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Research Article

COMPARATIVE STUDY OF INTRAVENOUS PARACETAMOL AND INTRAVENOUS DICLOFENAC ANALGESIA WITH RESPECT TO EFFECT ON RENAL FUNCTION, BLEEDING TIME, AND CLOTTING TIME IN POST-OPERATIVE CASES UNDERGOING LSCS UNDER SPINAL ANESTHESIA

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ABSTRACT

Objectives: The aims and objectives of the study are to compare paracetamol and diclofenac for post-operative analgesia, efficacy, and safety profiles in patients undergoing LSCS under spinal anesthesia.

Methods: Fifty-eight patients undergoing LSCS under spinal anesthesia were included in this study. Out of these 58 patients, 30 patients received paracetamol (Group P) and the remaining 28 patients received diclofenac (Group D). Post-operative pain was assessed using the Visual Analog Scale. Rescue analgesic used was buprenorphine intravenous at a dose of 1 µg/kg. Injection buprenorphine was given to the patient with a VAS score of more than three in addition to the routine dose of the study drug. Pre-operative and post-operative values of blood urea, serum creatinine, bleeding time, and clotting time were compared in both groups. $p<0.05$ were taken as statistically significant.

Results: The mean age of patients in both groups was found to be comparable with no statistically significant difference ($p=0.3849$). In post-operative period at 150, 180 min, and 210 min, Group P reported significantly higher pain scores as compared to Group D with p-values indicating statistical significance ($p<0.05$). The analysis of pre- and post-operative renal function tests, bleeding time, and clotting time showed that there was no significant difference in the pre- and post-operative renal function tests, bleeding time, and clotting time of the patients in Group P and Group D.

Conclusion: Intravenous diclofenac is found to have a superior analgesic effect as compared to intravenous paracetamol. Both paracetamol and diclofenac were found to have no significant side effects on renal functions, bleeding time, or clotting time.

Keywords: Post-operative analgesia, LSCS, Paracetamol, Diclofenac

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INTRODUCTION

The administration of effective analgesia in the post-operative period is a crucial aspect of surgical care, ensuring not only patient comfort but also facilitating early mobilization and recovery. In the specific context of obstetric surgery such as lower segment cesarean section (LSCS), the choice of analgesic is important due to its potential impact on both the mother and the neonate. Suboptimal analgesia in post-operative may be associated with the poor establishment of breastfeeding and its consequences on maternal as well as neonatal well-being. In some cases, though uncommon, suboptimal pain management after LSCS is associated with prolonged immobility and its consequences such as deep vein thrombosis or atelectasis [1].

IN post-operative period opioids, non-opioid analgesics, and adjunctive medications can be used for pain management after LSCS under spinal anesthesia. Opioids, such as morphine fentanyl, and hydromorphone, act on the central nervous system to provide potent analgesia, however, their use is often limited by concerns over respiratory depression and sedation necessitating careful patient selection and monitoring [2]. Non-opioid analgesics including NSAIDs such as ibuprofen, diclofenac, and paracetamol offer effective pain relief with a lower risk of respiratory depression. These agents act primarily by inhibiting cyclooxygenase enzymes or modulating pain pathways at the central level, presenting a safer option for mild-to-moderate pain and as part of multimodal pain management strategies to reduce opioid consumption. Adjunctive medications, such as gabapentin, muscle relaxants, and local anesthetics, may also be used to target specific pain pathways, enhance analgesia, or manage pain components not adequately addressed by opioids or non-opioids alone [3].

Intravenous paracetamol as well as diclofenac sodium are common analgesics being routinely used for post-operative analgesia in these patients. The choice between non-opioid analgesic drugs (like paracetamol) and non-steroidal anti-inflammatory drugs (NSAIDs) (like diclofenac sodium) involves considering their analgesic efficacy, mechanism of action, and side effect profiles [4]. Paracetamol, with its central analgesic and antipyretic properties, presents a favorable option for post-operative pain management. It has minimal impact on platelet function and gastrointestinal lining. On the other hand, diclofenac sodium (a potent NSAID) has strong anti-inflammatory and analgesic effects but carries a risk of adverse effects on renal function and hemostasis, particularly relevant in the surgical population [5].

Renal function is a critical consideration in the post-operative management of patients undergoing major surgeries, including LSCS. Both paracetamol and diclofenac are metabolized through the liver and excreted by the kidneys. In many cases, their use has been reported to be linked to alterations in renal blood flow and function [6]. In the setting of LSCS where fluid shifts and hemodynamics changes are a common occurrence, the impact of these analgesics on renal function needs careful examination. The assessment of renal parameters post-administration of these drugs provides valuable insights into their safety profile [7].

In addition to its effect on renal functions, these analgesics also have an effect on bleeding time and clotting time which are another vital aspect of post-operative care. In cases of obstetric surgeries where the risk of hemorrhage is heightened particular, this aspect needs to be given careful consideration [8]. The influence of analgesics on

platelet function and the coagulation cascade is well known. NSAIDs are potential inhibitors of platelet aggregation and are known to prolong bleeding time. It is therefore important to carefully maintain the balance between effective analgesia and the hemostatic integrity in cases receiving paracetamol or diclofenac sodium for post-operative analgesia [9].

This comparative study focuses on two widely used intravenous analgesics, paracetamol, and diclofenac, examining their efficacy and safety profiles in the post-operative setting of patients undergoing LSCS under spinal anesthesia. The investigation extends to evaluate the effects of these analgesics on renal function, bleeding time, and clotting time, parameters critical to the post-operative recovery process and patient safety.

METHODS

This was a comparative study conducted in the department of anesthesiology of a tertiary care medical institute. The Institutional Ethical Committee approved the study. Fifty-eight patients undergoing LSCS under spinal anesthesia were included in this study on the basis of a pre-defined inclusion and exclusion criteria. These 58 patients were divided into two groups. Thirty patients received injection paracetamol (1 gm in 100 ml IV fluid) infused over 15 min (Group P) and 28 patients received diclofenac 75 mg in 100 ml infused over 15 min (Group D). The sample size was calculated on the basis of a pilot study done on the topic of post-operative analgesia, assuming 90% power and 95% confidence interval, the sample size required was 50 patients; therefore, we included 58 patients who had undergone LSCS under spinal anesthesia during the study period.

A thorough pre-anesthetic evaluation was done with special emphasis on cardiac, respiratory, nervous, and endocrinal abnormalities. Previous anesthetic exposure and drug sensitivity were inquired. A thorough general and systemic examination was carried out for baseline parameters and airway assessment. An informed consent was taken. Moreover, following investigations were done. Beyond routine investigations, pre-operative bleeding time, clotting time, urea, and creatinine were done. These investigations were repeated after the second dose of analgesic postoperatively.

Tablet ranitidine 150 mg orally was given on the previous night. Patients were kept nil orally for 8 h before surgery. On the day of surgery, baseline bleeding time, clotting time, urea, and creatinine were sent. In the premedication room, an injection of ranitidine 50 mg and an injection of metoclopramide 10 mg were given 45 min before surgery. Intravenous access was secured with an 18G venous cannula and patients were pre-loaded with 500 m1 of lactated ringer's solution. All patients received supplemental oxygen through facemask. Patient was put in a lateral position and under aseptic precaution, a subarachnoid block was given with 2.2 m1 of 0.5% hyperbaric bupivacaine at L3–L4 interspace, the patient was then positioned supine with the left lateral tilt of 15° achieved by keeping a wedge under the right hip and surgical procedure ensued. Once the baby was delivered, 20 units of oxytocin were started in 1 L of normal saline as an infusion. Study drug was started at the same time through a three-way cannula and infused over 15 min time by a nurse who was not involved in the study. The time of administration of the study drug was noted by the nurse who administered the drug. The dose of paracetamol was repeated after 6 h and that of diclofenac was repeated after 12 h. Toward the end of the surgery, the patient was shifted to the post-operative ICU. Post-operative pain was assessed using the Visual Analog Scale. Rescue analgesic used was buprenorphine IV at a dose of 1 μg/kg. Injection buprenorphine was given to the patient with a VAS score of more than 3 in addition to a routine dose of the study drug. One hour after the second dose of the study drug, investigations such as urea, creatinine, bleeding time, and clotting time were repeated.

Both the groups were compared for renal function, bleeding time, and clotting time. Statistical analysis was done using the SPSS version 21.0 software. Quantitative data were presented as mean and standard deviation. For quantitative data, an unpaired t-test will be applied and for qualitative data, a Chi-square test will be used. $p<0.05$ will be taken as statistically significant.

Inclusion criteria

The following criteria were included in the study:

1. Patients undergoing LSCS under spinal anesthesia.
2. ASA Grade II patients.
3. Those gave informed and written consent to be part of the study.

Exclusion criteria

The following criteria were excluded from the study:

1. Patients who refused consent to be part of the study.
2. Patients of ASA Grade III or higher.
3. Patients allergic to any of the study drugs.
4. Patients with known renal diseases, bleeding, or clotting disorders.

RESULTS

The analysis of the patients on the basis of mean age showed that the mean age of patients in Group P was 27.48±2.77, whereas in Group D, the mean age of patients was 26.71±3.87. The mean age of patients in both groups was found to be comparable with no statistically significant difference ($p=0.3849$) (Table 1).

The comparison of VAS scores at various time intervals showed that Group P had slightly higher scores at the 30-min and 60-min intervals compared to Group D with non-significant p-values indicating no statistically significant difference in pain levels. At 120 min, Group P patients' pain score increased more noticeably than Group D, yet the difference was not statistically significant ($p=0.2329$). However, at 150 and 180 min, Group P reported significantly higher pain scores (2.50 and 3.90) compared to Group D (1.7 and 3.14), with p-values indicating statistical significance ($p<0.0001$ and $p=0.0100$, respectively). At 210 min, Group P's score decreased to 3.60, still higher than Group D's 2.11, with a significant p-value ($p=0.0038$). By the 300-min mark, both groups reported lower pain scores (Group P: 2.32, Group D: 2.10) with no significant difference between them ($p=0.3429$) (Table 2).

The analysis of pre- and post-operative renal function tests, namely blood urea and serum creatinine, showed that there was no significant difference in the pre- and post-operative renal function tests of the patients in Group P as well as Group D ($p>0.05$) (Table 3).

The analysis of pre- and post-operative bleeding time and clotting time in both the groups showed that there was no significant difference in the pre- and post-operative bleeding time and clotting time in Group P as well as Group D ($p>0.05$) (Table 4).

DISCUSSION

Both paracetamol and diclofenac are effective analgesics for managing post-operative pain; however, their impact on renal function and hemostatic parameters can differ significantly, which is crucial in the post-operative management of patients [10]. Paracetamol, with its relatively safe profile, does not significantly affect renal function in most patients. It is metabolized primarily in the liver, with minimal renal excretion of its metabolites. Thus, its use in the post-operative setting, especially after LSCS under spinal anesthesia, is less likely to compromise renal function. In addition, paracetamol does not significantly impact bleeding time or clotting time, making it a safer choice for analgesia in patients where bleeding risk is a concern [11].

On the other hand, diclofenac, a non-steroidal anti-inflammatory drug (NSAID), can affect renal function due to its mechanism of inhibiting prostaglandin synthesis. Prostaglandins play a protective role in maintaining renal blood flow, especially in states of hypoperfusion [12]. Therefore, diclofenac's use in the post-operative period could potentially lead to altered renal function, particularly

Table 1: Comparison of mean age of the patients in both groups

	Group P		Group D	
	Number of cases	Percentage	Number of cases	Percentage
18–25 years	16	27.59	13	22.41
26–30 years	9	15.52	11	18.97
Above 30 years	5	8.62	4	6.90
Total	30	51.72	28	48.28
Mean Age	27.48±2.77		26.71±3.87	

p=0.3849

Table 2: Mean VAS scores at different time intervals in both groups

Time interval (min)	Group P (Mean VAS)	Group D (Mean VAS)	p-value
0	0	0	-
5	0	0	-
10	0	0	-
15	0	0	-
20	0	0	
30	0.16+0.22	0.15+0.12	0.832
60	0.42+0.32	0.36+0.28	0.4518
120	0.93+0.56	0.76+0.51	0.2329
150	2.50+0.62	1.7+0.53	<0.0001*
180	3.90±1.24	3.14±0.89	0.0100*
210	3.60+1.87	2.11+1.89	0.0038*
300	2.32+0.94	2.10+0.80	0.3429

*Significant

Table 3: Comparison of pre- and post-operative renal function tests in studied groups.

	Pre-operative	Post-operative	p-value
Serum Creatinine (mg/dl)			
Group P	0.56±0.14	0.52±0.13	0.2652
Group D	0.54±0.13	0.50±0.11	0.2127
Blood urea (mg/dl)			
Group P	14.33±2.87	13.72±2.10	0.3624
Group D	13.14±1.48	13.57±1.53	0.2813

Table 4: Comparison of pre- and post-operative bleeding time and clotting time in studied groups

	Pre-operative	Post-operative	p-value
Bleeding time (seconds)			
Group P	102±21.71	108±33.97	0.423
Group D	106±21.34	111.42±33.52	0.462
Clotting time (seconds)			
Group P	220.00±19.82	223±20.14	0.5699
Group D	226.78±21.09	227.1422.52	0.950

in patients with pre-existing renal impairment or those at risk of hypoperfusion. Furthermore, by affecting platelet function, diclofenac can potentially prolong bleeding time, although its impact on clotting time is generally minimal. This effect on hemostasis warrants cautious use, especially in surgical patients [13].

In this study, the comparison of analgesic effects of paracetamol and diclofenac as assessed by mean VAS showed that the mean VAS score was more in Group P as compared to Group D at 150 min, 180 min, and 210 min postoperatively and the difference was statistically significant ($p<0.05$). At other times, the mean VAS scores were found to be comparable in both groups ($p> 0.05$). Pal A *et al*. conducted a study to compare the efficacy of injectable diclofenac intramuscularly (IM), injection paracetamol intravenously (IV), or a combination of both to provide post-operative analgesia in patients undergoing lower abdominal gynecological surgeries [14]. For this purpose, 90 female patients, classified as American Society of Anesthesiologists (ASA) I and II, aged between 20 and 50 years, and scheduled for elective total abdominal hysterectomy, with or without bilateral salpingo-oophorectomy, were divided randomly into three groups. Group D received 75 mg of intramuscular diclofenac every 8 h, Group P was administered 1 g of intravenous paracetamol at the same interval, and Group PD was given a combination of both treatments every 8 h for a 24-h period starting from the beginning of the surgery. The primary endpoint of the study was the need for additional analgesia (tramadol). Secondary endpoints included the Visual Analog Scale (VAS) scores for pain assessment, the duration until the first request for rescue analgesic, scores of patient satisfaction, and the observation of any adverse effects. The requirement of rescue analgesia was significantly lower in Groups D and PD compared to Group P. Mean (standard deviation) tramadol requirement during 24 h was 56.67 (62.60) mg, 20.00 (40.68) mg, and 20.00 (40.68) mg in the Groups P, D, and PD, respectively. On the basis of these findings, the authors concluded that injection diclofenac IM is more effective than paracetamol IV in terms of rescue analgesic requirement. A similar superior analgesic effect of diclofenac over paracetamol has also been reported by the authors such as Shah *et al*. [15] and Yoganarasimha *et al*. [16].

In our study, the pre-operative and post-operative renal function tests such as blood urea and serum creatinine were found to be comparable in both groups with no statistically significant difference. Forrest JB *et al*. conducted a study to compare the risk of serious adverse effects with ketorolac vs diclofenac or ketoprofen in adult patients after elective major surgery [17]. For this purpose, the authors undertook a prospective, randomized multicenter trial that evaluated the risks of death, increased surgical site bleeding, gastrointestinal bleeding, acute renal failure, and allergic reactions, with ketorolac vs diclofenac or ketoprofen administered according to their approved parenteral and oral dose and duration of treatment. A total of 11,245 patients completed the trial at 49 European hospitals. Of these, 5634 patients received ketorolac and 5611 patients received one of the comparators. 155 patients (1.38%) had a serious adverse outcome, with 19 deaths (0.17%), 117 patients with surgical site bleeding (1.04%), 12 patients with allergic reactions (0.12%), 10 patients with acute renal failure (0.09%), and four patients with gastrointestinal bleeding (0.04%). There were no differences between ketorolac and ketoprofen or diclofenac. The study found diclofenac to be an effective analgesic with no significant effects on renal functions. A similar safety profile of paracetamol for post-operative analgesia was reported by authors such as Kiliçaslan *et al*. [18] and Ozmete *et al*. [19].

There was no significant derangement in either bleeding or clotting time in any of the groups and mean pre-operative as well as post-operative bleeding time and clotting time were found to be comparable in both the groups. Osojnik I *et al*. conducted a study to establish whether the use of diclofenac reduces the administration of opioids and how it affects bleeding and platelet function after major cardiac surgeries. The study found that diclofenac in clinically administered doses does not interfere with the function of platelets and does not cause increased bleeding. Lower CRP in the diclofenac group may indicate a reduced inflammatory response after CPB. Therefore, diclofenac could be safe for use in patients undergoing major surgeries. A similar safety profile of paracetamol has been reported by the authors such as Kashif *et al*. [20]

CONCLUSION

In this study, intravenous diclofenac was found to be associated with superior analgesia as compared to intravenous paracetamol. Neither of

these drugs was found to have any effect on renal functions, bleeding time, or clotting time.

CONFLICT OF INTEREST

None.

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