabolized in liver & hepatotoxic in heavy doses and on prolonged use. It interacts with warfarin, isoniazid, CYP450-inducing drugs. Paracetamol above all does not have any effect on acid- base balance, cardiovascular system and it doesn't cause respiratory depression.

NSAIDs (Non-steroidal anti-inflammatory drugs) always act on both COX-1 & COX-2 & it has an increase the risk of upper gastro-intestinal bleeding unlike paracetamol.

Aims and Objectives

To compare the degree of safety, efficacy and acceptability of paracetamol & tramadol as post operative analgesic after Caesarean Section.

Materials and Methods

It is a comparative prospective observational study carried between April 2021-October 2022 (18 months) in the post recovery ward of the department of Obstetrics & Gynaecology Chittaranjan Seva Sadan College of Obstetrics Gynaecology & Child Health, 200 patients undergoing caesarean section under spinal anesthesia, excluding the patients who fall under the exclusion criteria.Out of 200 patients, 100 patients were chosen randomly, Group 1 received intravenous paracetamol 1gm infusion over 10-15 minutes 6 hourly for 4 doses & Group 2 received 100 mg tramadol infusion over 10-15 minutes in 100 ml normal saline 8 hourly for 3 doses**.**

Degree of pain relief was measured on numerical rating scale (NRS). Pain was assessed 2,6,12,24 hours after completion of surgery. Additional analgesia (rescue analgesia) before 8 hrs, if required (NRS Score>=6) was managed by giving injection pethidine 50 mg. intramuscularly. The sample size was determined using the formula:

$n=z^2pq/e^2$
z =1.96 at 95% confidence interval
p = 0.8452
q = (1-p) =0.1548
e = allowable error (5%)
Hence, n = 201.05 ~ 200

Exclusion Criteria for Tramadol

- Patients with known contraindication/ allergy to tramadol.
- Patients suffering from acute intoxication with alcohol, hypnotics, analgesic, opioid orpsychotropic medical product.
- Patients who are receiving monoamine oxidase inhibitor or who have taken them within the last 14 days.
- Patients with epilepsy not adequately controlled by treatment.

Exclusion Criteria for Paracetamol

- Patients with allergy to paracetamol
- Acute liver failure, disease/abnormal LFT, acute inflammation of the liver due to hepatitis C virus
- Severe renal impairment
- Acetaminophen overdose

Interpretation

After administration of analgesia, degree of pain relief was measured on NRS. If the NRS score of the patient remained below 4 at all-time of assessment it indicated good pain management. If a single dose of analgesia provided good pain relief for 8 hrs. Then it was considered adequate pain relief. If an analgesic was unable to provide good pain relief for 8 hours, then rescue analgesia was administered. The analgesic drugs which provided least side effects was considered the better one.

Results

Statistical Analysis was performed with help of Epi Info (TM) 7.2.2.2 EPI INFO is a

trademark of the Centers for Disease Control and Prevention (CDC). Descriptive statistical analysis was performed to calculate the means with corresponding standard deviations (s.d). Test of proportion was used to find the Standard Normal Deviate (Z) and to compare the difference proportions and Chi- square test was performed to find the associations. If any one of the cell frequencies was zero, corrected Chi-square test was used. If Chi-square was invalid due to null cell frequency/ frequencies, Fisher Exact test was used. t-test was used to compare means. $p<0.05$ was taken to be statistically significant. Row - Provides the comparison between two groups (PCM and Tramadol) Col- Provides the comparison within a group (PCM or Tramadol).

The patients in the two groups were in the ratio 1:1. The Corrected Chi-square test showed that there was no significant association between the age of patients in the two groups (p=0.21). t-test showed that there was no significant difference in mean age of the patients of the two groups ($t_{198}=0.97$;p=0.33). The Corrected Chi-square test showed that there was no significant association between the occupation of patients between the two groups (p=0.77).

In both the groups there was no significant association between socio-economic status between the two groups (p=0.52). Corrected Chi-square test showed that there was no significant association between gravida in two groups (p=0.09).

t-test showed that there was no significant difference in mean gravida of the patients of the two groups ($t_{198}=1.07$; p=0.28).

There was no significant association between the previous history of the mode of delivery in the two groups (p=0.27).

Past history of drugs and allergy had no significant association in the patients of two groups (p=0.84).

Comparative level of SpO2 between two groups had no significant association (p=0.26).

History of patients having tea and coffee addiction no significant association between the two groups (p=0.88). Thus, habit of drinking tea/coffee was more or less equally distributed over the patients of the two groups and it had no effect on the outcomes of the patients of the two groups. Thus, this was not a confounding factor in my study.

The past history of medicine use between the two groups no significant association (p=0.65). Thus, it was not a confounding factor in my study.

There was no significant association between type of LSCS (Emergency or Elective) between the two groups (p=0.78).

Thus, in table 1, t-test showed that the mean post-operative (PO) NRS of the patients treated with Tramadol was significantly higher than the patients treated with PCM ($p<0.0001$).

Since in table 2, one of the cell frequencies was zero, Chi-square test could not be applied. Fisher exact test showed that proportion of side effects was higher in Tramadol group (12.0%) as compared to PCM group (0.0%) ($p<0.0001$). There was no side effect in PCM group.

Table 1: Calculation of NRS (Pain Score at different interval after LSCS)

NRS	Group	Mean	s.d	t	P
PO at 2hour	PCM	1.79	1.64	5.71	<0.001 S
	Tramadol	3.16	1.75		
PO at 6hour	PCM	3.32	1.29	3.96	<0.001 S
	Tramadol	4.01	1.17		
PO at 12hour	PCM	3.33	1.60	4.70	<0.001 S
	Tramadol	4.48	1.85		
PO at 24hours	PCM	1.04	0.99	4.63	<0.001 S
	Tramadol	1.83	1.39		

Table 2: Comparison of side-effects between Paracetamol and Tramadol

Side effects	PCM	Tramadol	TOTAL
Yes Row %Col %	0 0.0 0.0	12 100.0 12.0	12 100.0 6.0
No Row %Col %	100 53.2 100.0	88 46.8 88.0	188 100.0 94.0
Total Row %Col %	100 50.0 100.0	100 50.0 100.0	200 100.0 100.0

Discussion

Reddy MS *et al* [1] (2021) found that one of the most important aspect of postoperative care is pain management which plays an important role in early recovery and improves patient's general condition. His study included patients between age 19-28 years. Mean duration of surgery (minutes) in each group were- Group A-56.5±7.49, Group B-58.27±8.06 and Group C- 56.97±6.78, respectively. In our study, the mean Age was higher in group 2 (Tramadol) [25.41± 3.78] than in group 1(PCM) [24.90± 3.64], but this was not statistically significant (p=0.21).We found that, most of the patients were in the age group of 25-29 years [106 (53.0%)].Most of the patients in our study were homemakers, [90(90.0%)] in group 1(PCM) group 2(Tramadol) 88.0%)] Most of the patients in our study belonged to lower Middle class, [61(61.0%)] in group 1(PCM) than in group 2 (Tramadol) [54(54.0%)]. Primigravida were more in group 2 (Tramadol) [(57.0%)] than group 1 (PCM) [(55.0%)].

45(51.1%) patients of group 1(PCM) and 43(48.9%) patients of group 2 (Tramadol) had history of previous obstetrics intervention like caesarean sections, vaginal deliveries, uterine evacuations but there was no significant association of the same with either of the two groups(p=0.27). Association of Parity of the patients with either of the two groups was not statistically significant (p=0.28). 9 patients in group 1(PCM) and 5 patients in group 2 (Tramadol) had oxygen saturation (SpO2) slightly less than 95% before the administration of the analgesics. All of them recovered after administration of moist oxygen for 2-4 hours. There was no deterioration of SpO2 after administration of the analgesics. Derry CJ *et al* [2] (2014) found that the addition of caffeine, in more than 100 mg dose in addition to the analgesics provided a good relief of pain in a good proportion of patients. In my study 55patients

of group 1(PCM) and 56 patients of group 2 had habit of drinking tea or coffee, but there was no significant association between the habit of drinking tea and coffee and the patients of the two groups (p=0.88). Though these habits may be associated with pain control but it was more or less equally distributed over the patients of the two groups. Thus, it was not a confounding factor to control pain other than PCM and Tramadol.

In the studies by Jonville-Bera *et al* [3] (2010), Taugourdeau S *et al* [4] (2011) and Mugunthan N *et al* [5] (2012) found that there was a recent trend of tramadol-induced hypoglycemia and have suggested that a very consideration should be make for such complications while using tramadol as analgesia. No such evidence of hypoglycemia was found in my study.

5(5.0%) patients of group 1(PCM) and 5(5.0%) patients of group 2 (Tramadol) had history of

intake of labetalol. 11(11.0%) patients of group 1(PCM) and 8(8.0%) patients of group 2(Tramadol) had history of intake of levothyroxine. History of intake of metformin was present in 3(3.0%) patients of group 1(PCM) and 1(1.0%) patients of group 2(Tramadol). The drug history of the patients was not significantly associated with either of the two groups (p=0.65).

Garba JA *et al* [6] (2021) in their study found that the median pain scores among those that had emergency and elective caesarean section ranged between 2 and 3 at all points of pain assessment. The satisfaction was good among 66.1% that had emergency caesarean section and 71.2% among those that had elective caesarean section. However, the difference was not statistically significant (χ = 0.546, p = 0.761). The participants had adequate pain relief and satisfied. In my study there was no significant association between the type of caesarean section (emergency and elective) and the patients of the two groups(p=0.78).

The mean weight of the patients in kg was more in group 1(PCM) [mean=55.83, s.d =4.20] than in group 2 (Tramadol) [mean=55.49, s.d=3.86],which was not statistically significant(p=0.55).

We found that, the mean SBP was less [117.80± 11.28] in group 2(Tramadol) than in group 1(PCM) [120.86±11.75] which was not statistically significant (p=0.06).

The mean DBP was less [76.68±7.69] in group 2(Tramadol) compared to group 1(PCM) [76.90±7.71] but this was not statistically significant (p=0.54).

In my study we found that, the mean pulse rate was more [78.90± 7.01] in group 2(Tramadol) than in group 1(PCM) [76.75± 6.93] (p=0.21).

The mean body temperature was not significantly more [97.786±0.59] in group1 (PCM) compared to group 2 (Tramadol) [97.641± 0.88] (p=0.17).

In the study by Kiliçaslan A *et al* [7] (2010) the effects and side effects of intravenous paracetamol application combined with patient-controlled intravenous tramadol analgesia were investigated in elective caesarean operations for postoperative pain control and its tramadol-sparing effect. Fifty ASA I-II patients scheduled for caesarean operation were enrolled in this study. At the end of surgery, tramadol was given via pain-*controlled* analgesia device and pain score along with sedation score was assessed after 1. 3, 6, 12, and 24 hours respectively following surgery. Adverse effects with tramadol were noted more with tramadol and the pain score with paracetamol infusion was significantly lower compared with the control group (p<0.05)

Apfel CC *et al* [8] (2013) in their systematic review and meta-analysis demonstrated that prophylactic acetaminophen given

intravenously reduced nausea and vomiting in the post operative period. The results from their meta-regression suggest that the antiemetic effect of i.v. acetaminophen was not mediated through the reduction of postoperative opioid consumption, but through direct mechanisms or through the reduction of postsurgical pain.

Rani KU *et al* [9] (2016) found that caesarean section is one of the commonest surgeries performed in obstetrics. This was a comparative study between the analgesic efficacy and the safety profile of paracetamol versus tramadol after Caesarean section. The requirement for rescue analgesia was comparable in both the groups (16% vs. 10%, p = 0.372). However maternal side effects were more in Tramadol group (8% vs. 34%, p = 0.001). The study concluded that the analgesic effect of both the drugs were satisfactory but there were more side effects with tramadol. This was comparable with our study in which side effects in the form of nausea & vomiting were more in group 2(Tramadol) [12(12.0%)] than in group 1(paracetamol)[0(0%)],& this was statistically significant($p<0.0001$).

Conclusion

In the post-operative period innumerable analgesics are available for control of pain but our study shows that efficacy, safety & acceptability of paracetamol infusion is better than intravenous tramadol and thus paracetamol infusion may be opted for better post-caesarean section pain management.

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