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Research Paper

ASSESSMENT OF PAIN RELIEF AND TOLERABILITY OF COX - 2 INHIBITORS

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Pain is an unavoidable outcome of every surgery, and most of the time it is sub- optimally treated. Conventional postoperative analgesics are opioids and non-selective NSAIDs, which have moderate to severe adverse effects profile. Parecoxib is the only parenterally administered selective cyclooxygenase-2 inhibitor available. This study was done to assess the pain relief and tolerability of cyclooxygenase-2 specific inhibitor after giving first dose postoperatively. This was a observational and comparative study between parecoxib 40 mg IV and Diclofenac 75 mg IM as postoperative analgesic. After baseline score subsequent scores were taken at an intervals of 30 minutes, 1, 4 and 8 hrs, after administering analgesic. Analgesic efficacy was assessed in terms of mean pain intensity score difference and tolerability assessment was done by monitoring general adverse events. 40 patients were enrolled in the study, 20 patients in each group. Demographic data was similar between two groups. Mean pain intensity score at baseline was 3.35 and 3.36 in parecoxib and Diclofenac group respectively. The difference in pain score between the groups was not significant in total 8 hours of study. Reduction in mean pain intensity upto 50 % was achieved in 30 min and 1 hr in parecoxib and Diclofenac group respectively. At the end of 8 hours, 15 (75 %) patients in parecoxib group experienced 'no pain', while in Diclofenac sodium group it was only with 8 (40 %) patients. Only mild adverse events like nausea, vomiting, and headache were present. The results of the study indicate that selective single dose of COX-2 inhibitor parecoxib sodium 40 mg IV is comparable to single dose of Diclofenac sodium 75 mg IM Both the drugs are found to be equally and well tolerated as single dose postoperative analgesic.

Keywords: Postoperative pain, Opioids, NSAIDs, cyclooxygenase-2 inhibitor.

INTRODUCTION

Postoperative pain is an expected outcome for each person who undergoes surgery, yet biomedical evidence published over the past 30 years indicates that variety of patient populations experience sub optimally treated pain.[1]

Despite the increased attention there is overwhelming evidence that pain in hospitalized patients remains sub optimally treated. This observation is important because pain has clinical, economic and human consequence, such as change in immune system function, decreased healing and diminished ability to function.[2]

Effective treatment of acute pain should be of high agenda of all staff looking after postoperative patient.

The drug therapy for treating postoperative pain involves opioids and non- opioid drugs. Non-opioid drugs mainly consist of non steroidal anti inflammatory drugs (NSAIDs), non selective Cyclooxygenase-1(COX-1)

inhibitors and recently developed selective Cyclooxygenase 2 (COX-2) inhibitors.[3]

The three main types of opioid receptors that have been described so far are μ, δ and κ receptor. In the dosage range typically used to treat patients with acute postoperative pain, μ receptor agonist has no therapeutic ceiling effect. Therefore unlike non-opioid analgesics dosage of these drugs are adjusted upwards until satisfactory pain control is achieved or adverse effect become intolerable.[4]

The adverse effect most commonly associated with opioids are respiratory depression, sedation, nausea, vomiting, constipation, urinary retention and itching. Other adverse effects include confusion, hallucination, nightmares, multifocal myoclonus and dizziness. These effects can adversely affect the ability to recuperate from a surgical procedure. The adverse effects of opioids and the advent of ambulatory surgery with rapid rehabilitation has led to a reappraisal of postoperative pain management and a shift away from reliance on powerful opioids as the sole postoperative analgesics.[5]

The use of NSAIDs is one of the most common non-opioid analgesic approaches currently used for management of postoperative pain. NSAIDs inhibit the COX enzyme, which are involved in the synthesis of prostaglandins responsible for inflammation, pain and fever.[6]

the enzyme COX exist in two iso-forms (COX-1 and COX-2). COX-1 mediates gastric mucosal integrity and renal and platelet function, while COX-2 is expressed after injury to contribute to inflammation and hyperalgesia.[7]

Non-selective NSAIDs blocks both the COX iso-forms (COX-1 and COX-2). Inhibition of COX-1 is associated with gastrointestinal and antiplatelet adverse events.

Parecoxib is the prodrug of valdecoxib, a selective COX-2 inhibitor, developed for parenteral administration. Approved COX-2 selective inhibitors such as, celecoxib, rofecoxib, and valdecoxib are only available for oral administration. Therefore, parecoxib is the novel option for acute postoperative management and may not produce adverse effects associated with non-selective COX inhibitors. In addition, postoperative patients with nausea and vomiting would benefit from an analgesic, anti-inflammatory COX-2 selective inhibitor available via the parenteral route.[8]

Based on phase-III clinical trials in post surgical pain management the effective dose of parecoxib is 20 or 40 mg and can be administered via the intravenous (IV) or intramuscular (IM) routes. Parecoxib has been shown to be safe and effective in all the clinical trials and most of the studies conducted so far.[9]

Cardiovascular risks of COX-2 inhibitor remain controversial, and more recent evidence suggests that rofecoxib and valdecoxib are notorious for causing increasing number of reports of rise in incidence of myocardial

infarction, stroke following prolonged use and since then have been withdrawn from the market by the respective pharmaceutical companies.[10]

Due to very well evident and documented adverse effect profile of the conventional treatment of postoperative pain, which includes opioids and non- selective NSAIDs, there is a need to develop a treatment for safe and equally effective postoperative analgesia. This promoted us to study the pain relief and tolerability of parecoxib sodium in comparison with the conventional analgesic, diclofenac sodium as a postoperative analgesic.[11]

METHODS

The study was conducted at bedded tertiary care hospital equipped with modern diagnostic and treatment facilities. The patients prescribed with Parecoxib sodium and Diclofenac sodium will be identified and a total of 40 patients who met the inclusion criteria will be selected for the study.

Inclusion Criteria

- Patients of either sex undergone general surgery with age group 18 and above
- Patients who were given selective COX-2 inhibitor parecoxib sodium or Diclofenac sodium as their first analgesic for postoperative pain, after recovering from anesthesia.

Exclusion Criteria

- Patient with clinically significant abnormalities on physical and laboratory examination.
- Patients with known hypersensitivity to NSAIDs.
- Patients who had gastric or duodenal ulcers and bleeding tendencies, significant renal impairment, and hepatic impairment.
- Patients on concomitant therapy with drugs such as warfarin, antiepileptics, fluconazole, and ketoconazole.
- Patients not willing to comply with the study procedure.

Methods of Data Collection

Patient data will be collected using a specially designed data collection form, which consist of the patient's demographic data, current medications, laboratory investigation, past medical and medication history will be collected from the patient's progress record, treatment chart, laboratory reports and patient history record.

Pain assessment

Pain assessment was done through Visual Analog Scale (VAS). It is a simple 10 cm horizontal and straight line extending from "no pain" to the extreme limit of pain as defined by several phrases, e.g., "pain as bad as it could possibly be" or "worst pain I have ever experienced" or "the worst pain I could imagine" or "agonizing pain."35

VAS is one of the most frequently used measurement scales in health care research.

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The VAS is most commonly known and used for measurement of pain.

RESULTS

Total 40 patients were taken in the study according to their post operative analgesic, 20 patients in each, parecoxib sodium 40 mg I.V. group and Diclofenac sodium 75 mg I.M. group. Out of 40 patients counseled for postoperative surgery, 8 (20.0%) belonged to lower socio-economic class and 5 (12.5%) belongs to upper socio-economic class. Among the patients recruited for the study, 31(77.5%) patients out of 40 had co-morbid

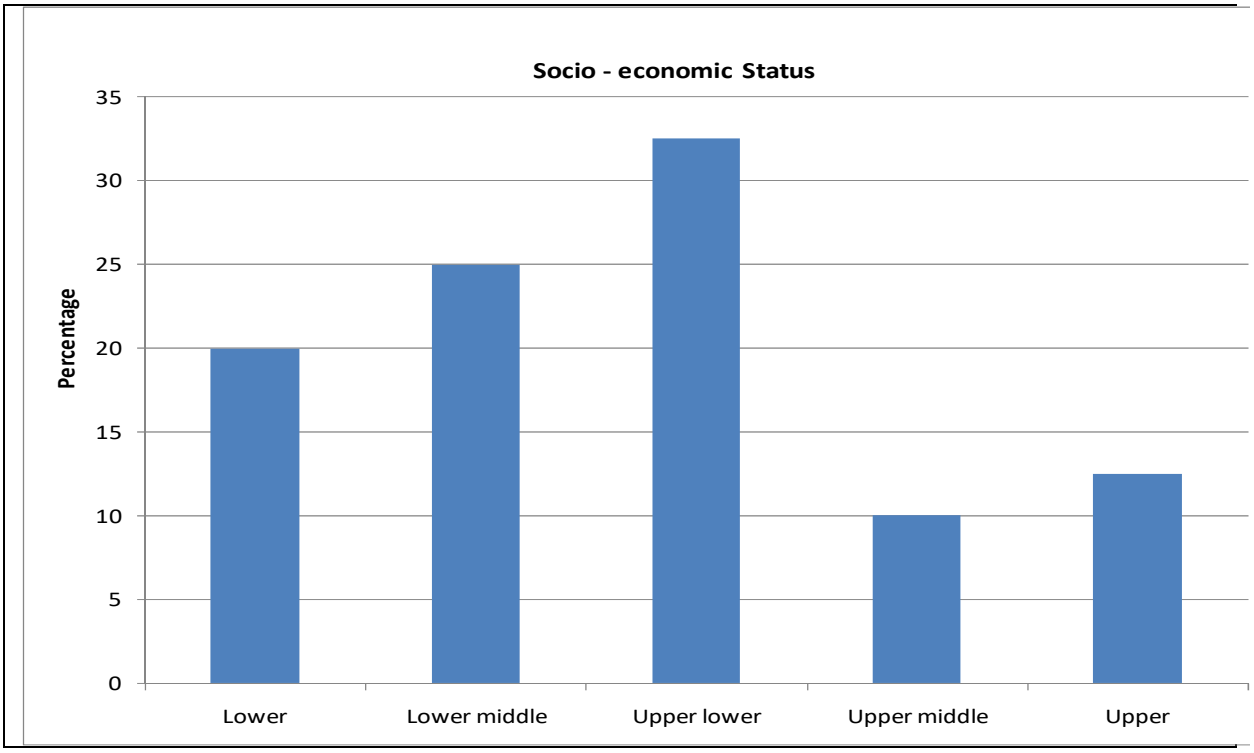

Fig. 1: Patients Socio-economic status treating with Postoperative Analgesics

Table 1: Co-morbid conditions among study population

Number of Co-Morbidities	No of patients	Percentage (%)	Overall Percentage (%)
Single	29	27.4	55.7
Double	15	14.2	
Triple	12	11.3	
More than 3	3	2.8	
None	47	44.3	44.3
Total (N)	106	100	100

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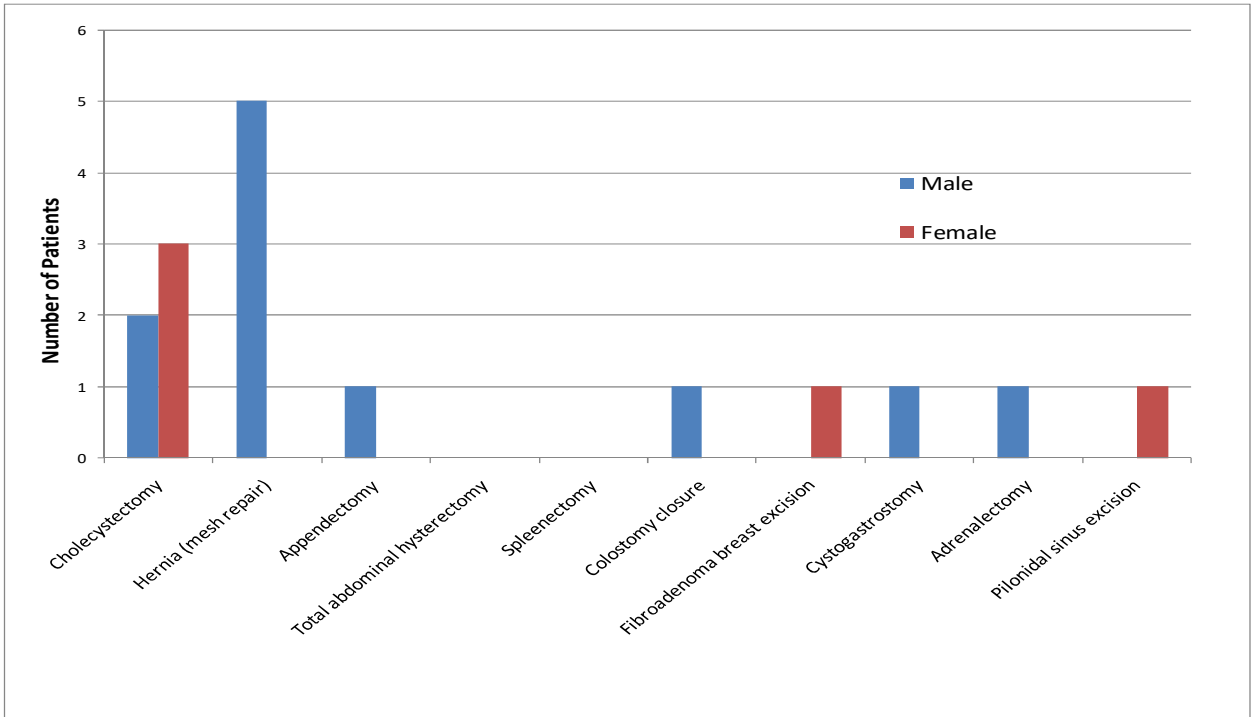

Fig. 2: Use of Parecoxib Sodium in different type of Surgery

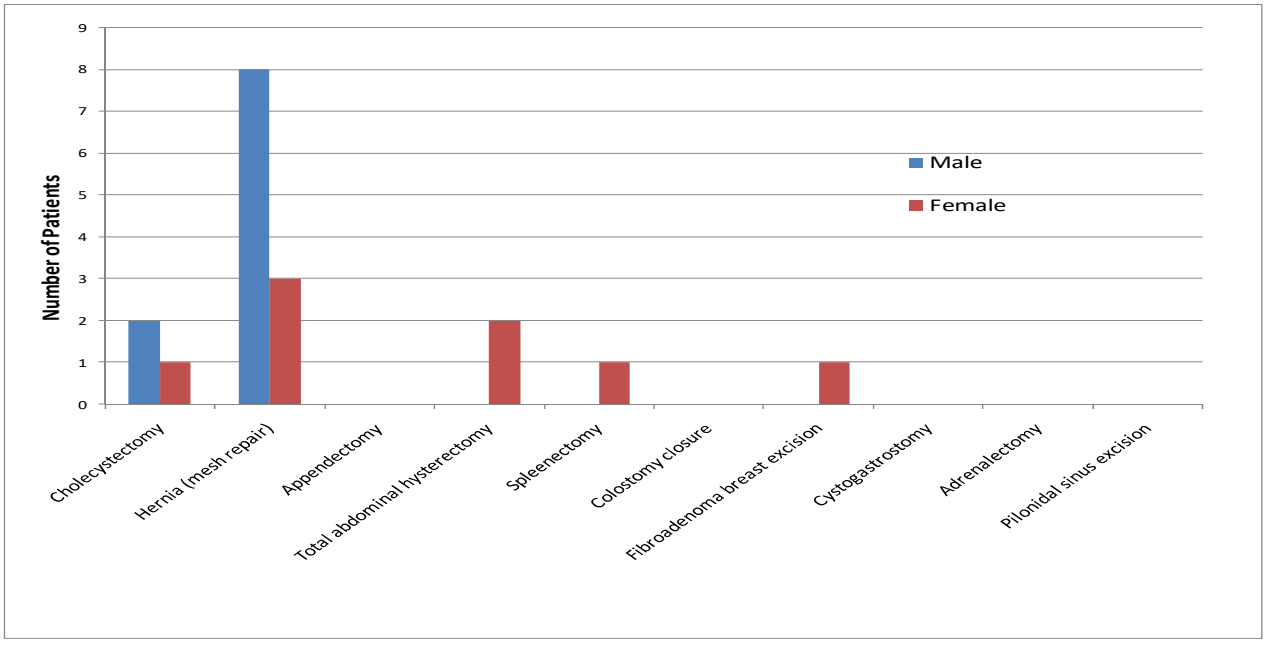

Fig. 3: Use of Diclofenac Sodium in different type of Surgery

conditions. The details of co-morbid condition are shown in Table 9. Majority of patients [18(45.0%)] had a single co-morbid condition, followed by 10 (25.0%) and 3 (7.5%) exhibiting double and triple co-morbid conditions respectively.

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Different types of surgeries performed and postoperative analgesic use is described in the below mentioned table.

Mean pain intensity score at baseline in parecoxib sodium group was 3.35 and in Diclofenac sodium group was 3.6 which did not differ significantly. The difference in pain score between the groups was not significant in total 8 hours of study.

After treatment, at 30 minutes mean pain score showed a reduction of 55.23 % with parecoxib sodium and 26.38 % with Diclofenac sodium. At the end of 1 hour, fall was 79.1 % in parecoxib sodium group and 54.16 % in Diclofenac sodium from baseline. At the end of 4 hours and 8 hours, fall in parecoxib sodium group was 89.55% and 92.53 % from baseline respectively, and similarly in Diclofenac group fall in pain intensity was 83.33 % and 80.55 % at the end of 4 hours and 8 hours from the baseline respectively.

Reduction in mean pain intensity up to 50%, in parecoxib sodium group was achieved in 30 minutes whereas the same was achieved in Diclofenac sodium group in 1 hour.

An increase in mean pain intensity score was observed in Diclofenac sodium group at 8th hour assessment compared to 4th hour assessment.

After taking first pain score representing the baseline score, the patients were administered analgesics. First pain score after administering the analgesic was taken after 30 minutes, subsequent scores were taken at an intervals

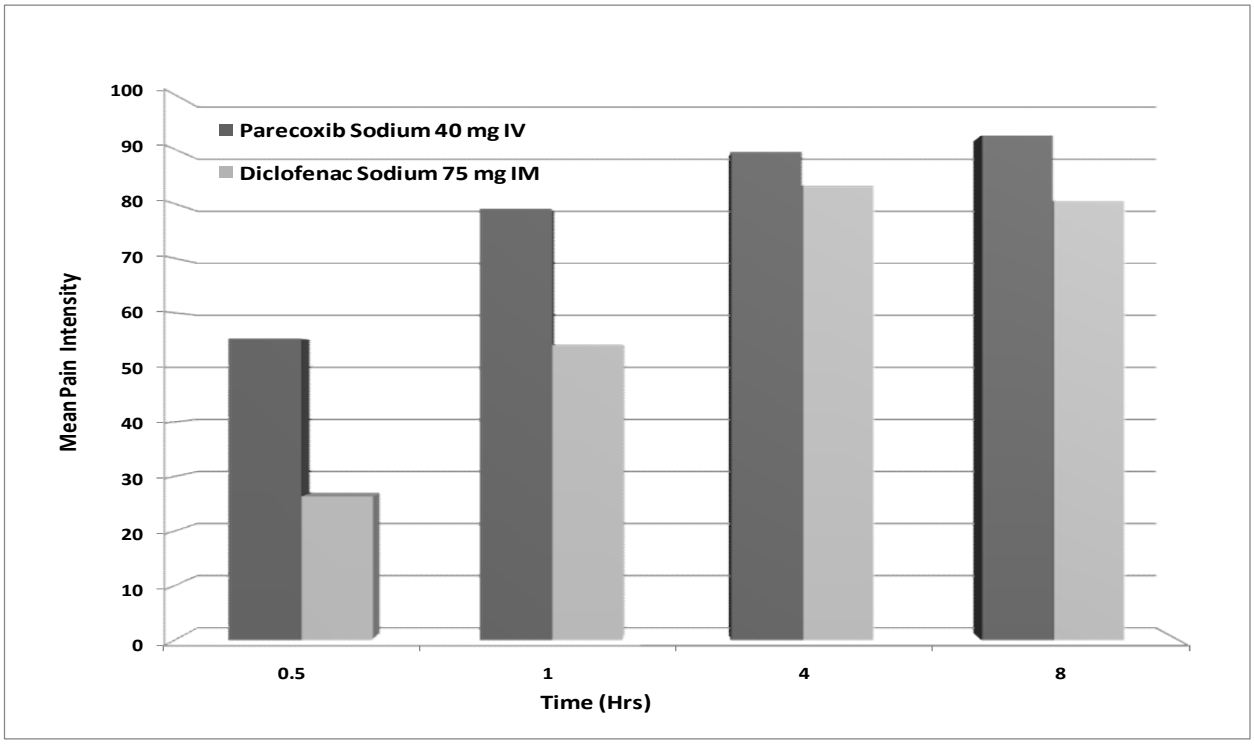

Fig. 4: Percentage fall in pain intensity from base line

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Table 2: Pain at the time of 0.0 hours

Nature of pain	Parecoxib sodium (n=20)	Diclofenac sodium (n=20)
No pain	0	0
Little	6	0
Some	4	9
Mild	8	10
Moderate	1	1
Severe	1	0
Agonizing	0	0

Table 3: Pain at the end of 0.5 hours

Nature of pain	Parecoxib sodium (n=20)	Diclofenac sodium (n=20)
No pain	0	0
Little	12	0
Some	6	9
Mild	2	9
Moderate	0	2
Severe	0	0
Agonizing	0	0

Table 4: Pain at the end of 1.0 hours

Nature of pain	Parecoxib sodium (n=20)	Diclofenac sodium (n=20)
No pain	7	1
Little	12	6
Some	1	12
Mild	0	1
Moderate	0	0
Severe	0	0
Agonizing	0	0

Table 5: Pain at the end of 4.0 hours

Nature of pain	Parecoxib sodium (n=20)	Diclofenac sodium (n=20)
No pain	13	9
Little	7	10
Some	0	1
Mild	0	0
Moderate	0	0
Severe	0	0
Agonizing	0	0

Table 6: Pain at the end of 8.0 hours

Nature of pain	Parecoxib sodium (n=20)	Diclofenac sodium (n=20)
No pain	15	8
Little	5	10
Some	0	2
Mild	0	0
Moderate	0	0
Severe	0	0
Agonizing	0	0

from the time of taking baseline scores, of 1 hr, 4 hr and 8 hrs.

At the end of 0.5 hours, 12 (60 %) patients who received parecoxib sodium 40 mg IV experienced 'Little pain', while in Diclofenac sodium group there was no patient in this category. At the end of 1.0 hours, 7 (35 %) patients who received parecoxib sodium 40 mg IV

experienced 'no pain', while in Diclofenac sodium group it was only 1 patient.

At the end of 4.0 hours, 13 (65 %) patients who received parecoxib sodium 40 mg IV experienced 'no pain', while in Diclofenac sodium group it was only 9 (45%) patient.

At the end of 8 hours, a good number, 15 (75 %) patients who received parecoxib sodium 40 mg IV experienced 'no pain', while in Diclofenac sodium group it was only with 8 (40 %) patients.

50 % of the total patients in Diclofenac sodium group complained 'little pain' after 8 hours of treatment while only 25 % of the patients who received parecoxib sodium complained 'little pain'.

No patients in the either group asked for rescue analgesic during the 8 hour pain assessment.

CONCLUSION

The results of the study indicate that selective single dose of COX-2 inhibitor parecoxib sodium 40 mg IV is comparable to single dose of Diclofenac sodium 75 mg IM. Both the drugs are found to be equally and well tolerable as single dose of postoperative analgesic. Additional studies involving larger number of patients will be needed to clearly validate the safety of selective COX-2 inhibitor parecoxib with regard to platelet, renal, and gastrointestinal effects.

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