ABSTRACT: Post-operative pain management has been a constant challenge to many of the surgeons. There is a need for developing newer modalities which can provide good analgesia with fewer side effects. A randomized clinical trial was designed with a sample size of 60 patients, which were divided into two groups. These were randomized to receive intramuscular diclofenac sodium injection (Group A) or diclofenac diethylamine transdermal patch (Group B) after 1 hour from the time of spinal anaesthesia. Statistical analysis was done using UNPAIRED t-test and Mann-Whitney test. It was concluded that diclofenac diethylamine transdermal patch is effective in the management of post-operative pain after inguinal hernia mesh repair. Pain scores were significantly lower in diclofenac patch group. Meantime of rescue analgesia is longer in diclofenac patch group. Demand for rescue analgesia is lower in diclofenac transdermal patch group. However there is a need for broader studies to confirm the above results.

KEYWORDS: Post-operative pain, NSAID's, Diclofenac transdermal patch.

INTRODUCTION: Despite recent advances in the treatment of post-operative pain, it remains one of the prevalent problems in health care today. Most patients receive some form of post-operative pain management, yet it is estimated that approximately 50% to 75% of patients have inadequate pain relief.\(^1\) It is of prime concern to the surgeon and the patient alike because it causes considerable anxiety, adds to the patients suffering and increases the hospital stay and morbidity.

Nonsteroidal anti-inflammatory drugs (NSAID's) are among the most widely used therapeutic classes of analgesic compounds.\(^2,3,4,5\) Unfortunately, while NSAID’s are effective at relieving the pain, they carry the potential for significant adverse reactions that can affect the gastrointestinal tract, liver and Kidneys.\(^5,7,6,9\)

Transdermal systems are an innovative delivery mechanism commonly replacing oral dosage forms and other traditional forms of administration. The drug contained on the transdermal patch enters the body through the skin in contact with the patch.\(^10,11\)

It is designed for the continuous and systemic release of diclofenac following its application to an intact skin it contains diclofenac diethylamine as the active ingredient. Transdermal patch is designed to remain at the site of the application for 24 hours. The device
has been evaluated in osteo-arthritis, musculo-skeletal dis-orders and gynecologic surgery induced post-operative pain and has demonstrated similar efficacy to the oral tablets.\textsuperscript{12, 13, 14} The patches have shown excellent safety profile, adverse local reactions at the site of the application have been mild and transient (Redness, itching).\textsuperscript{15}

This study elaborates by effectiveness of diclofenac transdermal patch as compared that of conventional intra muscular diclofenac injections in the management of post-operative pain.

\textbf{MATERIAL & METHODS:} This study was done on cases of inguinal hernia planed for mesh repair under spinal anaesthesia in a surgical unit of a tertiary care hospital over a period of one year. After obtaining approval from the institutional ethics committee, written informed consent was taken from all the patients who are included in the study.

\textbf{Design of the Study:} Randomized clinical trial of 60 cases.

All adult patients (more than 18 years) undergoing Inguinal Hernia Mesh Repair under spinal Anaesthesia were included.

Patients with allergative NSAID’s/ to other components of transdermal patch, any signs of strangulation or obstructed hernia, emergency/Non elective surgery, Analgesic usage 6 hours prior to scheduled surgery time, any history of hepatic or renal disease, any history of active peptic ulceration within last 6 months, pregnant or lactating women, surgery under Epidural or General Anaesthesia were excluded from the study.

\textbf{The sample size of 60 was randomized into 2 groups as follows:}

\textbf{Group A:} 30 patients received injection diclofenac sodium 75mg IM, one hour after administering spinal anaesthesia.

\textbf{Group B:} 30 patients received diclofenac transdermal patch 100mg, containing diclofenac diethylamine BP 100mg with an absorption area of 50 cm. Sq, one hour after administering spinal anaesthesia.

Postoperative pain measurement was done using 10cm visual analogue scale (VAS) and postoperative pain scores was noted after 2\textsuperscript{nd}, 4\textsuperscript{th}, 6\textsuperscript{th}, 12\textsuperscript{th}, 18\textsuperscript{th} and 24\textsuperscript{th} hour after surgery. During the entire 24 hours postoperative period the patient will receive rescue analgesic (Injection Butrophanol 2mg IM) only if the pain score is more than 5 cm and adverse effects were also recorded on the proforma. These two groups were also compared in terms of adverse effects like skin irritation, itching, rashes, erythema, induration, potential of the patch to adhere to the applied area in diclofenac transdermal patch group and pain at the injection site, dyspepsia, abdominal pain, nausea, vomiting etc in intramuscular diclofenac sodium injection.

\textbf{Statistical Analysis:} Unpaired t-test-Mean pain scores.

Mann-Whitney test- amount of rescue analgesia consumed.

\textbf{OBSERVATION AND RESULTS:} At the end of the study the whole data was analyzed. All subjects were males except one subject was female in group A as inguinal hernia is rare in females.
**Table 1: Age distribution of the patients**

<table>
<thead>
<tr>
<th>Age in years</th>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;18 years</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>18-25</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>26-35</td>
<td>5</td>
<td>9</td>
</tr>
<tr>
<td>36-45</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>46-55</td>
<td>11</td>
<td>6</td>
</tr>
<tr>
<td>56-65</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>&gt;65 years</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Mean</td>
<td>41.3</td>
<td>38.8</td>
</tr>
<tr>
<td>S D</td>
<td>15.03</td>
<td>15.39</td>
</tr>
<tr>
<td>p-value</td>
<td>0.527</td>
<td></td>
</tr>
</tbody>
</table>

Mean age in group-A was 41.3 years and mean age in group-B is 38.8 years. Statistical analysis was done with chi-square test. P-value was 0.527 which was not significant. Indirect inguinal hernia were more common than direct inguinal hernia i.e., about 68.33% cases.

Length of the incision in group A was ranging from 6.5 cm to 9.5 cm with a mean length of incision was 7.5 cm and SD of 0.8066, in group B the length of incision was 6.5 cm to 10 cm with a mean length of incision was 7.9 cm and SD of 0.8137.

Mean time of rescue analgesia in group A was 7.455 hours and standard deviation of 2.536 hours and in group B was 17.397 hours, standard deviation of 4.990 hours. Data analyzed using statistical tests has been represented in the table below:

**RESULTS:**

<table>
<thead>
<tr>
<th>Mean</th>
<th>Group A</th>
<th>Group B</th>
<th>Analysis</th>
<th>P value</th>
<th>Statistical Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>41.3±15.03</td>
<td>38.8±15.39</td>
<td>unpaired t-test</td>
<td>0.5269</td>
<td>No</td>
</tr>
<tr>
<td>Length of incision (cm)</td>
<td>7.657±0.768</td>
<td>7.913±0.847</td>
<td>unpaired t-test</td>
<td>0.2238</td>
<td>No</td>
</tr>
<tr>
<td>2nd hour (VAS)</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
<td>-</td>
</tr>
<tr>
<td>4th hour (VAS)</td>
<td>1.527±1.373</td>
<td>0.27±0.837</td>
<td>unpaired t-test</td>
<td>0.001</td>
<td>Yes</td>
</tr>
<tr>
<td>6th hour (VAS)</td>
<td>3.391±1.476</td>
<td>0.77±1.271</td>
<td>unpaired t-test</td>
<td>&lt;0.001</td>
<td>Yes</td>
</tr>
<tr>
<td>12th hour (VAS)</td>
<td>3.467±1.0693</td>
<td>1.32±1.052</td>
<td>unpaired t-test</td>
<td>0.003</td>
<td>Yes</td>
</tr>
<tr>
<td>18th hour (VAS)</td>
<td>-</td>
<td>2.594±1.407</td>
<td></td>
<td></td>
<td>-</td>
</tr>
<tr>
<td>24th hour (VAS)</td>
<td>-</td>
<td>2±1.758</td>
<td></td>
<td></td>
<td>-</td>
</tr>
<tr>
<td>Time of rescue analgesia (HRS)</td>
<td>7.455±2.54</td>
<td>17.4±4.99</td>
<td>unpaired t-test</td>
<td>&lt;0.001</td>
<td>Yes</td>
</tr>
<tr>
<td>Dose of rescue</td>
<td>1.429±0.504</td>
<td>0.933±0.37</td>
<td>Mann-Whitney</td>
<td>0.0024</td>
<td>Yes</td>
</tr>
</tbody>
</table>
DISCUSSION: Dealing with post-op pain remains an arena for never ending research with better formulations and modalities rapidly replacing the obsolete ones. Clinician perpetually strives for an analgesic modality which provides profound analgesia and best tolerability to the patient and hence ensuring patient compliance. The pain in the postoperative period demands relief not only on humanitarian grounds but also to reduce the physical morbidity following the surgery. Opioids and NSAID’s still remain as the cornerstone in the treatment of postoperative pain. Because of their side effects most of the analgesic dosage is inadequate. There is need for developing newer modalities which can provide good analgesia with fewer side effects.

In our study we observed that newly developed diclofenac diethylamine transdermal patch is effective and safe in the treatment of postoperative pain relief after inguinal hernia meshplasty. Patients receiving diclofenac diethylamine transdermal patch had statistically significant reduction in pain scores as compared to that of intramuscular diclofenac injection group. The mean time of rescue analgesia is significantly longer in patients receiving diclofenac diethyamine transdermal patch.

In terms of safety, the diclofenac diethylamine transdermal patch was well tolerated and did not lead to systemic side effects. Minor adverse reactions like erythema, induration seen in 5 patients and peeling off the patch was seen in 3 patients. Adverse effects were minor which did not warrant any special care. However, we did not calculate the cost effectiveness between the two groups.

Topically applied NSAID’s are effective in decreasing both acute and chronic pain, they inhibit prostaglandin synthesis, and decrease the inflammatory response. Topical NSAID’s offer the advantage of enhanced local drug delivery to the affected tissues with a lower incidence of adverse systemic effects as a result of decreased plasma concentrations.\(^{15}\) In addition, topical NSAID’s have been associated with a lower incidence of gastrointestinal adverse effects compared with systemic administration of these medications.\(^{16}\)

There was a study to evaluate the pharmacokinetic profile of new matrix-type transdermal delivery system: diclofenac diethylamine patch. The patches were subjected to in vitro permeation enhancement studies through rat skin using a specially designed diffusion cell. The pharmacokinetic parameters calculated from blood levels of drug reveal of profile similar to a sustained-release formulation, with ability to maintain adequate plasma levels of 24 hours (i.e., upto the next application). Author concludes that the amount of drug bioavailable for targeting the sites of action is lower than oral route, but the absorbed dose appears to be adequate for therapeutic use, particularly because of the absence of side effects.

There was a study to investigate the clinical efficacy and safety of a newly developed diclofenac patch in the topical treatment of blunt impact injuries. This was a randomized, placebo
controlled, double blind, multicentre study in 120 patients with traumatic blunt soft tissue injury. They found that the diclofenac patch was significantly effective than placebo, the patch produced rapid pain relief as reflected by the time to reach resolution of pain at the injured site which was significantly shorter compared to placebo. The patch was well tolerated. The most frequently observed adverse events were cutaneous adverse reactions (pruritus, rash) of minor severity occurring with the frequency as in the placebo group.¹

There was a study to compare pain management of standard analgesic and Standard analgesic plus diclofenac transdermal patch in patients who undergo laparoscopic gynecologic surgery. Author concluded that diclofenac transdermal Bhninistration seems a valid help to standard analgesic treatment in postoperative pain control and could also help to reduce the period of hospitalization of patients who undergo laparoscopic benign gynecological surgery.¹²

Topical preparations of NSAIDs have also been tested in various clinical trials arc they were found to have a therapeutic role in minimizing chronic or acute.¹⁷,¹⁰,¹⁵,¹⁸ The plasma concentrations achieved by the topical or the transdermal listration of NSAIDs is considerably lower than that produced by oral NSAIDs.¹⁹ But the lower plasma concentration also led to a lower incidence of systemic adverse effects. Hence, the topical NSAIDs have carved out a niche for themselves as therapeutic analgesic modalities with established benefits and lower incidence of adverse events.

Through our study proved that diclofenac transdermal patch is effective in management of postoperative pain, there are certain limitations. Pain being multifactorial the assessment and conclusion of any intervention involving it is difficult. It is therefore required to conduct broader and multi-setting trails to confirm the above findings.

CONCLUSION: This randomized clinical trial comparing the effectiveness of transdermal diclofenac patch and intramuscular diclofenac injection in postoperative pain relief after inguinal hernia mesh repair concludes that.

Diclofenac diethylamine transdermal patch is effective in the management of postoperative pain after inguinal hernia mesh repair. Pain scores were significantly lower in diclofenac diethylamine transdermal patch group when compared to that of intramuscular diclofenac injection group. Mean time of rescue analgesia is longer in diclofenac diethylamine transdermal patch group. However, we did not calculate the cost effectiveness between the two groups. Diclofenac patch was well tolerated and was patient friendly.

Pain being multi-factorial, the assessment and conclusions of any intervention involving it is difficult. It is therefore required to conduct broader and multi-setting trials to confirm the above findings.

BIBLIOGRAPHY:

AUTHORS:
1. P. Ravikumar Reddy
2. Rajashekar S. B.
3. Karthik U. S.

PARTICULARS OF CONTRIBUTORS:
1. Assistant Professor, Department of Surgery, VIMS, Bellary.
2. Assistant Professor, Department of Surgery, VIMS, Bellary.
3. Post Graduate, Department of Surgery, VIMS, Bellary.

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:
Dr. P. Ravikumar Reddy,
Assistant Professor,
Department of Surgery,
VIMS, Bellary.
E-mail: draviredyy@gmail.com

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