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COMPARATIVE STUDY IN MANAGEMENT OF POST OPERATIVE PAIN WITH DICLOFENAC PATCH VERSUS DICLOFENAC INJECTION

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ABSTRACT

Adequate management of post operative pain has been a goal of all surgeons since the advent of surgery. Over the decades the endeavour has been to find an ideal analgesic with minimal or no side effects. This ideal analgesic is still elusive. The most terrible period postoperatively is the first 24 hours when severity of pain and vital signs are fluctuating. If patients are kept pain free during this period, they can cope with the circumstances well, leading to early recovery. In this study we compared the analgesic effects of diclofenac transdermal patch (100mg)-Nupatch and diclofenac intramuscular injection (75mg) in the management of post operative pain, to observe the efficacy, duration, quality of analgesic effect on visual analogue scale and to observe any adverse effects of diclofenac patch and diclofenac injection in short term use.

Keywords: *Transdermal Patch, Nupatch, Postoperative Analgesia, Intramuscular Injection*

INTRODUCTION

The word pain is derived from the latin ‘poena’ meaning punishment, a penalty, or tourniquet. It is defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage (Hughes, 2008).

The most frequent indication of any kind of surgery is to relieve the patient of some type of pain. A large majority of the patients who seek medical attention and subsequently undergo surgical operation do so because of the compelling influence of pain. Therefore, it seems paradoxical that a surgeon, in accomplishing his or her mission of relieving pre-operative pain, induces pain in the early postoperative period which, usually, is much more severe than the original complaint.

Pain, is an important cause of post operative complications. Excessive pain result in poor mobility, increased arterial pressure and myocardial work which may result in increased morbidity or mortality following surgery (Chaturvedi, 1987).

Effective postoperative pain control is an essential component of the care of the surgical patient. Various types drugs are used for postoperative analgesia, of which narcotics and NSAIDS are the most important ones. Narcotics are known to cause drowsiness, constipation, urinary retention, haemodynamic and respiratory disturbances as compared to minimal side effects by NSAIDS. Diclofenac is one of the most commonly used NSAID. Oral administration is the route of choice in daily practice but it becomes impractical before and after surgery because of high first pass metabolism. Its parenteral preparation is irritating and hence it is very painful at the site of administration. Development of skin, subcutaneous and even muscle tissue necrosis (Nicolau syndrome), abscess formation, etc. are rare but serious complications of intramuscular injections of NSAIDS (Lie *et al.*, 2006). As the understanding of pain pathophysiology and treatment is increasing, new routes of drug delivery are being discovered with the objective of attempting to block pain at peripheral sites, with maximum active drug and minimal systemic effects. Topical (Transdermal) preparations are the result of such exploration, which are expected to be free of the drawbacks of oral, parenteral diclofenac. Administration is also very simple, noninvasive and only once in 24 hrs (Prausnitz *et al.*, 2004; Scheindlin, 2004).

Transdermal Patch

Composition

The main components of a transdermal drug delivery system are:

- Release liner—protects the patch during storage and is removed before its use;

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- Drug—drug solution in direct contact with the release liner;
- Adhesive—adheres the components of the patch together and sticks the patch to the skin;
- Membrane—controls the release of the drug from reservoir and multi-layer patches;
- Backing laminates—protects the patch from the environment;
- Permeation enhancers.

Diclofenac patch has been in a use for a long time now. Predel *et al.* in 2004 used diclofenac patch for acute traumatic blunt soft tissue injuries and they found that the diclofenac patch was effective, well tolerated and reported no significant adverse events with diclofenac when compared to placebo.

Allesandri *et al.*, (2006) in their study on one hundred twenty patients requiring laparoscopic surgery for gynecologic benign diseases found that the rate of discharge in patients receiving diclofenac patch was comparable to patients receiving standard analgesia.

Lionberger and Brennan in 2010 studied the efficacy of diclofenac patch in treating pain due to soft tissue injury and found that topical NSAID is clinically effective in treating acute pain due to soft tissue injuries, producing clinical benefit within several hours of the first application and significant pain relief relative to placebo

So Overall, transdermal drug delivery offers compelling opportunities to address the low bioavailability of many oral drugs; the pain and inconvenience of injections; and the limited controlled release options of both.

Aim of our study was to compare diclofenac transdermal patch with standard diclofenac injection in terms of:-

1. Post operative analgesia
2. Side effects
3. Cost effectiveness
4. Patient compliance

MATERIALS AND METHODS

100 patients undergoing surgery in the department of General Surgery at Sri Guru Ram Das Institute of Medical Sciences and Research, Amritsar were selected randomly and were divided into two groups of 50 patients each.

Group A: Received diclofenac transdermal patch (100 mg) one hour before end of surgery.

Group B: Received intramuscular injection of Diclofenac sodium (75 mg) half an hour before end of surgery



Figure 1: Diclofenac Patch (Nupatch)

Inclusion Criteria

Patients of age group 10-70 yrs with major surgical operations including cholecystectomy, hernial repair, open prostatectomy, radical cystectomy, pyelolithotomy, pyeloplasty, nephrectomy, modified radical mastectomy, ano-rectal surgeries like fistulectomy and haemorrhoidectomy.

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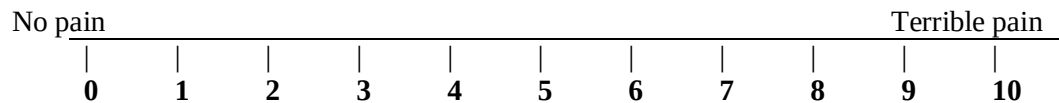
Exclusion Criteria

1. Pregnant women
2. Mentally confused or mentally handicapped patients
3. History of allergy to drug
4. Severe kidney disease
5. Patients with neuropathies or nerve injuries
6. Patients with pain due to cause, other than presenting disease
7. Age <10 years and >70 years

Assessment

The selected patients were examined, thoroughly investigated and explained about the interpretation of visual linear analogue scale to determine the level of pain during the postoperative period. This was carried out with a 10 cm line marked on paper. The end marked with zero would mean no pain and other end marked 10 would mean maximum pain. Pain score was interpreted as follows:

- 1-3 cm - Mild pain
- 4-6 cm - Moderate pain
- 7-10 cm - Severe pain



Quantitative measurement of pain was done on visual linear analogue scale at:

- Immediately after extubation
- 4 hours after operation
- 8 hours after operation
- 12 hours after operation
- 24 hours after operation

In addition to recordings of Pain score; pulse rate, blood pressure, respiratory rate & temperature, were considered. Besides this, the timing of the rescue analgesia (VAS score>5) in the form of additional dose or additional other analgesic required was also noted.

Observations

For better comparison the number of patients of a particular operation was kept same in both the groups. The age and sex difference was also not significant in the 2 groups. The mean age in group A was 46.46 ± 12.413 and Group B was 46.30 ± 12.329 years with $p = 0.949$

Table 1: Visual analogue score postoperatively

Visual analogue score	Group A (n=50)	Group B(n=50)	t value	p value
Before surgery	$1.78 \pm .648$	$1.80 \pm .535$	-0.168	.867
Immediately after extubation (Mean $\pm$ S.D.)	3.14 ± 0.833	3.10 ± 0.735	.255	.800(NS)
At 4 hour (Mean $\pm$ S.D.)	3.20 ± 0.700	3.26 ± 0.633	-.450	.654(NS)
At 8 Hour (Mean $\pm$ S.D.)	6.26 ± 1.006	6.16 ± 1.095	.476	.635(NS)
At 12 Hour (Mean $\pm$ S.D.)	3.24 ± 0.687	3.46 ± 0.788	-1.488	.140(NS)
At 24 Hour (Mean $\pm$ S.D.)	3.44 ± 0.951	3.18 ± 0.748	1.520	.132(NS)

S- Significant; NS- Non – Significant; S.D. – Standard Deviation

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Duration of surgery was comparable in the two groups with no significant difference.

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 7.21 hours and in group B was 7.43 hours. The p value calculated came out to be 0.128 which is non significant.

Table 2: Average Time of First Supplemental Dose Required Postoperatively

Group	TIME	T value	p value
Group A	7.21 HOUR		
Group B	7.43 HOUR	1.1399	0.128

So both diclofenac patch and diclofenac injection have same analgesic efficacy with diclofenac patch being advantageous over injection group in having lesser skin side effects, only in 2% of the patients as compared to 14% in injection group.

Table 3: Incidence of adverse effects postoperatively

	Group A	Group B	
Absent	49(98%)	43(86%)	92
Present	1(2%)	7(14%)	8
Total	50	50	100



Figure 2: Diclofenac Injection Adverse Effects

DISCUSSION

As the understanding of pain pathophysiology and treatment increases, new routes of drug delivery are being discovered with the objective of attempting to block 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.

Based on contents, there are two primary types of analgesic patches:

1) **Patches containing** counterirritants-contain ingredients such as capsaicin, methyl salicylate, camphor, or menthol, which are thought to mask pain signals by causing other sensations (itching, warmth, or cooling) in the areas they are applied to.

2) **Patches containing narcotics or NSAIDs**- e.g. fentanyl, Buprenorphine and diclofenac patch.

In the present study two modes of diclofenac analgesia i.e. Transdermal and intramuscular were compared. A total of 100 patients in all were divided into 2 groups of 50 patients each. The various

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parameters recorded postoperatively were; Pulse Rate, Blood Pressure, Respiratory Rate, Temperature, and Intensity of pain on VAS (visual analogue scale) at 0, 4, 8, 12, 24hr. Score of 5 or more on VAS was considered to represent the need of rescue analgesia (tramadol 2mg/kg). The mean time at which first rescue analgesia administered in study group was 7hr 21min and in control group was 7hr 43min which is comparable. Study group (patch) had advantage over control in being almost free of deleterious local side effects like skin erythema, pruritis, oedema, abscess, necrosis etc and secondly patch is easy to use as compared to injection. These results of the present study are comparable to the studies performed earlier by many workers in terms of efficacy and side effects of diclofenac patch.

Hsieh *et al.*, in 2010 studied the efficacy and side effects of diclofenac patch in treatment of patients with myofascial pain syndrome of trapezius. In this study diclofenac sodium patches were compared with control menthol patches in randomized, double blind, placebo-controlled trial and the treatment to control ratio was 2:1. Efficacy and safety parameters were assessed before the patch was applied (day 0), three days (day4) and seven days after (day8). The findings in this study demonstrated that treatment with diclofenac patch produced significantly greater pain reduction and earlier mobilization of involved muscles than similar treatment with a control menthol patch and the most frequently observed adverse effects in either group was skin irritation and erythema: with 16%–18% in the control group and 3%–6% in the treatment group. So in overall diclofenac sodium patch was superior to placebo in terms of reducing VAS scores and improving functional outcomes, and did not cause significant adverse effects.

Krishna and Natraj in 2012 conducted a study on 60 patients, randomly divided into 2 groups of 30 each to compare the efficacy of single dose of diclofenac patch with diclofenac injection as a pre-emptive post-operative analgesia. Diclofenac patch 100mg was applied at the start of surgery in study group and diclofenac injection 75mg was given intramuscularly half an hr before the end of surgery in control group. The pain was assessed postoperatively at 2, 6 and 12 hr 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 6 min (patch group) which was comparable. The various studies support our study in terms of efficacy and side effects of transdermal patch. Only thing of concern is its slow onset of action after application, so it has to be applied in anticipation to pain and not after the pain sets in. The other minor problem that we faced during the study was poor adhesiveness. The patch would loosen and peel off when applied in summers (due to sweating) or to loose mobile skin parts of the body such as arms or gluteal region. So from the above discussion it is clear that 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 like skin erythema, pruritis, 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.

Conclusion

Diclofenac sodium patch is as effective as Diclofenac sodium intramuscular injection in providing post-operative analgesia. Only concern about patch is that it has longer onset of action, so if applied by proper planning; patch has many advantages as listed below:-

- Self administration and self termination.
- Having lesser local side effects like skin erythema, pruritis, oedema, abscess and necrosis.
- Drugs avoid first pass metabolism in the liver as drugs enter the systemic circulation directly
- Useful when patients cannot swallow.
- Useful even before and after surgery.
- Useful even if the patient is nauseous or vomiting.
- Drug destruction by stomach and digestive enzymes does not occur.

Precautions We Should Take While Using

➤ Do not apply more or fewer patches or apply patches more often than prescribed by your doctor.

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- Do not apply diclofenac patches to skin that is broken, damaged, cut, infected, or covered by a rash.
- Do not wear a patch while bathing or showering. Plan to bath or shower after you remove a patch and before you apply the next patch.
- Do not apply to hairy skin

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