(e) ISSN Online: 2321-9599

(p) ISSN Print: 2348-6805

ORIGINAL ARTICLE

To evaluate the effects of tramadol and diclofenac, both alone and in combination, on pain experienced after a cesarean section

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ABSTRACT:

Aim: To evaluate the effects of tramadol and diclofenac, both alone and in combination, on pain experienced after a cesarean section. **Material and methods:** After obtaining approval from the hospital's ethical council, a group of 120 patients who were undergoing lower segment cesarean section were included in the study. A cohort of 120 patients was recruited for the experiment and were allocated randomly into three groups, each including 40 patients. The groups were categorized as follows: Group T was administered tramadol, Group D was administered diclofenac, and Group TD was administered both tramadol and diclofenac. Before the therapy, all patients received a comprehensive explanation of the Visual Analog Scale (VAS). **Results:** The values for the onset of analgesia (in minutes) are as follows: 37.09±2.32 for group T, 25.21±2.65 for group D, and 18.84±1.83 for group TD. The duration of analgesia was 549.69±5.65 minutes in group T, 409.55±5.48 minutes in group D, and 541.15±5.29 minutes in group TD. The Visual Analog Scale (VAS) scores at 1 hour were 2.91±0.27, 2.81±0.33, and 1.99±0.32 in group T, group D, and group TD, respectively. The Visual Analog Scale (VAS) scores at 3 hours were 2.39±0.34, 2.31±0.43, and 1.51±0.65 in group T, group D, and group TD, respectively. The Visual Analog Scale (VAS) scores at 6 hours were 3.22±0.54, 3.18±0.16, and 2.11±0.59 in group T, group D, and group TD, respectively. The number of dosages administered during a 24-hour period was 2.72±0.39, 3.83±0.37, and 2.47±0.59 in group T, group D, and group TD, respectively. **Conclusion:** The results of our study suggest that using a multimodal approach for post cesarean care, which involves the simultaneous use of tramadol and diclofenac, led to more effective pain alleviation compared to taking each medicine alone. Moreover, this strategy also resulted in a reduction in the frequency of adverse occurrences.

Keywords: Tramadol, Diclofenac, Post-cesarean, pain

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This article may be cited as: Krishna CS. To evaluate the effects of tramadol and diclofenac, both alone and in combination, on pain experienced after a cesarean section. J Adv Med Dent Scie Res 2016;4(3):239-243.

INTRODUCTION

Pain, as per the definition provided by the International Association for the Study of Pain, refers to an unpleasant combination of sensory and emotional experiences that is associated with actual or potential harm to tissues, or may be described in terms of such harm [1]. Pain is a widespread issue in public health and remains the main motivation for individuals to seek medical guidance and be hospitalized [2]. Pain affects individuals across all demographics, including age, gender, socioeconomic status, race, and geographic location [2]. Severe pain, the most common kind of pain, may result from several factors including accident, serious illness, surgery, or arthritis. Comprehending the source of sudden pain requires a complex and multidisciplinary method [2, 3]. The global prevalence of postoperative pain varies from 14 to 70%, with a notably high occurrence in India, where more than 80% of patients have postoperative pain [3].

A caesarean section is necessary when there is a danger to either the baby or the mother during a vaginal birth. The rise in cesarean delivery rates has been attributed to the relaxation of criteria for fetal distress and elective repeat sections. Caesarean section is often performed in cases when the fetal state is not reassuring, there is a failure to proceed in the delivery, there is a mismatch between the size of the baby's head and the mother's pelvis, the baby is in an abnormal position, or the mother has had previous surgery on her uterus[4]. Currently, Caesarean section is a widely done surgical procedure around the globe. The international health community has established an optimal rate for cesarean sections, which is between 10% and 15%. The caesarean section rate in public institutions in India is 12%, whereas in private sectors it is much higher at 28%. Similar to other significant surgical operations, cesarean birth may cause intense postoperative pain and suffering. It is well known that insufficiently managed pain can have negative effects on the health of the mother and may result in various postoperative problems. Effective pain management after a cesarean section is crucial for promoting the prompt movement of the mother and enabling her to attend to her newborn as soon as feasible[5]. Failure to address surgical pain might lead to maternal problems such as basal atelectasis caused by decreased breathing and deep vein thrombosis (DVT) owing to delayed walking. Furthermore, engaging in early ambulation may help enhance the process of wound healing [6]. The unimodal approach to pain treatment often results in insufficient pain relief due to the cautious use of lower pharmacological doses to avoid potential side effects. Considering the complex

nature of pain, the use of many medicines with distinct mechanisms of action in multimodal analgesia has been seen to enhance the overall pain-relieving impact. Consequently, there is a growing trend towards using a multimodal strategy to provide sufficient pain relief after surgery. An incremental method using a multimodal combination of agents, namely the use of two or more pain drugs with distinct mechanisms of action, may empower obstetricians to accurately tailor pain treatment for women throughout the postpartum period. Multiple case series in the literature provide evidence for the effectiveness of a multimodal strategy to pain treatment [7,8].

Opioids and nonsteroidal anti-inflammatory medications (NSAIDs) have historically been used for the purpose of delivering efficient pain relief after surgery. Opioids induce somnolence, which hampers the mother's ability to engage with the infant in an efficient manner. Administering NSAIDs as a standalone treatment is insufficient to provide adequate pain relief. Hence, a multimodal strategy was implemented, whereby analgesics are administered in conjunction to enhance effectiveness and minimize adverse effects. Analgesic combinations must meet two crucial criteria: first, the combination of components should exhibit additive or synergistic analgesic effects; second, this interaction should enable the use of lower dosages of each agent in combination, leading to an enhanced safety profile[9,10]. This review emphasizes the therapeutic potential of combining analgesics with distinct mechanisms of action, namely a nonsteroidal anti-inflammatory drug (NSAID) such as diclofenac with an opioid such as tramadol. The objective of this study was to compare the effectiveness of the centrally acting drug tramadol and the peripherally acting drug diclofenac, both alone and in combination with reduced doses, in providing postoperative pain relief and reducing side effects in patients undergoing elective cesarean delivery under spinal anesthesia.

MATERIAL AND METHODS

Following the permission of the hospital ethical committee, a cohort of 120 patients who were receiving lower segment cesarean section were included in the research. Prior to their inclusion, informed agreement was acquired from either the patient or a close family. The research comprised patients between the ages of 18 to 35 who had a lower segment cesarean section performed under spinal anesthesia and had an American Society of Anesthesiologists Class 1 or 2 classification. The research excluded patients who had a documented allergy to diclofenac or tramadol, a history of peptic ulcer or gastrointestinal bleeding, recent use of opioids within the last 30 days, pre-eclampsia or eclampsia, pulmonary illness, or had difficulties during surgery or required a modified surgical technique.

A total of 120 patients were selected for the trial and were randomly assigned to three groups, with each group consisting of 40 patients. The groups were designated as follows: Group T received tramadol, Group D received diclofenac, and Group TD received both tramadol and diclofenac. Prior to the treatment, all patients were provided with a detailed explanation of the Visual Analog Scale (VAS). Throughout the perioperative and anesthetic processes, standardized practices were adhered to. Spinal anesthesia was administered using a 27-gauge Whitacre needle in either the L2-3 or L3-4 vertebral area. The anesthesia was achieved by injecting 0.5% bupivacaine with dextrose, following the typical clinical dosage of 1.8-2.0 ml. The established intravenous fluid regimen included administering 20 ml per kilogram of modified Ringer lactate solution prior to the initiation of spinal anesthesia. A 1-liter amount of ringer lactate solution was administered every 8-12 hours for a duration of 24 hours after the surgical procedure. The condition of abnormally low blood pressure, known as hypotension, was addressed by administering a rapid injection of 5 mg of ephedrine via an intravenous route. No further opioids were administered simultaneously. Patients were provided study medicines when they emerged from anesthesia after surgery and reported discomfort. Consult Table 1 for specific medicine dosages.

The Visual Analog Scale (VAS) that was described to the patient before the surgery was used to evaluate the level of discomfort. Pain severity and pain alleviation were evaluated in all patients using a Visual Analog Scale (VAS), which measures pain on a scale of 0 to 10 cm. A score of 0 cm indicates no pain, while a score of 10 cm represents the most severe agony imaginable. The pain was assessed at 0, 1, 3, 6, 12, 18, and 24 hours, and the beginning of pain relief was recorded. An additional dosage was administered anytime the Visual Analog Scale (VAS) score exceeded 5 or if the patient requested it. The duration of effective pain relief was measured until the first instance when more pain relief was needed. The total number of administered dosages was recorded. Additionally, the researchers compared the side-effects that were encountered after undertaking the various treatment plans.

STATISTICAL ANALYSIS

The data analysis was conducted using SPSS software version 25.0. The data were presented as the mean value plus or minus the standard deviation. The pain ratings were examined using the Kruskall-Wallis test, followed by the Mann-Whitney test for comparing the different groups. The data on the onset of pain, duration, and number of dosages was evaluated using Analysis of Variance (ANOVA), followed by the Least Significant Difference (LSD) test for post-hoc analysis. The side-effects were compared using a Chi-square test. A p-value less than 0.05 was deemed statistically significant.

Table 1: Drug doses

	Drug and dose
GroupT	Tramadol Hcl 100mg IM, 2ml normal saline IM one in left and one in right gluteal regions
Group D	Diclofenac75mg IM, 2ml normal saline IM one in left and one in right gluteal regions
GroupTD	Tramadol Hcl 50 mg IM, diclofenac 50 mg IM one in left and one in right gluteal regions

RESULTS

A total of 120 patients were allocated randomly into three groups, with each group consisting of 40 patients. The patients were administered either tramadol, diclofenac, or a combination of tramadol and diclofenac intramuscularly when they experienced pain that was tolerable following surgery. There were no significant differences in the patients' characteristics across the three groups. Vital signs such as pulse, blood pressure, and respiration rate were monitored every hour for a duration of 6 hours during the early postoperative phase. The data indicate that there is no notable clinical variance. The combination of tramadol and diclofenac resulted in much earlier pain relief compared to either tramadol or diclofenac alone. This might be attributed to the synergistic impact resulting from the combination. Patients who were administered diclofenac alone saw a considerably earlier start of effects compared to those who were given tramadol. The delayed start of pain relief in the tramadol group may be attributed to reduced sensitivity, since all patients were pregnant. Patients who were given tramadol either alone or in combination with diclofenac needed a considerably lower number of doses compared to those who got diclofenac alone. This might be attributed to the extended duration of action of tramadol and its active metabolite. The concurrent administration of tramadol and diclofenac resulted in a reduction in the occurrence of adverse effects. This might be attributed to the reduced dosages of medications when administered in combination. Nevertheless, no substantial disparity was seen among the groups (Tables 2-4).

Table 2 displays the mean age of the individuals in group T, group D, and group TD as 21.79±2.46, 23.11±2.65, and 22.97±2.84, respectively. The height (in centimeters) of the individuals in group T, group D, and group TD was recorded as 154.89±3.38, 155.68±3.84, and 155.59±3.44, respectively. The gestational age (in weeks) of the participants was 38.55±2.64, 38.79±2.87, and 38.59±2.39 in group T, group D, and group TD, respectively.

Table 2: Patient characteristics and demographic data.

	Group T (n=40)		Group D (n=40)		Group TD (n=40)		P value
Age (years)	21.79	2.46	23.11	2.65	22.97	2.84	0.15
Height (cm)	154.89	3.38	155.68	3.84	155.59	3.44	0.11
Gestational age (weeks)	38.55	2.64	38.79	2.87	38.59	2.39	0.23

Table 3 displays the onset of analgesia in different groups. The values for the onset of analgesia (in minutes) are as follows: 37.09±2.32 for group T, 25.21±2.65 for group D, and 18.84±1.83 for group TD. The duration of analgesia was 549.69±5.65 minutes in group T, 409.55±5.48 minutes in group D, and 541.15±5.29 minutes in group TD. The Visual Analog Scale (VAS) scores at 1 hour were 2.91±0.27, 2.81±0.33, and 1.99±0.32 in group T, group D, and group TD, respectively. The Visual Analog Scale (VAS) scores at 3 hours were 2.39±0.34, 2.31±0.43, and 1.51±0.65 in group T, group D, and group TD, respectively. The Visual Analog Scale (VAS) scores at 6 hours were 3.22±0.54, 3.18±0.16, and 2.11±0.59 in group T, group D, and group TD, respectively. The number of dosages administered during a 24-hour period was 2.72±0.39, 3.83±0.37, and 2.47±0.59 in group T, group D, and group TD, respectively.

Table 3: Onset and duration of analgesia among the study groups

	Group T (n=40)		Group D (n=40)		Group TD (n=40)	
Onset of analgesia (min)	37.09	2.32	25.21	2.65	18.84*	1.83
Duration of analgesia (min)	549.69	5.65	409.55	5.48	541.15*	5.29
VASat1hr	2.91	0.27	2.81	0.33	1.99*	0.32
VASat3hr	2.39	0.34	2.31	0.43	1.51*	0.65
VASat6hr	3.22	0.54	3.18	0.16	2.11*	0.59
Numberofdosesin24 hr	2.72	0.39	3.83	0.37	2.47*	0.59

VAS: Visual Analog Scale. *denotes $p < 0.05$ and considered significant

Table 4: Incidence of side effects

	Group T (n=40)		Group D (n=40)		Group TD (n=40)	
Nausea	13	32.5	19	47.5	7	17.5
Vomiting	7	17.5	2	5	2	5

Drowsiness	18	45	11	27.5	9	22.5
Dizziness	14	35	9	22.5	7	17.5

DISCUSSION

Postoperative pain is categorized as acute pain caused by surgical trauma, which stimulates an inflammatory reaction and the activation of sensory neurons. Postoperative discomfort after a cesarean section is a common cause of acute pain in the field of obstetrics. The postoperative pain is a major hindrance to the recovery process after a surgical treatment, as it affects both the surgical outcome and the effects of anesthesia. Our research suggests that the combination of tramadol and diclofenac produces more pain-relieving benefits than either medicine alone, as shown in previous studies. Patients who received a combination of tramadol and diclofenac had lower pain ratings compared to those who were given either tramadol or diclofenac alone.

The literature extensively suggests the use of a multimodal strategy to pain management, which involves the combination of medications that target pain relief via several pathways. Tramadol is a centrally acting pain reliever that binds strongly to μ receptors and weakly to κ and δ receptors. Tramadol not only acts as a μ opioid agonist, but also improves the functioning of the spinal descending inhibitory pathways by preventing the absorption of nor epinephrine and 5-hydroxytryptamine by neurons. Additionally, it stimulates the release of 5-HT before the synapse. NSAIDs, like diclofenac, reduce the generation of prostaglandins in peripheral tissues in response to injury, instead of blocking afferent signals. There is data indicating that NSAIDs have a key role in reducing the flow of sensory information via the nonopioid supraspinal nociceptive reflex[13]. Due to its ability to block prostaglandin production, diclofenac may have a more significant impact on reducing pain caused by uterine contractions. As a result, it may provide superior analgesia in the postoperative period compared to tramadol.The tramadol group in this research had analgesia onset at 37.09±2.32 minutes, which was sooner than the findings of a study conducted by Norman R. Rosenthal et al[14], where the onset was 51 minutes. The reason for this may be attributed to the oral route of administration of tramadol used in their investigation. The analgesic effect of diclofenac started after an average of 25.21 ± 2.65 minutes, which was longer than the duration reported in a previous research conducted by Zuniga et al[15], where it was 18 minutes. This might be attributed to the pain model they examined, which specifically focused on postoperative molar extraction.In this research, the length of pain relief provided by tramadol (549.69±5.65) was similar to the duration reported in a study conducted by Dellikan et al[16], which was 559 ± 86.43. The analgesic effect of diclofenac in our research lasted for an average of 409.55±5.48 minutes, which is similar to the length reported by Prabhakar et al[17], where it was 400.00 ± 75 minutes.The occurrence of negative side effects of each specific medicine may be reduced by decreasing the dosage for each drug. In our research, we observed a reduction in the occurrence of vomiting, sleepiness, and dizziness in the group of participants who received a combination of diclofenac and tramadol. The occurrence of nausea and vomiting in the current investigation was similar to the study conducted by Smith et al[18]. The prevalence of somnolence in the current investigation was lower than that reported in the research conducted by Smith et al. This might be attributed to the use of morphine as a supplementary analgesic in their research. The occurrence of tiredness and dizziness in the tramadol group is similar to the findings reported by Ahmed et al[19] in their research. The occurrence of vomiting and sleepiness in the diclofenac group is similar ($p > 0.05$) to the findings of the research conducted by Prabhakar et al[16].

CONCLUSION

Our findings indicate that using a multimodal strategy for post cesarean treatment, including the administration of both tramadol and diclofenac, resulted in superior pain relief compared to using each medication individually. Furthermore, this technique also led to a decrease in the occurrence of adverse events. An integrated approach to pain relief is both more effective and beneficial. Additional research is necessary to assess the effectiveness in diverse clinical situations and to investigate various alternative medication combinations for improved pain relief.

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