

RESEARCH ARTICLE

Comparative effect of intravenous nalbuphine versus intravenous paracetamol for post-operative obstetric analgesia

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ABSTRACT

Background: Management of the post-operative pain after cesarean section (CS) requires a balance between the pain relief and undesirable side effects of drugs. To improve the post-operative pain management after CS, we compared analgesic efficacy of i.v nalbuphine versus i.v paracetamol for post-operative CS pain. **Aim and Objective:** The aim of the study was to compare the efficacy and safety of single-dose intravenous nalbuphine versus intravenous paracetamol for post-operative analgesia CS pain. **Materials and Methods:** This was a hospital-based retrospective study in the department of obstetrics, gynecology, among 120 patients of CS. We enrolled 120 patients in our prospective randomized trial after an uneventful elective CS under the spinal anesthesia. Group A patients received i.v paracetamol infusion and Group B patients received i.v nalbuphine on the first complaint of pain. The results were analyzed by t-test; $P < 0.05$ was taken as significant. **Results:** The numeric rating score for pain and need for rescue analgesia were significantly lower in i.v nalbuphine group as compared to i.v paracetamol group. Changes in pulse rates were found statistically significant in patients receiving nalbuphine with the mean pulse rate within 74.90 ± 3.93 BPM in comparison to patients receiving paracetamol with the mean pulse rate within 81.09 ± 4.32 BPM ($P < 0.05$). Changes in systolic blood pressure (SBP) were found statistically significant in patients receiving nalbuphine with mean SBP 118 ± 2.68 mmHg in comparison to patients receiving paracetamol with mean SBP 114 ± 2.82 mmHg ($P < 0.05$). Changes in diastolic blood pressure (DBP) were found statistically significant in patients receiving nalbuphine with mean DBP 79.1 ± 2.07 mmHg in comparison to patients receiving paracetamol with mean DBP 74 ± 2.19 mmHg ($P < 0.05$). None of the patients had hypotension in both groups. In our study, both paracetamol and nalbuphine are found to be having better hemodynamic stability. Further rescue analgesics used were significantly high in paracetamol group with maximum 8 ± 1.08 rescue analgesic doses used and in nalbuphine group maximum 2 ± 1.02 rescue analgesic doses were used. **Conclusion:** Our results showed improved pain control, more hemodynamic stability, and less need for the rescue analgesia with i.v nalbuphine in post-operative period in patients of CS.

KEY WORDS: Post-operative pain; Nalbuphine, Paracetamol; Cesarean section

INTRODUCTION

Cesarean section (CS) delivery rates are increasing worldwide. The effective post-operative pain management plays a key role in the priority of women undergoing lower segment CS (LSCS). Inadequate pain management in acute post-operative period is associated with complications such as persistent

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pain, delayed functional recovery, and increased postpartum depression. Thus, it requires effective post-operative pain management, which reduces these complications, anxiety, morbidity, cost, and length of hospital stay, and allows the mother to ambulate early.^[1-3] To improve the post-operative pain management after CS, we compared analgesic efficacy of i.v paracetamol infusion versus i.v nalbuphine injection for post-operative CS pain.

Pain is defined as an unpleasant sensory or emotional experience associated with actual or potential tissue damage, often evoked by external or internal noxious stimulus.^[3,4] Analgesic agents are the drugs possessing significant pain relieving mechanism by acting on the CNS or on peripheral pain receptors.^[5,6] Opioids and nonsteroidal anti-inflammatory drugs (NSAIDs) are most commonly used agents for the post-operative pain, but they have their own advantages and disadvantages.^[7,8] Although opioids are the main choice for acute postoperative pain, they are not devoid of undesirable side effects such as post-operative nausea and vomiting, sedation, and respiratory depression in higher doses.^[9,10] IV paracetamol is a safer alternative to opioids. Paracetamol is preferred in most surgical patients because it does not affect mental status, bleeding, respiratory drive, gastric mucosa integrity, or renal function with significant opioid-sparing effect.^[11-13] Due to its better analgesic benefits and early recovery characteristics, we have taken IV paracetamol in this study to compare its analgesic action with IV nalbuphine. However, paracetamol has disadvantages such as allergic reactions, gastric irritation, and hepatorenal derangement, more volume of the drug for IV infusion.^[5,6]

These disadvantages can be overcome with nalbuphine which is a partial opioid antagonist having lesser respiratory depressant effect, better safety profile than other opioids, minimum circulatory effects, providing good sedation, and lower incidence of nausea and vomiting^[8] with significant analgesia. Hence, we had compared analgesic efficacy of i.v paracetamol infusion versus i.v nalbuphine injection for post-operative CS pain.

MATERIALS AND METHODS

Place of Study

This study was conducted at the department of obstetrics gynecology.

Type of Study

It is prospective open label comparative study with 120 pregnant women (60 controls+60 study subjects) who are undergoing elective LSCS without any risk factors.

Sample Collection

The sample size was 120.

Complete blood picture, random blood sugar, serum urea, serum creatinine, liver and function tests were done for each patient.

Sampling Methods

This was a consecutive sampling.

Patients are divided into two groups through computerized randomization. Group A subjects are given injection paracetamol 1 g i.v, while Group B subjects are given injection nalbuphine 20 mg i.v.

Drugs

1. Group A – injection paracetamol 1 g i.v. infusion
2. Group B – injection nalbuphine 20 mg i.v.

Inclusion Criteria

Age group 20–35 years, female sex, and pregnant women undergoing elective LSCS were included in the study.

Exclusion Criteria

The following criteria were excluded from the study:

- Age group <20 and >35 years
- Patients undergoing emergency LSCS
- Patients with other risk factors such as PIH, and eclampsia
- Non-obstetric patients, individuals taking other analgesic drugs
- Tobacco consumers and alcoholics
- Patients with liver and kidney diseases
- Patients taking tranquilizers
- Patients with serum creatinine >1.4 mg/dl.

Statistical Analysis

Data were presented in the form of statistical tables and charts. SPSS software version 20 was used for statistical analysis.

Ethical Approval

Approval was taken from the Institutional Ethics Committee before commencement of the study.

It is prospective open label comparative study with 120 pregnant women (60 controls+60 study subjects) who are undergoing elective LSCS without any risk factors. Patients are divided into two groups through computerized randomization. Group A subjects are given injection paracetamol 1 g i.v, while Group B subjects are given injection nalbuphine 20 mg

i.v. Base line investigations including complete blood picture, random blood sugar, serum urea, serum creatinine, and liver function tests were done for each patient.

Description of the Procedure^[8-10]

Before participation in the study, the informed consent was taken from all participants. After base line investigations and physical examination, Group-A patients (controls) managed with i.v paracetamol and Group-B patients (test subjects) managed with i.v nalbuphine. Vitals (PR, RR, temperature, and BP) were assessed for every 15 min during first 1 h, for every half an hourly during 2nd h, and for every one hourly there after till 6 h postoperatively. The assessment of pain by visual analogue score (VAS) was done immediately after surgery and shifting the patient to post-operative care unit. VAS values are as follows:

- 0: No pain
- 1–4: Mild pain
- 5–7: Moderate pain
- 8–10: Severe pain.

As the VAS again reaches seven or more rescue analgesic was administered in the form of injection diclofenac sodium 1.5 mg/kg IV diluted till 10 ml in NS. Time of drug administration, time of onset, and duration of drug action and VAS scores were noted. Statistical analysis was performed by applying students *t*-test using SPSS software and $P < 0.05$ was considered statistically significant.^[11-13]

RESULTS

In this study, the onset of action for paracetamol was 20 ± 3.45 min and for nalbuphine group was 7 ± 2.96 min which was significant. Duration of action for both groups was ≥ 6 h (VAS scores reaching more than 7). The measured vital signs indicated significant differences in mean pulse rate, blood pressure (systolic and diastolic blood pressure [DBP]), and VAS between the two groups during the course of study as presented in Figures 1-4, respectively.

Changes in pulse rates were found statistically significant in patients receiving nalbuphine with the mean pulse rate within 74.90 ± 3.93 BPM in comparison to patients receiving paracetamol with the mean pulse rate within 81.09 ± 4.32 BPM ($P < 0.05$) [Figure 1 and Table 1]. None of the patient experienced the bradycardia in either group. In this study, we did not observe any significant side effects of drugs in either group.

Changes in systolic blood pressure (SBP) were found statistically significant in patients receiving nalbuphine with mean SBP 118 ± 2.68 mmHg in comparison to patients receiving paracetamol with mean SBP 114 ± 2.82 mmHg ($P < 0.05$) [Figure 2]. None of the patients had hypotension in both groups.

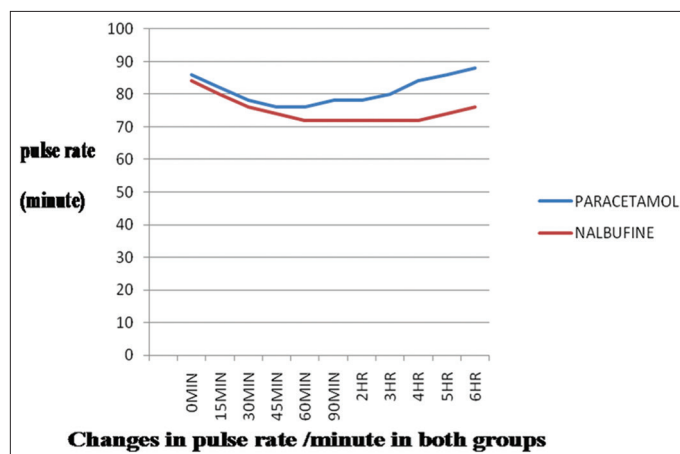


Figure 1: Comparison of pulse rate/minute (mean) between both groups

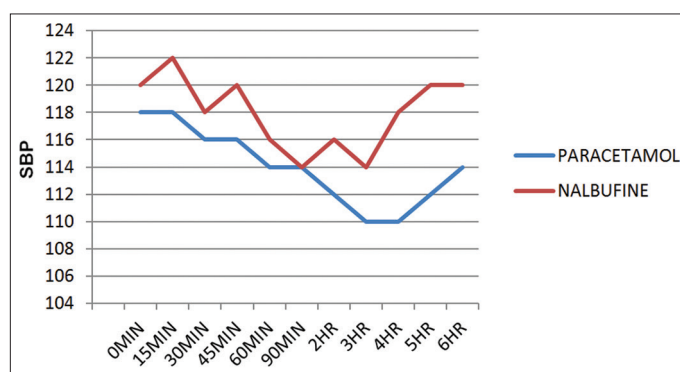


Figure 2: Comparison of mean systolic blood pressure (mmHg) between both groups

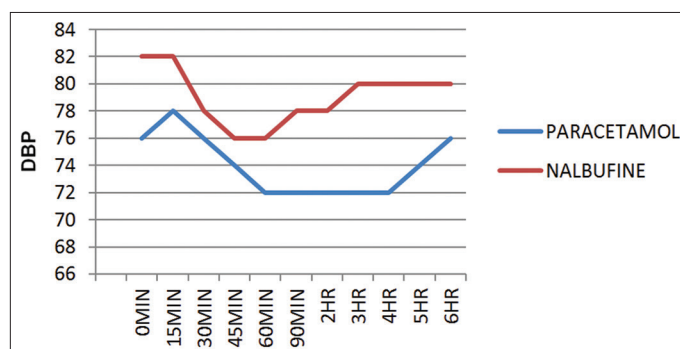


Figure 3: Comparison of mean diastolic blood pressure (mmHg) between both groups

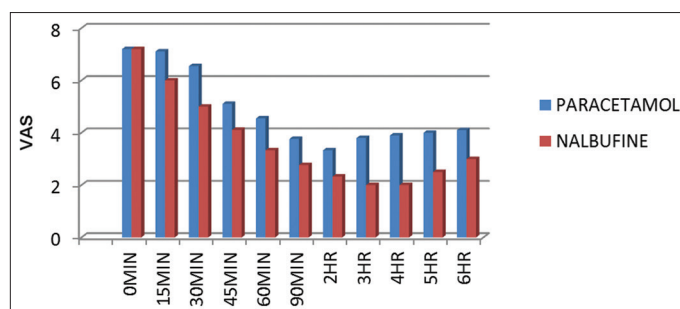


Figure 4: Comparison of pain relief by mean visual analogue score in both groups

Changes in DBP were found statistically significant in patients receiving nalbuphine with mean DBP 79.1 ± 2.07 mmHg in comparison to patients receiving paracetamol with mean DBP 74 ± 2.19 mmHg ($P < 0.05$) [Figure 3].

VAS in both groups were found statistically significant in patients receiving nalbuphine with mean 3.66 ± 1.73 in comparison to patients receiving paracetamol with mean 4.85 ± 1.42 ($P < 0.05$) [Figure 4].

Further rescue analgesics used were significantly high in paracetamol group with maximum 8 ± 1.08 rescue analgesic doses used and in nalbuphine group maximum 2 ± 1.02 rescue analgesic doses were used.

DISCUSSION

This study is concerned in comparing the analgesic effect of intravenous paracetamol versus intravenous nalbuphine after elective CS. Also compares the changes occurring in pulse rate, SBP, and DBP as a result of difference in perception of pain without neglecting to watch on any adverse events of drugs in this study. This study is a result of our perception in the need for a safe and excellent analgesic agent with minimal side effects. Nalbuphine is a semi synthetic opioid agonist-antagonist of the phenanthrene series, structurally related to the agonist oxymorphone and the antagonist naloxone^[9,10,14] which was synthesized in an attempt to provide analgesia without the undesirable side effects of a mu agonist, notably respiratory depression, and drug dependence, with a lower incidence of nausea and vomiting than other opioids. It has been shown to be safe and effective for the treatment of conditions such as burns, multiple traumas, orthopedic injuries, gynecology, and intra-abdominal conditions.^[15,16] It does not affect the mental status, bleeding, respiratory drive, gastric mucosal integrity, or renal function.^[17,18]

Many previous studies have studied the possibility of opioids being more efficacious in females than in males and a study by Gear *et al.* in 1999 found this property of sexual dimorphism (more efficacious in females) to be more prominent for kappa agonists, that is, nalbuphine.^[19,20] Paracetamol is a non-opioid analgesic and related to NSAIDs group of analgesics. Its analgesic action is probably mediated by the serotonergic mechanism and by weak inhibition of cyclooxygenase-1 and cyclooxygenase-2 and antipyretic action is through inhibition of cyclooxygenase-3 in the hypothalamus. The injectable paracetamol for IV infusion was introduced in 2002. It is preferred in most surgical patients because it does not affect mental status, bleeding, respiratory drive, gastric mucosa integrity, or renal function with significant opioid-sparing effect.^[11-13] A study on patients of LSCS, in which IV paracetamol was compared with oral ibuprofen, IV paracetamol group showed better pain control compared to ibuprofen group.^[19] Hence, this study was

undertaken to compare the analgesic efficacy of nalbuphine with paracetamol in LSCS.^[21-24]

In this study, the pulse rate, SBP, DBP, and pain score by VAS were assessed at 0 min, 15 min, 30 min, 60 min, and 90 min, 2 h, 3 h, 4 h, 5 h, and 6 h intervals for both groups in post-operative room. The measured vital signs indicated significant differences in mean values of pulse rate, blood pressure (systolic and DBP), and VAS between the two groups as presented in Figures 1-5.

Our study shows that mean onset of action for paracetamol is 20 ± 3.45 min and for nalbuphine group is 7 ± 2.96 min which is significant. The duration of action for both groups in this study is ≥ 6 h. Uchiyama *et al.*^[25] demonstrated that nalbuphine provides a faster onset of action, probably because of its lipophilic properties. In a study by Solanki *et al.*, the onset of action of nalbuphine was 7.95 ± 3.94 min.^[23] The changes in pulse rates were found statistically significant in patients receiving nalbuphine with the mean pulse rate within 74.90 ± 3.93 BPM in comparison to patients receiving paracetamol with the mean pulse rate within 81.09 ± 4.32 BPM ($P < 0.05$) [Figure 1 and Table 1]. None of the patient had experienced bradycardia in either group. Changes in SBP were found statistically significant in patients receiving nalbuphine with mean SBP 118 ± 2.68 mmHg in comparison to patients receiving paracetamol with mean SBP 114 ± 2.82 mmHg ($P < 0.05$) [Figure 2]. Changes in DBP were found statistically significant in patients receiving nalbuphine with mean DBP 79.1 ± 2.07 mmHg in comparison to patients receiving paracetamol with mean DBP 74 ± 2.19 mmHg ($P < 0.05$) [Figure 3]. None of the patients had hypotension in both groups. In our study, both paracetamol and nalbuphine are found to be having better hemodynamic

Table 1: Mean pulse rate, SBP, DBP, and VAS of both groups

Groups (n=60)	Pulse rate/minute	SBP	DBP	VAS
Group-A -paracetamol	81.09 ± 4.32	114 ± 2.82	74 ± 2.19	4.85 ± 1.42
Group-B -nalbuphine	$74.90 \pm 3.93^*$	$118 \pm 2.68^*$	$79.1 \pm 2.07^*$	$3.66 \pm 1.73^*$

All the results were represented as mean $\pm$ SEM. * $P < 0.05$ = significant SBP, DBP, and VAS

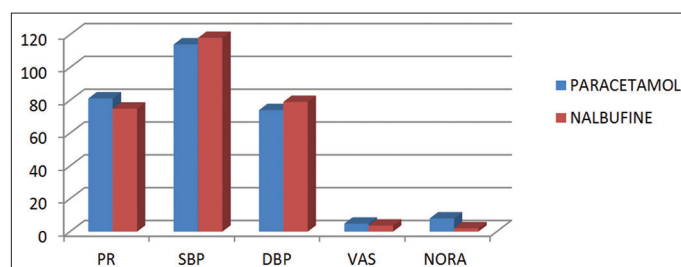


Figure 5: Mean pulse rate, systolic blood pressure, diastolic blood pressure, visual analogue score, and number of rescue analgesics of both groups

stability. Siddiqui and Chohan and Lake *et al.* also showed better hemodynamic stability with nalbuphine compared to tramadol in perioperative settings.^[24-26] Soltani *et al.* reported better hemodynamic stability with paracetamol in CS by general anesthesia.^[27]

This study shows that nalbuphine IV injection may be adequate for post-operative pain and paracetamol IV infusion may be used for mild-to-moderate post-operative pain. Studies by Yeh *et al.*^[28] have also described adequate post-operative analgesia for various surgical procedures using nalbuphine.^[26-29] Studies by Sinatra *et al.*^[13] and Alhashemi *et al.*^[19] found that IV paracetamol provided rapid and effective analgesia in patients of orthopedic surgeries and LSCS, compared to placebo or ibuprofen. In this study, we did not observe any significant side effects of drugs in either group. Lake *et al.* have also reported fewer side effects, less cardiac depression with nalbuphine in comparison to morphine.^[26] Nalbuphine acts through kappa-opioid receptors and may attenuate mu-opioid-receptor related side effects. Woolland *et al.* have also showed that nalbuphine has less adverse effects than paracetamol.^[16] Further rescue analgesics used were significantly high in paracetamol group with maximum eight doses used and in nalbuphine group maximum two doses were used. Minai and Khan^[30] proved that the need for supplemental analgesia was lower with patients in nalbuphine group for intraoperative and post-operative analgesia. This study found that the use of i.v nalbuphine is more effective than acetaminophen i.v in relieving post-operative pain after cesarean surgeries. Similarly, in a study by Ahmed *et al.* demonstrated that using nalbuphine IV has more effective and prolonged analgesia with a more safety margin than acetaminophen IV.^[17]

CONCLUSION

Nalbuphine appears to be a better analgesic of choice for the relief of moderate to severe pain in post-operative CS patients. It provides good sedation, hemodynamic stability, early post-operative recovery, better pain control, lesser need for rescue analgesics, and lesser adverse effects in comparison with IV paracetamol. Paracetamol is also an effective and safe drug for managing mild-to-moderate post-operative pain with a significant opioid-sparing effect.

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