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COMPARATIVE STUDY OF TRAMADOL SUPPOSITORY VERSUS IV TRAMADOL IN PATIENTS UNDERGOING CESAREAN SECTION SURGERY: POST OPERATIVE PAIN RELIEF

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ABSTRACT

Background

Effective pain management during the perioperative period is crucial for optimizing patient outcomes following surgery. Proper pain relief not only facilitates early mobilization but also contributes to quicker discharge. In the early postoperative phase, oral medications are typically not an option, making injectable analgesics the standard approach for pain management.

Material and Methods

We assessed 60 patients, with 30 participants in each group. All the participants were classified as ASA II, aged between 18 and 50 years, and underwent cesarean sections under spinal anesthesia. Following the surgery and post-vaginal toileting, Group A received 100 mg of tramadol intravenously, while Group B received 100 mg of tramadol suppository rectally. Intraoperative and perioperative vital signs were recorded, and side effects such as nausea, vomiting, and pruritus were monitored. If at any point the visual analog scale (VAS) score reached 6 or higher, an intravenous injection of paracetamol (15 mg/kg) was administered, and the study was concluded. The timing of the rescue analgesic administration was recorded, and patients were monitored postoperatively at 6, 12, and 24 hours. The total number of rescue analgesics administered within the 24-hour postoperative period was also documented.

Results

In our study, the tramadol suppository group showed mean VAS scores was 0, 2.6 ± 0.67, 3.03 ± 0.71, 4.53 ± 0.77, at 0, 6, 12, and 24 hours respectively and the IV tramadol group had mean VAS score was 0, 3.47 ± 0.50,3.97 ± 0.8, 4.87 ± 0.81 at 0, 6, 12 and 24 hours respectively. The mean Visual Analogue Scale (VAS) score was significantly lower in the suppository group compared to the IV tramadol group. In the suppository group, out of 50 patients, 4 (8%) required rescue analgesia at 6 hours, 8 (16%) at 12 hours, and 12 (24%) at 24 hours postoperatively. In contrast, in the IV tramadol group, 16 patients (32%) needed rescue analgesia at 6 hours, 20 (40%) at 12 hours, and 20 (40%) at 24 hours postoperatively.

Conclusions

The suppository group experienced prolonged analgesia and required fewer rescue analgesics compared to the IV group. Additionally, nausea and vomiting were less frequent in the suppository group. Rectal tramadol provides more effective postoperative pain relief after cesarean section than intravenous tramadol, offering longer-lasting pain control and fewer side effects.

Keywords: Caesarean section, diclofenac sodium, postoperative analgesia, suppository, tramadol

Introduction

Pain is described as an uncomfortable sensory and emotional experience associated with actual or potential damage to tissues [1]. It is an unpleasant sensation localized in specific areas of the body, triggered by the activation of sensory nerve endings known as nociceptors, which are activated by the release of substances such as prostaglandins and chemical signals from damaged or inflamed cells [2].

Postoperative pain is a common form of acute pain, and its management is an integral part of patient care, playing a pivotal role in the transition from the recovery unit to discharge home [3,4]. Untreated postoperative pain can have significant psychological and physiological effects, including anxiety, depression, and stress responses, which may lead to hypertension, tachycardia, and an increased risk of myocardial infarction [2]. Pain can also delay mobilization, leading to venous thrombosis, pressure sores,and the development of chronic pain [5]. Ineffective pain control, apart from being inhumane, results in increased mortality and morbidity.

Various treatments and pharmaceuticals are employed to manage postoperative pain, including epidural procedures, local anesthetic infiltration, opioids, NSAIDs, and patient-controlled analgesia (PCA) pumps [3]. Opioids and NSAIDs are cost-effective and widely used for this purpose [6]. Any postoperative analgesic method must fulfill three essential criteria: effectiveness, safety, and predictability.

Opioids have been utilized for centuries to alleviate anxiety and surgical pain. However, systemic opioid administration can lead to side effects such as vomiting, nausea, respiratory depression, constipation, itching, and dizziness [7]. These issues limit the use of opioids like tramadol for postoperative pain relief, particularly in procedures such as day surgery or oropharyngeal surgery (e.g., tonsillectomy), where avoiding postoperative nausea and vomiting is crucial. In such cases, rectal administration of tramadol may serve as an alternative. This method is convenient, and established for treating postoperative pain in adults, and studies indicate that rectal administration of tramadol is safer, easier, more dependable, and less painful compared to intravenous administration [8].

Systemic NSAIDs may cause adverse effects such as rash, analgesic nephropathy, and bleeding [9].

Tramadol, classified as an atypical opioid, has a moderate affinity for mu-opioid receptors and a weak affinity for delta and kappa opioid receptors. Tramadol not only acts as a mu-opioid agonist but also blocks norepinephrine and serotonin absorption in neurons and increases presynaptic serotonin release, which improves the spinal descending inhibitory pathway. Tramadol produces much less sedation, respiratory depression, cardiac depression, and dizziness than morphine does. Furthermore, tramadol carries a lower risk of addiction and abuse [10,11].

Nausea and vomiting are the primary troublesome side effects of tramadol, but they can be managed effectively with antiemetic medications [11]. Tramadol is offered in multiple formulations, such as oral, intramuscular, intravenous, intrathecal, and rectal preparations.

Materials And Methods

This study involved 60 female patients classified as ASA grade II, aged between 18 and 50 years, who were primigravida and undergoing cesarean section surgery under spinal anesthesia. Patients who met the inclusion criteria were randomly selected to participate in the study. Institutional ethics committee approval (IESC/FP/2021/96) was obtained before the initiation of this prospective, comparative, randomized study.
Written informed consent was obtained from all the participants.

Participation criteria

Female patients aged 18-50 years, ASA grade II classification, primigravida, undergoing cesarean section under spinal anesthesia, hemodynamically stable, normal results from routine preoperative tests, and no other underlying health conditions were included. Patients with ASA physical status III or higher, history of previous cesarean sections, contraindication to spinal anesthesia, and co-existing conditions such as diabetes, hypertension, neurological disorders, psychiatric disorders, or neurovascular disorders, known drug allergies were excluded.

Preoperative Evaluation

A comprehensive preoperative evaluation was

conducted, which included a detailed medical history, general and systemic examinations of the cardiovascular, respiratory, and central nervous systems, and routine laboratory testing. Patients were instructed to fast for eight hours before the procedure. Written informed consent was obtained from all participants.

Baseline Measurements

Preoperative recordings of heart rate (HR), oxygen saturation (SpO2), systolic (SBP) and diastolic blood pressure (DBP), mean arterial pressure (MAP), and electrocardiogram (ECG) were made. An 18 G IV cannula was used to establish peripheral venous access, and patients were preloaded with 10 ml/kg of Ringer's lactate.

Intraoperative Procedure

Upon arrival in the operating theater, patients were monitored using non-invasive blood pressure (NIBP), pulse oximeter, and ECG. Following aseptic precautions, patients were positioned sitting for a lumbar puncture at the L3-L4 level, performed by a consultant anesthesiologist using a 26G Quincke's spinal needle. Once a free and transparent flow of cerebrospinal fluid (CSF) was observed, 2.2 ml of 0.5% heavy bupivacaine was administered. Patients were then positioned supine, and an adequate sensory blockade at the T6 level was confirmed.

Drug Administration

After delivery of the baby, 4 mg of IV ondansetron was administered slowly to both groups, followed by 20 units of Pitocin in 100 ml of normal saline. Post-surgery, Group A received 100 mg of tramadol suppositories per rectal route, while Group B received 100 mg of IV tramadol.

Monitoring and Data Collection

The following time points were recorded: T0: Administration of spinal anesthesia, T1: Start of surgery, T2: End of surgery, T3: Administration time and route of the study drug. Vital signs were monitored throughout the procedure and postoperatively at 6 hours, 12 hours, and 24 hours. Any side effects, such as nausea, vomiting, and itching, were noted. In case of discomfort indicated on a visual analog scale (VAS), the study was concluded for that participant, and 15 mg/kg of IV paracetamol was administered as rescue medication.

VAS Score

A visual analogue scale (VAS) was used to assess pain intensity. Participants marked their perceived pain level on a 10 cm line ranging from "no pain" to "worst possible pain". This score provided a quantitative measure of pain severity [12].

Statistical Analysis

Data was entered into Microsoft Excel 360 and analyzed using SPSS version 26. Descriptive statistics, such as frequencies and percentages, were used for qualitative variables. Mean and standard deviation were calculated for quantitative data. The chi-square test was applied to assess differences in the distribution of qualitative variables across groups, while the independent samples t-test was used to compare mean values between two groups. Repeated Measures Analysis of Variance (RM-ANOVA) was employed to examine changes in mean values across groups for variables measured repeatedly. A significance level of $p < 0.05$ was used to determine statistical significance.

Results

The demographic traits, including age and weight, were comparable between both groups, eliminating any potential bias-related disparities. The mean age in Group A was 28.4±3.9 years, while in Group B it was 28.24±3.4 years. The difference was statistically insignificant, with a p-value >0.05 (p=0.86), as determined by an independent t-test.

The mean weight in Group A was 75.4±8.08 kg, while in Group B it was 76.7±7.7 kg. The mean weights were similar between the two groups, with a p-value >0.05 (p=0.11), indicating no statistical significance.

The Visual Analog Scale (VAS) scores for pain were recorded at multiple time points for both Group A and Group B, each consisting of 30 participants. At 0 minutes, both groups had a mean VAS score of 0, indicating no initial pain. However, significant differences emerged at subsequent time points. At 6 hours, Group A had a higher mean VAS score of 4.13±0.7 compared to Group B's 3.33±1.2, with a p-value of 0.002, indicating statistical significance. At 12 hours, the mean VAS score for Group A increased to 6.13±1.1, while Group B's score was 4.33±1.2, with a p-value < 0.0001, again showing a significant difference. Finally, at 24 hours, Group A had a mean VAS score of 5.27±1.1, whereas Group B's score

significantly decreased to 2.33±1.2, with a p-value < 0.0001, demonstrating a statistically significant difference in pain levels between the two groups at all measured time points after the initial assessment (Table *1*).

Variable	Group A (n=30)		Group B (n=30)		p-value
VAS	Mean	SD	Mean	SD	-
At 0 minutes	0	0	0	0	0
At 6 hours	4.13	0.7	3.33	1.2	0.002*
At 12 hours	6.13	1.1	4.33	1.2	< 0.0001*
At 24 hours	5.27	1.1	2.33	1.2	< 0.0001*

Table 1: Comparison of VAS scores

VAS= Visual analog scale
*Statistically significant

Rescue analgesia	Group A (n=30)	Group B (n=30)	p-value
At 0 minutes	0	0	0
At 6 hours	12 (40%)	2 (6.7%)	0.002*
At 12 hours	6 (20%)	8 (26.7%)	0.54
At 24 hours	0	1 (3.3%)	0.31

Table 2: Comparison of rescue analgesia required

*Statistically significant

Rescue analgesia data for both groups was analyzed at various time points. At 0 minutes, neither group required rescue analgesia, resulting in no significant difference. At 6 hours, a notable difference was observed, with 12 participants (40%) in Group A requiring rescue analgesia compared to only 2 participants (6.7%) in Group B, yielding a p-value of 0.002, which is statistically significant. At 12 hours, the need for rescue analgesia was 20% in Group A and 26.7% in Group B, with a p-value of 0.54, indicating no significant difference between the groups. By 24 hours, no participants in Group A required rescue analgesia, while 1 participant (3.3%) in Group B did, with a p-value of 0.17, showing no significant difference at this time point.(Table 2)

Side Effect	Group A (n=30)	Group B (n=30)	p-value
Nausea	7(23%)	3 (10%)	0.18
Vomiting	6 (20%)	0	0.009*
Respiratory Depression	0	0	-

Table 3: Comparison of side effects

***statistically significant**

We further analyzed the side effects in each group. Group B, 3 participants (10%)

experienced nausea, and there were no cases of vomiting or respiratory depression. In contrast, Group A reported a higher incidence of side effects, with 7 participants (23%) experiencing nausea and 6 participants (20%) experiencing vomiting. Both groups had no cases of respiratory depression.

Discussion

The route of tramadol administration significantly influences its onset, duration, efficacy, and side effect profile [8,11]. Oral administration is often impractical during the postoperative period when patients are nil by mouth, potentially causing nausea or vomiting [13]. Intramuscular administration can be painful, while intravenous administration achieves rapid peak concentrations but is associated with a higher incidence of postoperative nausea and vomiting. These factors limit the widespread use of tramadol in the postoperative setting.

Rectal administration of tramadol via suppositories offers a viable alternative. In our study, we compared IV versus rectal tramadol for postoperative analgesia in patients undergoing lower segment cesarean section (LSCS). Patients generally find rectal drug administration uncomfortable when awake. To mitigate this, in our study, tramadol suppositories were introduced under the influence of spinal anesthesia at the end of surgery, ensuring patient comfort. We administered a rectal dose of 100 mg, guided by therapeutic considerations [14].

Tramadol undergoes rapid distribution following intravenous administration, characterized by a fast onset and an initial distribution half-life of 6 minutes [10,11,15]. After rectal administration, tramadol has been observed in dogs from 5 minutes to up to 10 hours, indicating rapid absorption of the active ingredient [16].

Tramadol is extensively metabolized in the body into several metabolites, including N-desmethyl-tramadol (M2) and N, O-desmethyl-tramadol (M5) [17]. In our study, the tramadol suppository group showed mean VAS scores of 0, 4.13± 0.7, 6.13 ±1.1, and 5.27±1.1 at 0, 6, 12, and 24 hours respectively and the IV tramadol group had mean VAS score of 0, 3.33±1.2,4.33± 1.2, 2.33 ±1.2 at 0, 6, 12 and 24 hours respectively. The mean VAS in the suppository group was comparatively lower than the IV tramadol group. Additionally, of the 30 patients in group A, 12 (40%) needed rescue analgesia at 6 hours, and 6(20%) at 12 hours after surgery. Similarly, of the 30 patients in group B, 2 (6.7%) needed rescue analgesia at 6 hours, 8 (26.7%) at 12 hours, and 1 (3.3%) at 24 hours after surgery. It depicts that, more rescue analgesics were required in IV tramadol as compared to the suppository group.

When comparing side effects between the two groups, three of the patients in the suppository group experienced nausea as a side effect. In contrast, among the 30 patients in the IV tramadol group,7 patients (23%) reported nausea, and 6 patients (20%) experienced vomiting.

Our findings align with several previous studies. Lotfalizade et al. [18] investigated the analgesic efficacy of diclofenac suppositories compared to intravenous tramadol and their combination in cesarean section, reporting a mean analgesic duration of 134.7 minutes in the intravenous tramadol group. Gadani et al. [8] investigated adult tonsillectomy patients and found that rectal tramadol extended the duration of pain relief significantly compared to intravenous tramadol (504±146.96 min vs. 426±80.36 min). Moreover, they reported a lower incidence of postoperative nausea and vomiting (PONV) in the rectal tramadol group (5%) compared to the intravenous group (15%). Joshi et al. studied the use of rectal tramadol and diclofenac suppositories in cesarean sections, observing a low PONV rate (3.33%) in the rectal tramadol group. Khazin et al. [19] investigated postoperative pain management using rectal tramadol and indomethacin for diagnostic curettage and early pregnancy termination. Their findings indicated that rectal tramadol provided superior pain relief with minimal adverse effects.

These studies highlight the potential benefits of rectal tramadol administration in different surgical settings, including prolonged analgesia duration and reduced incidence of PONV, compared to intravenous tramadol.

In summary, our study's outcomes are consistent with previous studies, affirming the efficacy and advantages of rectal tramadol administration in various surgical settings. This study presents several limitations that should be considered. The relatively limited sample size may impact the ability to draw broad or definitive conclusions from the results.

Additionally, the analysis did not cover cost-effectiveness, which could have provided further insights into the economic aspects of the treatment options. The study focused exclusively on ASA II primigravida patients without significant underlying health conditions, which may limit the generalizability of the findings to other patient groups. Furthermore, the age range of participants was restricted to 18 to 60 years, and all participants were female, which may also affect the applicability of the results to a broader population. The use of the Visual Analog Scale (VAS) for assessing pain is inherently subjective and may vary among patients, influencing the consistency of pain measurement. Lastly, patients undergoing emergency procedures were not included, which may affect the relevance of the findings to urgent surgical scenarios.

Conclusions

Our study concludes that rectal tramadol suppositories may serve as a superior alternative to intravenous tramadol for postoperative pain management, particularly in patients undergoing cesarean sections. The findings suggest that rectal tramadol provides extended pain relief compared to its intravenous counterpart, which is advantageous for postoperative care. Additionally, rectal administration is associated with fewer side effects, making it a more favorable option for managing pain while minimizing adverse reactions. This method of administration not only enhances patient comfort but also offers a practical solution for effective pain control with reduced risk of complications, underscoring its potential benefits in surgical recovery and pain management.

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