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Transdermal Diclofenac Patch versus Intra Muscular Diclofenac Injection for the Management of Pain in the Post Operative Patients in a Teritiary Teaching Institute

Chaitanaya[1], Karri Naga Venkata Harish[2]

Author's Affiliation: [1]Assistant Professor, [2]Post Graduate, Department of Anesthesia, Maharajah's Institute of Medical Sciences, College of Allied Health Sciences, Vazhayoor, Karad, Malappuram 673633, Kerala, India.

Corresponding Author: Karri Naga Venkata Harish, Post Graduate, Department in Anesthesiology, Maharajah's Institute of Medical Sciences, Vizianagaram, Andhra Pradesh 535217.

E-mail: drharish34@gmail.com

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Abstract

Background: Pain management in immediate postoperative period is an extremely important but herculean task. As oral medication is not possible at this stage, it is injectable analgesia which is put to task. In countries like India, where efficacy and cost both count, intramuscular diclofenac is the most commonly employed analgesic.

Methodology: The study was cross sectional by using questionnaire in 80 healthy adult subjects of either sex undergoing Hernia correction surgery under spinal anaesthesia. The subjects were assigned into two groups (Group I and Group P) by computer generated randomization table to receive intramuscular diclofenac 75mg or transdermal diclofenac patch 100mg immediately after spinal anaesthesia. The patients were monitored for pain using Visual Analogue Scale. Duration of analgesia and request for rescue analgesic (Tramadol 2mg/kg) were noted in both the groups. The study ended when patients had a VAS > 8 or at first request for analgesic.

Result and Conclusion: It was concluded that if applied with proper planning, diclofenac patch was as effective as diclofenac injection but at the same time administration of patch is devoid of pain, local side effects, drug destruction by stomach and digestive enzymes and first pass metabolism in liver.

Keywords: Diclofenac; Transdermal Patch; Intra Muscular Injection; Postoperative analgesia; Hernia surgeries.

Introduction

Pain is defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage.[1] Pain, an important cause of post-operative complications, results in poor mobility, increased arterial pressure and myocardial work which may result in increased morbidity or mortality following surgery.[2]

Post operative pain is a unique and common form of acute pain. Although ample evidence indicates than an efficacious post operative pain treatment reduces patient morbidity and improves patient outcome, recent studies demonstrate that about 50–70% of patients experience moderate to severe pain after surgery indicating that post operative pain remains poorly treated. The management of post operative pain is an essential and integral part of care given to the patient that assumes an important role in transition from the recovery unit to the home environment.[3,4]

Peripheral tissue injury as seen in post operative patients provokes two kinds of modification in the responsiveness of nervous system-peripheral

sensitization and central sensitization resulting in an overall hypersensitivity state in the post operative period. Prevention and establishment of this hypersensitivity state could lead to reduced post operative pain, which forms the basis of pre-emptiveanalgesia.[5,6] Opioids have been administered for hundreds of years to allay anxiety and to reduce the pain associated with surgery. Though they are very useful in relieving post-operative pain, they are associated with many side effects.[7] There is a need to reduce peri-operative opioid consumption.[8,9]

Non-steroidal anti-inflammatory drugs exert anti-inflammatory and analgesic effects through the inhibition of prostagland in synthesis, by blocking the activity of cyclo-oxygenase.[10,11] They have been shown to have opioid sparing effects.[12,13,14] Diclofenac is a well established non-steroidal anti-inflammatory agent but the commonly used intramuscular route is associated with patient resentment, pain on injection, peak to trough variability. The transdermal route of diclofenac delivery, which is recently introduced in India appears to be an attractive alternative in view of better patient acceptance, avoidance of first pass hepatic metabolism, sustained absorption and bio-availability and reduced incidence of systemic side effects. However due to its prolonged onset time, it may not be useful for treatment of acute pain but can be used as pre-emptive analgesic to reduce post-operative pain.

The advantages of transdermal diclofenac patch over the orally administered drug are evaluated in acute blunt injuries, sports injuries,[15] osteoarthritis[16] etc, but pre-emptive use of transdermal diclofenac patchin reducing post-operative pain has not been much studied. Hence the present study was undertaken in patients undergoing elective lower abdominal surgery like hernia repair,under spinal anaesthesia with an objective to evaluate the efficiency of transdermal diclofenac patch against the routinely used intramuscular diclofenac injection for post-operative pain relief.

Transdermal patch

Composition

Components of a transdermal diclofenac delivery system are:

1. release liner-protects the patch during storage and is removed before its use;
2. drug-drug solution in direct contact with the release liner;
3. adhesive-adheres the components of the patch together and sticks the patch to the skin;
4. membrane-controls the release of the drug from reservoir and multi-layer patches;
5. backing laminates-protects the patch from the environment;
6. Permeation enhancers.

Methods

The present prospective randomised clinical study was conducted in a teaching hospital attached to a medical college to evaluate transdermal diclofenac patch as pre-emptive analgesic compared to intramuscular drug in providing post-operative pain relief. Institutional ethical committee approval was taken. Data was collected in pre-tested proforma meeting the objectives of the study.

Inclusion Criteria: Normal adult patients of either sex between 20–60 years admitted for hernia correction surgeries done under spinal anesthesia.

Exclusion Criteria:

1. Pregnant females.
2. Patients posted for emergency surgeries.
3. Patients with co-morbid diseases like diabetes, hypertension,neurological, psychiatric or neuro-vascular disorders.
4. Patients having absolute contra indication for spinal anesthesia like raised intra cranial pressure, severe hypovolemia, bleeding diathesis and local infection.

Adult subjects in the age group between 20 years and 60 years of either sex belonging to ASA class I and class II posted for elective hernia repair surgeries without any co-morbid diseases are grouped randomly by computer generated numbers into 2 groups with 40 patients in each group.

Group I: Received intramuscular injection of diclofenac 75mg after giving spinal anesthesia at the beginning of the surgery.

Group P: Received a transdermal patch of diclofenac 100mg after giving spinal anesthesia at the beginning of the surgery.

Pre-operative assessment was done for each patient and written informed consent was taken. All the patients were pre-medicated on the night before surgery with Tablet Ranitidine 150mg and Tablet Alprazolam 0.5mg. Monitoring was done using

multi parameter monitor having pulseoximetry, ECG, NIBP and SPO_2. Intra venous fluids were administered through an 18G intra venous cannula.

Under aseptic precautions,with the patient in the lateral position,lumbar puncture was performed by the consultant anesthesiologist at the level of L3 – L4 through a mid line approach using 25G Quincke spinal needle and 3 ml of bupivacaine 0.5% heavy was injected after confirmation of needle tip in the subarachnoid space by free and clear flow of CSF. Subjects were made to lie down in the supine posture immediately with the table kept flat horizontally and supplementary oxygen was given.

After confirming the adequate level of sensory blockade for surgery, (level of 10^{th} thoracic dermatome at the level of umbilicus) after spinal anesthesia, transdermal diclofenac patch was applied on lateral aspect of contralateral thigh in patient in Group P and intramuscular diclofenac 75mg (3ml) was injected in the contra lateral gluteal region in the patients in Group I.

The following parameters are noted,

1. Time of administration of spinal anesthesia
2. Time of beginning of surgery
3. Time of administration of study drug and route

All subjects were monitored during the surgery and peri operative period till complete sensory and motor recovery employing multi parameter monitors which displays heart rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), ECG and SPO_2.

In the post operated period,Patients were asked to assess their post-operative pain on a visual analog scale using different facial expressions to grade the severity of pain from a scale of 0–10 where score 0 represents a very happy patient with no pain and score 10 representing hurting as much as we can imagine. Quantitative measurement of pain was done on visual linear analogue scale at:

1. Immediately after extubation
2. 4 hours after operation
3. 8 hours after operation
4. 12 hours after operation
5. 24 hours after operation.

At any time during the study, if visual analog scale is more than or equal to 8, then an intramuscular injection of tramadol 2mg /kg was administered as a rescue analgesia , and the study ended. The time at which rescue analgesia is given is noted.

Statistical Analysis

Data was entered in excel format and analysed using SPSS version 17, descriptive statistics like frequency, proportions were calculated.

Results

The age and sex difference was also not significant in the two groups. The mean age in group I was 45.34±13.64 and Group P was 46.40±12.46 years.

Table 1: Visual analogue score post operatively.

Visual Analogue Score	Group I	Group P
Before surgery	1.87±0.70	1.91±0.45
Immediately after extubation (Mean ± S.D.)	3.28 ± 0.72	3.26 ± 0.83
At 4 hour (Mean ± S.D.)	3.36 ± 0.68	3.42 ± 0.56
At 8 Hour (Mean ± S.D.)	6.86± 0.98	6.82 ± 1.02
At 12 Hour (Mean ± S.D.)	3.42 ± 0.78	3.64 ± 0.87
At 24 Hour (Mean ± S.D.)	3.34 ± 0.89	3.09 ± 0.73

Pain was assessed on VAS and was found that pain scores in both the groups were at their peak at or around 8 hours. Mean time of first supplement dose requirement in group A was 7.12 hours and in group B was 7.56 hours. The p value calculated came out to be non-significant (Table 1 and 2).

Table 2: Average time of first supplemental dose required post operatively.

Group	Time
I	7.12 Hours
P	7.56 Hours

Discussion

With the increase in understanding of pain pathophysiology and treatment, new routes of drug delivery are being discovered with the objective of blocking pain at peripheral sites, with maximum active drug and minimal systemic effects. Topical preparations are the result of such exploration. The goal of topical NSAIDs is to minimize systemic adverse effects and encourage compliance. Most topical preparations are available as transdermal patches, ointments or creams.

Acute pain in the perioperative setting is defined as pain that is present in a surgical patient because of pre-existing disease, the surgical procedure or a combination of disease related and procedure related sources.[17] Traditionally opioids have been the main-stay of acute postoperative pain management. They provide excellent analgesia. However they are not suitable for treatment of

somatic pain due to peripheral tissue injury. They are also associated with adverse outcomes like respiratory depressions, cardiovascular depressions, post-operative nausea and vomiting, impairment of bowel function, urinary retention, pruritus etc.

Hence there is a need to reduce perioperative opioid analgesic requirement, without compromising analgesia component. Several modalities have been tried to provide pre emptive perioperative pain relief which can reduce dependence on opioids. Some of them are regional anesthesia/analgesia, peripheral nerve block, field block, NSAIDs, alpha 2 adrenergic agonists etc.

Non steroidal anti inflammatory drugs (NSAIDs) are among the most widely used medications in the world because of their demonstrated efficacy in reducing pain and inflammation.[18] Their efficacy has been documented in a number of clinical disorders, including osteo-arthritis, rheumatoid arthritis, ankylosing spondylitis, gout, dysmenorrhea, dental pain and headache.[19–24]

The basic mode of action is inhibition of pro inflammatory enzyme cyclo-oxygenase (COX). Although effective at relieving pain and inflammation, NSAIDs are associated with a significant risk of serious gastro intestinal adverse events and potential cardio vascular side effects.[25,26]

An evidence based update on NSAIDs in 2007, has shown the NSAIDs to have pre-emptive effects and reduce post-operative analgesic and opioid requirement. Also this update noted that the parenteral route (intramuscular or intra venous) had the same risks of gastro intestinal toxicity as the oral route and that the NSAIDs given by the topical route are an exception as they are not associated with any gastro intestinal effects.[27]

Of the many NSAIDs available, diclofenac through intramuscular route, is commonly used in our institution for relief of post-operative pain. Systemic administration can lead to fluctuations in pain control levels and gastro-intestinal complications.

Absorptions of the drug is faster leading to rapid achievement of maximum plasma concentration followed by steep decline in plasma concentration of the drug. This manifests as rapid onset of analgesia which however is not sustained. Intramuscular injections are painful and resented by many patients.[28]

A newer route of diclofenac administration is now available with introduction of transdermal diclofenac patch. The transdermal drug delivery offers several advantages as it avoids the need for intravenous or intramuscular drug administration, and is an option in patients who are unable to swallow oral medications.

Transdermal drug administration also by-passes first pass metabolism in the liver[29] and overcomes concerns regarding drugs that are poorly absorbed in the gastro intestinal tract.

Application of diclofenac patch was shown to reduce the incidence and severity of post-operative sore throat[30] and succinyl choline induced myalgia in patients after ceaserian delivery under endotracheal general anaesthesia.[31]

Transdermal diclofenac sodium patch, which delivers the drug into systemic circulation through the skin, has been shown to produce higher pain tolerance and no gastro intestinal complications as compared to oral administration.[32] Transdermal diclofenac sodium patch has been shown to achieve better bioavailability with no marked peak to trough fluctuations.

The diclofenac transdermal patch bioavailability is approximately 1% that of oral diclofenac, with an elimination half-life of 12 hours.[33] The pharma cokinetic profile and systemic and local absorption of diclofenac following dermal patch application in Yokshire-Landrace pigs showed that it resulted in high tissue penetration and low systemic absorption.[34]

Topical diclofenac patch is shown to be effective and safe for the treatment of acute blunt impact injuries.[15] Galer et al conducted a multi-centre controlled clinical trial and showed that diclofenac patch is an effective and safe pain reliever for sports injury pain and the advantages of this novel therapy includes its ease of use and lack of systemic side effect. In the post operative setting, due to the long onset duration, this may be useful when applied in anticipation of pain, and not after the patient experiences the pain.[35]

Krishna et al. studied the analgesic effects of transdermal diclofenac patch in patients undergoing elective lower limb orthopaedic surgery under spinal anaesthesia.[36]

Allesandri et al compared pain management of standard skin medication plus a diclofenac transdermal patch and standard skin medication alone at all incisional areas in the patients who underwent laparoscopic gynaecologic surgery. They demonstrated that the diclofenac transdermal patch reduced post-operative analgesic requirements and hospital stay.[37]

Safinaz et al,[38] showed that the diclofenac patch and intramuscular injection were equally effective in the prevention of post-operative pain after laparoscopic surgery under general anaesthesia and that transdermal diclofenac patch was superior to intramuscular diclofenac injection for patient tolerance.

In our study, The two groups were comparable in terms of age and sex distribution. The duration and nature of surgery were also similar in both the groups. Krishna and Natraj conducted a study to compare the efficacy of single dose of diclofenac patch with diclofenac injection as a pre emptive post-operative analgesia.[36] The pain was assessed postoperatively at 2, 6 and 12 hrs postoperatively on VAS. The study ended when patients asked for rescue analgesia or VAS >5. The mean duration of analgesia in control group (injection group) was 7hr 28min and the study group was 8hr 6min (patch group) which was comparable to our study.

In the present study no local cutaneous or systemic adverse reactions were observed for transdermal diclofenac patch. This supports the previous findings that the lower plasma concentration achieved with topical NSAIDs application is associated with reduction in systemic adverse effects.

Conclusion

Diclofenac sodium patch is as efficient as Diclofenac sodium intramuscular injection in terms of analgesia when applied timely. Patch being advantageous over injection in having lesser local side effects likes skin erythema, pruritus, oedema, abscess and necrosis. In addition, transdermal systems are non-invasive and can be self-administered. They also improve patient compliance and are generally inexpensive. It is also an option in patients who are unable to swallow oral medications or in whom oral route is to be avoided due to GIT pathologies.

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