*ejpmr, 2020,7(3), 337-341*

**SJIF Impact Factor 6.222**

**EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH**

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

# INJECTABLE TRAMADOL VS DICLOFENAC AS AN ANALGESIC FOR POST-OPERATIVE HYSTERECTOMY

**Dr. Namrata Rajendra Pawar*[1], Dr. Yogita Surendra Karandikar[1] and Dr. Uma Anand Bhosale[2]**

[*1]Junior Resident II, Department of Pharmacology SKNMCGH.
[1]Professor, Department of Pharmacology SKNMCGH.
[2]Professor and HOD, Department of Pharmacology SKNMCGH.

***Corresponding Author: Dr. Namrata Rajendra Pawar**

Junior Resident II, Department of Pharmacology SKNMCGH.

**Article Received on 06/01/2020** **Article Revised on 27/01/2020** **Article Accepted on 17/02/2020**

## ABSTRACT

**Background:** Postoperative pain may be a significant reason for delayed discharge from hospital, increased morbidity, and reduced patient satisfaction. Nowadays opioids are the mainstay in the treatment of acute postoperative pain. Tramadol is an atypical opioid having an additional mechanism by inhibitory reuptake of NA and 5HT. But opioids produce side effects like nausea, vomiting, sedation, pruritis. Diclofenac is a non-selective NSAIDs with good tissue permeability. NSAIDs are particularly effective in cases of somatic inflammatory pain. **Objectives:** We conducted this study to compare the efficacy of Injection tramadol and Injection diclofenac as an analgesic for post-operative patients undergoing Hysterectomy. **Methods:** This was an open-label prospective study that included 60 female patients undergoing hysterectomy aged 20 years and above. Randomly allocated 30 patients were given Tramadol 50 mg IV three times a day and the rest 30 patients were given Diclofenac 75mg IV two times a day. Post-operative pain scores were recorded using the Visual Analog Scale (VAS) and Facial Rating Scale (FRS) at 6,12,24 and 48 hrs respectively and the ASSIST scale was recorded at 24hrs. Statistical analysis was done using unpaired t-test. **Results:** The mean pain score was found less in the diclofenac group compared to the tramadol group at all intervals by VAS and FRS ($p<0.05$). As per ASSIST, patient and caregiver satisfaction score was better in the diclofenac group. Nausea and dizziness were more commonly reported in the tramadol group. **Conclusion:** Diclofenac provides effective and better analgesia in acute post-hysterectomy pain than tramadol with fewer adverse effects.

**KEYWORDS:** Postoperative Pain, Tramadol, Diclofenac, VAS, FRS, ASSIST.

## INTRODUCTION

Pain after surgery is the main concern that a patient has to deal with.[1] It can lead to high morbidity, delay the discharge from hospital as well as reduced patient satisfaction.[2] Pain can be classified as acute or chronic; it is the acute pain that must be dealt with in the immediate postoperative period.[3]

Ideally, postoperative pain should be monitored concurrently during rest (important for comfort) and during movement (important for the functioning and postoperative complication), but this is often not done due to lack of time.[4,5] Post-operative pain management is a major concern following surgery. Abdominal hysterectomy is usually producing moderate to severe pain postoperatively.[2] The different classes of analgesics are used for pain relief; exert their effect through different mechanisms.[6] Opioids and NSAIDs are used for the management of postoperative pain and both the groups have their own pros and cons.

Nowadays opioids are the mainstay for the treatment of postoperative pain but opioids produce side effects like nausea, vomiting, sedation, pruritis and respiratory depression. Tramadol is a centrally acting analgesic that has a moderate affinity for μ receptors and weak kappa and delta-opioid receptors. It is 5 to 10 times less potent than morphine as an analgesic. In addition to μ receptor agonist, tramadol enhances the function of the spinal descending inhibitory pathway by inhibiting neuronal reuptake of 5-hydroxytryptamine and norepinephrine also inhibits the release of 5-hydroxytryptamine.

On the other hand, non-steroidal anti-inflammatory drugs are alternative to opioids as they are devoid of opioid-related side effects, yet provide effective analgesia along with antipyretic and anti-inflammatory action. Diclofenac is a non-selective NSAID belonging to an acetic acid group. NSAIDs inhibit the biosynthesis of prostaglandins by preventing the substrate arachidonic acid from binding to the COX enzyme active site. The COX enzymes are COX-1 and COX-2 isoenzymes. COX-2 expression can be induced by inflammatory

mediators in many tissues and has a role in the mediation of pain, inflammation, and fever. Peripheral blocking of prostaglandin synthesis and central inhibition of COX-2 plays a very important role in nociception.[7]

Pain that accompanies inflammation and tissue injury probably results from local stimulation of pain fibers and enhanced pain sensitivity. NSAIDs are particularly effective when inflammation has caused sensitization of pain. The aim of our study was to compare the efficacy of Injection tramadol and Injection diclofenac as an analgesic for postoperative patients undergoing Hysterectomy. We also aimed to assess the cost-effectiveness between Injection tramadol and Injection diclofenac.

## MATERIALS AND METHODS

This was an open-label prospective, comparative study conducted in gynaecology ward at a tertiary care hospital over a period of one year. 60 female patients aged above 20 undergoing abdominal hysterectomy were included in the study whereas patients who were sensitive to NSAID and opioids, patients who underwent malignancy surgery, patients with a history of chronic pain, peptic ulceration, bleeding disorders, patients with impaired renal or hepatic functions and patients who were not willing to fill consent form were excluded from the study. The Institutional Ethics Committee's permission was obtained beforehand in accordance with the Helsinki Declaration of 1975 that was revised in 2000. [IEC approval no: SKNMC/Ethics/App/2019/512].Written informed consent was provided by every participant at the time of recruitment. Each subject was informed in a detailed and comprehensive manner about the pain assessment scale. Patients fulfilling inclusion criteria were divided into two groups by simple convenient randomization.

- **Group T** (30 patients) – Tramadol 50mg Intravenous every 8 hours for 72 hours.
- **Group D** (30 patients) – Diclofenac 75 mg Intravenous every 12 hours for 72 hours.

All patients were given spinal anesthesia as per standard protocol (bupivacaine 0.5%+ Injection fentanyl 25 mcg) and received diclofenac suppository post-operative immediately followed by Injection tramadol or Injection diclofenac for 2days.

Assessment of pain was done using Visual Analogue Scale (VAS)[8] score, scored 0 to 10 where 0 indicates no pain, whereas 10 indicates 'Worst pain ever' and Facial rating scale (FRS).[9] Adults who have difficulty using the numbers on the visual/numerical rating scales were assisted with the use of six facial expressions suggesting various pain intensities. The patients were asked to choose the face that best describes how they feel. The far-left face indicates 'No hurt' and the far-right face indicates 'Hurts worst', The score was assessed postoperatively in the post-operative recovery room at 6, 12, 24 and 48 hours. ASSISIT[10] score was an objective type of questionnaire which included questions under 3 sub-headings - Pain score, Patients satisfaction score and Caregiver score and was recorded by an observer at 24 hrs postoperatively. Any side effects were carefully noted.

## STATISTICAL ANALYSIS

The data thus collected were tabulated and subjected to unpaired student t-test and analysed with Microsoft Excel office. The confidence limit of the study was kept at 95%, hence a "p" value less than 0.05 indicated a statistically significant association.

## RESULTS

**Table 1: Represents the vas score of both the groups at 6 hrs, 12 hrs, 24 hrs, 48 hrs time intervals. The score was significantly lower in the diclofenac arm up to 24hrs, thereafter scores were comparable between the groups.**

| VAS score | Group T | Group D | P-value |
|---|---|---|---|
| **6 hrs** | 8.3 | 7.53 | 0.008** |
| **12 hrs** | 7.33 | 6.63 | 0.013* |
| **24 hrs** | 5.3 | 4.7 | 0.034* |
| **48 hrs** | 1.33 | 0.9 | 0.079 |

*N=30 each, p<0.05*, p<0.01** when comparison done between groups by Student t-test.*

**Table 2: Represents the FRS score of both the groups at 6 hrs, 12 hrs, 24 hrs, 48 hrs time intervals. Similar to the VAS score, the FRS score was significantly lower in diclofenac arm up to 24hrs, thereafter scores were comparable between the groups.**

| FRS Scale | Group T | Group D | P-value |
|---|---|---|---|
| **6 hrs** | 4.467 | 4 | 0.006** |
| **12 hrs** | 3.933 | 3.566 | 0.017* |
| **24 hrs** | 2.933 | 2.566 | 0.035* |
| **48 hrs** | 0.833 | 0.566 | 0.065 |

*N=30 each, p<0.05*, p<0.01** when comparison done between groups by Student t-test.*

**Table 3: Represents The Mean Assist Score Recorded at 24hrs Postoperatively. The p-values were statistically Significant While Doing Movements or Activities In Bed As Well As out of Bed.**

| ASSIST score 24hr CHARACTERISTICS | Group T | Group D | P-value |
|---|---|---|---|
| **PAIN SCORE** | | | |
| Pain at rest | 4.33 | 3.33 | 0.059 |
| Pain at movement | 6.1 | 5.167 | 0.023* |
| Least pain in last 24 hr | 5.1 | 4.633 | 0.085 |
| Worst pain in last 24 hr | 8.233 | 7.5 | 0.016* |
| Severe pain in last 24 hr (%) | 55 | 49.33 | 0.105 |
| **PAIN SATISFACTION SCORE** | | | |
| Pain while doing activities in bed | 3.76 | 2.766 | 0.046* |
| Pain while doing activities out of bed | 4.4 | 3.133 | 0.007** |
| Falling asleep | 1.533 | 1.6 | 0.887 |
| Staying asleep | 0.9 | 0.533 | 0.202 |
| Pain relief using pain treatment (%) | 60 | 68.66 | 0.108 |
| **CARE GIVERS SCORE** | **6.733** | **7.2** | **0.251** |

*N=30 each, p<0.05*, p<0.01** when comparison done between groups by Student t-test.*

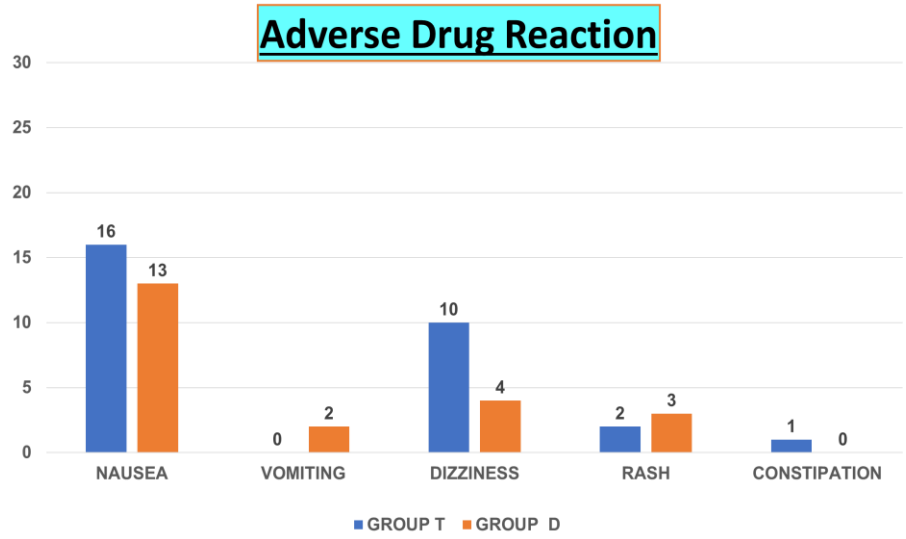


**Figure 1: Represents the adverse drug reactions which we came across during our study period. In the tramadol group, 16 patients experienced nausea, 10 patients experienced dizziness, 2 patients experienced rash and 1 patient experienced constipation. While in the diclofenac group, 13 patients experienced nausea, 2 patients experienced vomiting, 4 patients experienced dizziness and 3 patients experienced rash.**

We also calculated the Cost-Effective Ratio. Cost of Tramadol (50 mg) per patient for 3days treatment was Rs 207 and that of Diclofenac (75mg) was Rs 162. Effectiveness calculated for tramadol and diclofenac was 8.7 and 9.1 respectively. The cost-effective ratio for tramadol was 23.8 and 17.8 in the case of diclofenac, which was also in favor of the diclofenac group. (Table 4)

| Cost-effective Ratio | Cost | Effectiveness | Ratio (rs) |
|---|---|---|---|
| TRAMADOL (50mg) | 207 | 8.7 | 23.8 |
| DICLOFENAC (75 mg) | 162 | 9.1 | 17.8 |

## DISCUSSION

Recently the concept of postoperative pain relief is regarded as a time-dependant maximization of patient's comfort with safer and cheaper analgesics. Of the total surgeries in our hospital, Gynaecological are major contributors.

In our study, we observed, diclofenac was more efficacious up to 24 hrs postoperatively in both the VAS scale and the FRS scale. After 24 hrs efficacy was almost equivalent in both groups. No patient required rescue medication in either of the groups. To strengthen our study we also used the ASSIST score at 24 hrs which was an objective scale, according to this questionnaire pain at movement was comparatively less in the diclofenac group. According to the cost-effective analysis, diclofenac is more cost-effective compared to tramadol.

Shukla AK et all in their study observed that the analgesic effect of diclofenac in 1st 24 hrs is significantly greater than tramadol for postoperative pain[2]. Merrikhihaghi S et al, in their study, has demonstrated the analgesic effect of diclofenac is 3.21 times more cost-effective than tramadol with the same efficiency and for post-cesarean pain.[11] Sahil S et al concluded that the diclofenac suppository provides a better quality of postoperative analgesia as compared to tramadol when used as pre-emptive analgesia.[12] Joshi V et al in their study concluded that diclofenac suppository is a better alternative to tramadol because it has shown a better analgesic effect on postoperative pain[13]

The surgical procedure causes local tissue damage, resulting in the release of inflammatory mediators like prostaglandins, histamine, serotonin, bradykinin, substance P, and other mediators, production of noxious stimuli, and irritation of free nerve endings and nociceptors (nociceptive pain). Diclofenac being an NSAIDS causes inhibition of cyclooxygenase(COX), which catalyzes the formation of prostaglandins from arachidonic acid, this justifies that in postoperative inflammatory conditions diclofenac affords quick relief of pain and wound oedema.[14]

In contrast to this, Kumar, P.R. et al conducted a prospective, randomized comparative study on sixty patients of ASA I & II posted for elective surgery under general anaesthesia concluded intravenous tramadol hydrochloride and diclofenac sodium appears to have equipotent effect as postoperative analgesia.[15] Paudel Rama et al in their study compared the analgesic efficacy of tramadol with diclofenac sodium in patients with postoperative orthopedic pain and concluded that Tramadol has a more pronounced analgesic effect than diclofenac. Thus, tramadol can be considered as an effective alternative to traditional NSAIDs in the treatment of post-operative pain.[16] This could be due to the difference in the baseline pain threshold and type/ intensity of pain between gynaecology surgeries and orthopedic surgeries

There were a few limitations to the study. The sample size we considered was small. This was a short term study so we were unable to assess long term adverse reactions. Also, drugs were given by the same investigator, so blinding was not done.

Diclofenac is a peripherally acting analgesic agent, so the adverse effects were also relatively fewer as compared to tramadol which is a centrally acting agent.

As we had conducted the study in our hospital, and we considered the cost of the drug as per hospital formulary. We found that diclofenac is more cost-effective than tramadol in postoperative inflammatory conditions, the reason behind it is that the efficacy of diclofenac is more than tramadol as mentioned above. The other probable reason being the better compliance of the patient due to twice a day administration of diclofenac.

## CONCLUSION

Diclofenac provides effective and better analgesia in the post-hysterectomy pain than tramadol with fewer adverse effects. Diclofenac is more cost-effective. Also, Diclofenac requires less frequent administration. Though in the majority of hospital setups tramadol is preferred for postoperative pain management, in view of this study results we recommend that, tramadol should be replaced by a cost-effective and efficacious diclofenac therapy for post-operative pain management.

## ACKNOWLEDGMENTS

We would like to acknowledge Dr. Hemant Damle's professor of gynaecology for his support and guidance.

## REFERENCES

1. Farzi F, Naderi Nabi B, Mirmansouri A, et al. Postoperative Pain After Abdominal Hysterectomy: A Randomized, Double-Blind, Controlled Trial Comparing the Effects of Tramadol and Gabapentin as Premedication. *Anesth Pain Med*., 2016; 6(1): e32360. Published 2016 Jan 17. doi:10.5812/aapm.32360
2. Shukla AK, Srivastav AK. Comparative study of tramadol and diclofenac as analgesic for postoperative pain. *Int J Med Res Rev*., 2015; 3(11): 1311-1316. doi:10.17511/ijmrr.2015.i11.238.
3. Khobragade SM. Comparison of intramuscular diclofenac sodium, diclofenac sodium suppository and intravenous tramadol for postoperative analgesia in gynaecological surgeries done under spinal anaesthesia. Int J Res Med Sci., 2018; 6: 3034-41.
4. Ryhänen P, Adamski J, Puhakka K, Leppäluoto J, Vuolteenaho O, Ryhänen J. Postoperative pain relief in children. A comparison between caudal bupivacaine and intramuscular diclofenac sodium.Anaesthesia, Jan, 1994; 49(1): 57-61.
5. Rahman, M.H. and Beattie, J. Managing postoperative pain. Pharmaceutical Journal, July, 2005; 275; 145-8.
6. Pal A, Biswas J, Mukhopadhyay P, Sanyal P, Dasgupta S, Das S. Diclofenac is more effective for post-operative analgesia in patients undergoing lower abdominal gynecological surgeries: A comparative study. *Anesth Essays Res*., 2014; 8(2): 192–196. doi:10.4103/0259-1162.134502
7. Cummings K, Naguib Mohamed A. Stoelting's textbook of pharmacology and physiology in anaesthetic practice: 5th edition; Opioid agonists and antagonists, 2015; 217-241.
8. Hawker, G.A.Mian,S,Kendzerska,T. and French,M. Measures of adult pain:Visual Analog Scale for pain,McGill Pain Questionnaire,Short-Form McGill pain questionnaire, Chronic Pain Grade Scale, Short-Form-36 Bodily pain scale and Measure of Intermittent and Constant Osteoarthritis Pain.Arthritis care Res., 2011; 63: S240-S252.

9. Praveen Kumar, Laxmi Tripathi. Challenges in pain assessment:Pain Intensity Scales., 2014; 28(2): 61-70.
10. Subramanian B, Shastri N, Aziz L, et al. ASSIST - Patient satisfaction survey in postoperative pain management from Indian subcontinent. *J Anaesthesiol Clin Pharmacol*, 2017; 33(1): 40-47.
11. Merrikhihaji S, Farshchi A, Farshchi B, Farshchi S, Dorkoosh FA. Tramadol versus diclofenac in pain management after cesarean section: a cost nalysis study. J pharmacoeconomics and pharmaceutical management, 2015; 1(1): 22-4.
12. Sahil S, Mane M, Paranjape J. Comparison of diclofenac suppository with tramadol suppository for postoperative analgesia in abdominal hysterectomy patients. Medpulse-International medical J., 2017; 4(5): 606-9.
13. Joshi V S, Vyavahare R D, Khade G, Shiledar V, Jamadar N.P.: Comparative study ofanalgesic efficacy ofrectal suppository of tramadol versus diclofenac insuppressing postoperative pain after Cesarean section,International J. of Healthcare and Biomedical Research, 2013; 1(2): 32-37.
14. Málek J, Ševčík P, Bejšovec D. Postoperative pain management.chapter-2 Pathophysiology of acute postoperative pain :10-11Third updated edition Published by: Mladá fronta a. s., Mezi Vodami, 1952/9 143 00 Praha 4
15. Kumar, P.R. & Soumya, S. & Kumar, P.S. & Kumar, J.S.. The effectiveness of intravenous tramadol hydrochloride and diclofenac sodium as postoperative analgesia – A comparative study. International Journal of Pharmaceutical Sciences Review and Research, 2016; 36: 260-263.
16. Paudel, Rama & Deka, Anjali & Gupta, Hemant & Nepal, Hari. Comparative evaluation of analgesic efficacy of tramadol and diclofenac-sodium in post-operative orthopedic patients. International Journal of Basic & Clinical Pharmacology, 2017; 6: 2676.