

A Comparative Study To Evaluate The Efficacy Of Diclofenac And Tramadol Alone And In Combination In Obstetrics

Shreya Shekhar¹, Pramod Kumar², Pankaj Kumar Singh³, Md. Jamil Akhtar⁴

¹Tutor, Department of Pharmacology, Vardhman Institute of Medical Sciences, Pawapuri, Nalanda, Bihar, India

²Tutor, Department of Pharmacology, Vardhman Institute of Medical Sciences, Pawapuri, Nalanda, Bihar, India

³Tutor, Department of Pharmacology, Vardhman Institute of Medical Sciences, Pawapuri, Nalanda, Bihar, India

⁴Assistant Professor, Department of Pharmacology, Vardhman Institute of Medical Sciences, Pawapuri, Nalanda, Bihar, India

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Abstract

Background: Post-cesarean pain is a common cause of acute pain in the obstetrics. Pain in the postoperative period is an important impediment to recovery from surgery and anesthesia. **Aim:** This study was conducted to evaluate the efficacy of postoperative analgesia and incidence of side-effects of centrally acting drug tramadol with peripherally acting drug diclofenac alone and in combination in patients undergoing elective cesarean delivery under spinal anesthesia. **Methods:** The study population of 90 patients was randomly divided into three groups of 30 each to receive the following treatments: tramadol (Group T), diclofenac (Group D), tramadol and diclofenac at reduced doses (Group TD). **Results:** Combination of tramadol and diclofenac produced significantly early analgesia in comparison to tramadol or diclofenac alone and decrease in the incidence of side-effects. **Conclusion:** We conclude that a multimodal approach to post-cesarean management with a combination of tramadol and diclofenac produced better analgesia than individual drugs and a reduction in the side-effects. Such a combination approach to relieve pain is more effective and advantageous.

Keywords: Tramadol hydrochloride, Diclofenac sodium, Post-cesarean pain

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Introduction

Post-cesarean pain is a common cause of acute pain in obstetrics. There exists an inadequate relief from pain and satisfaction to the patient is still inadequate in many cases. The patients in this group are always healthy, young and active women and are eager to care for their infants. Early postpartum hours and days are important for the interaction between mothers and newborn and pain should not interfere with the mother's ability to nurse the baby[1]. Opioids and nonsteroidal anti-inflammatory drugs (NSAIDs) have been traditionally used to provide effective postoperative analgesia. Opioids cause drowsiness that impairs mother from effectively interacting with the baby. NSAIDs given alone do not suffice to provide effective analgesia. Therefore, a multimodal approach was adopted in which analgesics are given in combination to improve the efficacy and decrease side-effects. The two important criteria to be satisfied by analgesic combinations are - the combination of components should display additive or synergistic analgesia and this interaction should allow lower doses of each substance to be used in combination resulting in an improved safety profile[2]. This overview highlights the therapeutic potential of combining analgesics with a different mechanism of action, particularly a NSAID like diclofenac with an opioid like tramadol.

*Correspondence

Dr. Md. Jamil Akhtar

Assistant Professor, Department of Pharmacology, Vardhman Institute Of Medical Sciences, Pawapuri, Nalanda, Bihar, India

E-mail: drakhtar01@yahoo.co.in

The present study was conducted to compare the efficacy of postoperative analgesia and incidence of side-effects of centrally acting drug tramadol with peripherally acting drug diclofenac alone and in combination of both in decreased doses in patients undergoing elective cesarean delivery under spinal anesthesia.

Materials and Method

The present study was conducted at Department of Obstetrics and Gynaecology and Department of Pharmacology, at Vardhman Institute of Medical Sciences, Pawapuri. A total of 90 patients undergoing lower segment cesarean section were included in the study. The study was approved by institutional research and ethical research committee. An informed and written consent was obtained from either the patient or close relative before they were included in the study. Patients in the age group of 18-35 who underwent lower segment cesarean section under spinal anesthesia with American Society of Anaesthesiologists Class 1 and 2 were included in the study. Patients with known allergy to diclofenac or tramadol, history of peptic ulcer or GI bleeds, opioid use in last 30 days, pre-eclampsia/eclampsia, pulmonary disease, intra-operative complications/ modified surgical procedure were excluded from the study. The study population of 90 patients were randomly divided into three groups of 30 each to receive the following treatments: tramadol (Group T), diclofenac (Group D), tramadol and diclofenac (Group TD) [Table - 1].

Table 1: Drug doses

| Drug and dose | |
|--|--|
| Group T | Tramadol Hcl 100 mg IM, 2 ml normal saline IM one in left and one in right gluteal regions |
| Group D | Diclofenac 75 mg IM, 2 ml normal saline IM one in left and one in right gluteal regions |
| Group TD | Tramadol Hcl 50 mg IM, diclofenac 50 mg IM one in left and one in right gluteal regions |
| T: Tramadol, D: Diclofenac, TD: Combination of tramadol and diclofenac | |

All patients were explained about the Visual Analog Scale (VAS) and standardized perioperative and anesthetic procedures were followed. Spinal anesthesia was induced with a 27 gauge whitacre needle in the L2-3 or L3-4 vertebral space by 0.5% bupivacaine with dextrose dosed according to usual clinical standards (1.8-2.0 ml). The standard IV fluid protocol was 20 ml/kg of modified ringer lactate solution before the induction of spinal anesthesia. A volume of 1 L of ringer lactate was given every 8-12 hrs for 24 hrs after surgery. Hypotension (reduction of blood pressure greater than 20%) was treated with an IV bolus of 5 mg of ephedrine. No concomitant opioids were given. Study drugs were administered to the patients once they came out of anesthetic effect after the surgery and experienced pain. Table 1 can be referred for drug doses.

The VAS which was explained to the patient preoperatively was used to assess the pain. In all the patients, intensity of pain and pain relief following injection of the drug was assessed by VAS (pain score of 0-10 cm, where 0 cm = no pain and 10 cm = worst pain possible). Pain was evaluated at 0, 1, 3, 6, 12, 18, and at 24 hrs and onset of analgesia was noted. Additional dose was given whenever VAS is >5 or if patient demands. Duration of effective analgesia was measured until first requirement of rescue analgesia. Total number of doses given was recorded. Furthermore, the side-effects experienced after undergoing the different regimens were compared.

Statistical analysis

All data analysis was completed using SPSS software. Data were expressed as mean \pm SD. Pain scores were analyzed by using Kruskal-Wallis test followed by Mann-Whitney test for intergroup

comparison. Data of onset of pain, duration and number of doses was analyzed by Analysis of variance (ANOVA) followed by Least significant difference test for post-hoc analysis. Side-effects were compared by Chi-square test. $p < 0.05$ was considered as statistically significant.

Results

Ninety patients were randomly divided into three groups of 30 patients each to receive either tramadol or diclofenac or tramadol with diclofenac IM at the onset of bearable pain after surgery. The patients' characteristics did not differ significantly between the three groups. Monitoring of vital signs like pulse, blood pressure and respiratory rate in the early postoperative period was done hourly for 6 hrs. The results show no significant clinical variation. Combination of tramadol and diclofenac produced significantly early analgesia in comparison to tramadol or diclofenac alone. This might be because of the synergistic effect of the combination. Patients receiving diclofenac alone had significantly early onset than those receiving tramadol. The late onset of analgesia in tramadol group might be because of altered sensitivity as all the patients were pregnant. Patients receiving tramadol alone or in combination with diclofenac required significantly less number of doses than those who received diclofenac alone. This might be because of longer duration of action of tramadol and its active metabolite. Combination of tramadol and diclofenac produced a decrease in the incidence of side effects. This might be because of the decreased doses of drugs when given in combination. However, significant difference was not observed between the groups (Tables 2-4).

Table 2: Patient characteristics and demographic data.

| | Group T (n=30) | Group D (n=30) | Group TD (n=30) |
|-------------------------|-------------------|-------------------|-------------------|
| Age (years) | 21.90 \pm 2.29 | 22.43 \pm 2.78 | 22.30 \pm 2.87 |
| Height (cm) | 154.90 \pm 3.09 | 155.30 \pm 4.82 | 155.80 \pm 5.26 |
| Gestational age (weeks) | 38.60 \pm 1.15 | 38.70 \pm 1.36 | 38.40 \pm 1.67 |

T: Tramadol, D: Diclofenac, TD: Combination of tramadol and diclofenac

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

| | Group T (n=30) | Group D (n=30) | Group TD (n=30) |
|-----------------------------|--------------------|--------------------|---------------------|
| Onset of analgesia (min) | 36.50 \pm 9.21 | 24.17 \pm 9.21 | 18.33 \pm 6.74* |
| Duration of analgesia (min) | 551.67 \pm 94.44 | 412.00 \pm 72.93 | 539.00 \pm 89.65* |
| VAS at 1 hr | 2.87 \pm 0.82 | 2.77 \pm 0.77 | 1.97 \pm 1.35* |
| VAS at 3 hr | 2.40 \pm 1.00 | 2.27 \pm 0.94 | 1.47 \pm 1.14* |
| VAS at 6 hr | 3.27 \pm 0.83 | 3.20 \pm 1.10 | 2.13 \pm 1.17* |
| Number of doses in 24 hr | 2.67 \pm 0.5 | 3.70 \pm 0.6 | 2.50 \pm 0.4* |

VAS scores are expressed as Mean \pm SD, T: Tramadol, D: Diclofenac, TD: Combination of tramadol and diclofenac, VAS: Visual Analog Scale. *denotes $p < 0.05$ and considered significant

Table 4: Incidence of side effects.

| | Group T (n=30) | Group D (n=30) | Group TD (n=30) |
|------------|----------------|----------------|-----------------|
| Nausea | 9 (30.00) | 12 (40.00) | 5 (16.66) |
| Vomiting | 5 (16.66) | 2 (6.66) | 2 (6.66) |
| Drowsiness | 12 (40.00) | 8 (26.66) | 6 (20.00) |
| Dizziness | 9 (30.00) | 6 (20.00) | 5 (16.66) |

T: Tramadol, D: Diclofenac, TD: Combination of tramadol and diclofenac

Discussion

Postoperative pain is considered a form of acute pain due to surgical trauma with inflammatory reaction and initiation of an afferent

neuronal barrage[7]. Post-caesarean section pain is a common cause of acute pain in the obstetrics. Pain in the postoperative period is an important impediment to recovery from surgery and anesthesia.

Comparison of our results and those in the literature suggest that combination of tramadol and diclofenac improves analgesia from that of the drugs given alone. Patients who received a combination of tramadol and diclofenac had lower pain scores than those who received either tramadol or diclofenac alone. The concept of multimodal approach to pain control with the use of a combination of drugs that relieve pain by different mechanisms has been widely proposed in the literature. Tramadol is a centrally acting analgesic that has a strong affinity for μ receptors and weak affinity for κ and δ receptors. In addition to μ opioid agonist effects, tramadol enhances the function of the spinal descending inhibitory pathways by inhibition of neuronal reuptake of nor epinephrine and 5-hydroxytryptamine as well as presynaptic stimulation of 5-HT release[8] NSAID such as diclofenac decreases production of peripheral tissue prostaglandins in response to injury, rather than providing afferent block. There is some evidence suggesting a central role for NSAID in the reduction of afferent input through the nonopioid supraspinal nociceptive reflex[9]. It is possible that diclofenac, because of its prostaglandin synthesis-inhibiting effects, would have a greater contribution in relieving pain secondary to the uterine contraction, thus providing a better quality of analgesia in the postoperative period than tramadol. In this study, the onset of analgesia of tramadol group was 36.5 ± 9.21 min which was earlier than the study done by Norman R. Rosenthal et al.[10] where it was 51 min. This could be because of the route of administration of tramadol used in their study was oral route. The onset of analgesia in the diclofenac group was 24.17 ± 10.09 min which was more than the study done by Zuniga et al.[11] where it was 18 min. This might be because of the pain model that they studied was on postoperative molar extraction. The duration of analgesia of tramadol in the present study (551 ± 94.44) was comparable with the study done by Dellikan et al.[12] where it was 559 ± 86.43 . The duration of analgesia of diclofenac group in the present study 412.00 ± 72.93 min was also comparable to the study done by Prabhakar et al.[13] where it was 400.00 ± 75 min. The incidence of adverse effects of each independent drug by reducing the individual dose. A similar result was obtained in our study with decrease in incidence of vomiting, drowsiness and dizziness in the combination group of diclofenac and tramadol. The incidence of nausea and vomiting in present study was comparable to the study done by Smith et al.[14] The incidence of drowsiness in present study was less than the study done by Smith et al. This might be because morphine was used as rescue analgesic in their study. The incidence of drowsiness and dizziness in tramadol group are comparable to the results in the study done by Ahmed et al[15]. The incidence of vomiting and drowsiness in diclofenac group are comparable ($p > 0.05$) with the study done by Prabhakar et al.[13]

Conclusion

We conclude that a multimodal approach to post caesarean management with combination of tramadol and diclofenac produced better analgesia than individual drugs and a reduction in the side-effects. Such a combination approach to relieve pain is more effective and advantageous. Further studies are required to evaluate the efficacy in different clinical scenarios and various other drug combinations to be evaluated for better analgesia.

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