Original Article

"RANDOMIZED CONTROLLED STUDY ON EFFICACY OF DICLOFENAC SODIUM PATCH IN WOMEN WITH LOW BACK PAIN"

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ABSTRACT

Background: For the treatment of pain disorders including low back pain, nonsteroidal anti-inflammatory medications (NSAIDs) are frequently utilized. They come in several forms (such as transdermal, suppository, and oral). Simple processes can be used to deliver oral formulations; nevertheless, It is important to consider when to dose in relation to meals as it is typically advised not to take them without food. Furthermore, older adults frequently experience difficulty swallowing due to muscle weakening, which may make the administration of oral formulations contraindicated in this population. Rectal suppositories allow for quick absorption of drugs (via the rectal mucosa) independent of meal consumption and are safe to use even in elderly people.

Methodology: The present study is randomized double blinded controlled conducted in the department of Pharmacology and in association with Orthopedics in patients with low back pain after taking informed voluntary consent in the age group 30-60 years. The patinets with low back pain were randomly allocated into D (diclofenac patch) group and P (placebo) group. The study consisted of a 1-week washout period, a 1-week observation period, and a 2-week treatment period. After a 1-week washout of the prior analgesic treatment (NSAID or acetaminophen), during the observation period patients applied two placebo patches once daily for 1 week in a single-blind manner. Acceptable sites of application included the chest, abdomen, upper arm, upper and mid back, low back, and thigh. In principle, a different site from that used on the

previous day was to be used. Patients assessed their low back pain daily from the start of the washout period until the end of the study by using a 100-mm VAS.

Results: In the present study we enrolled total of 100 patients with low back pain, these patients were randomly allocated into two groups group D and group P consisting of 50 subjects in each group. The mean age in D group was 54.6±12.42 and in P group was 56.42±11.24 respectively. In D group 22 were males and 28 were females and in P group 20 were males and 30 were females. The 3 day VAS scores in D and P group were 62.24±10.98 and 61.42±11.68 respectively. Patient satisfaction at the start of the treatment were assessed, it is found that 12 patients were satisfied in D group and 15 were satisfied in P group. Efficacy outcome at one week and two weeks were assessed using 3 day VAS scores, it is evident that the VAS scores were decreased at one week and two weeks in both the groups, but in the D group it was statistically significant compared to the P group.

Conclusion: In the present study, the patients with low back pain, diclofenac sodium patch 75 mg administered once daily for 2 weeks has an adequate analgesic effect and is well tolerated. This systemically acting patch can be safely administered even to patients with trouble swallowing or who are at risk of aspiration without regard to the effect of food on drug absorption. Unlike locally acting formulations, the patch need not always be applied to the target site, so dosing is simple and the burden is not on one area of the skin. These advantages of the diclofenac sodium patch may make it a novel systemic NSAID option for pain control in low back pain.

Key words: diclofenac sodium patch, non-steroidal anti-inflammatory drugs, low back pain and placebo.

INTRODUCTION

For the treatment of pain disorders including low back pain, nonsteroidal anti-inflammatory medications (NSAIDs) are frequently utilized [1, 2, 3]. They come in several forms (such as transdermal, suppository, and oral) [4-6]. Simple processes can be used to deliver oral formulations; nevertheless, it is important to consider when to dose in relation to meals as it is typically advised not to take them without food [7]. Furthermore, older adults frequently experience difficulty swallowing due to muscle weakening, which may make the administration of oral formulations contraindicated in this population [8,9]. Rectal suppositories allow for quick absorption of drugs (via the rectal mucosa) independent of meal consumption and are safe to use even in elderly people [10].

Furthermore, certain patients—particularly the elderly or those with limited daily functioning—often require assistance from a caregiver to inject rectal suppositories, which can cause them to feel burdensome and uncomfortable. Transdermal formulations can be used even by individuals who have trouble swallowing pills because they circumvent the impact of food on drug absorption [6]. Compared to oral formulations, all currently available transdermal NSAID formulations have a significantly lower potential for gastrointestinal and other toxicities; however, they act locally and must always be applied to the target site, which increases the risk of physical skin irritation (such as contact dermatitis) from repeated application and, in the case of the patch, removal [11].

Topical versions of several NSAIDs have been made available, including ibuprofen cream/gel, piroxicam patch/cream, ketoprofen gel, and diclofenac preparations. There hasn't been much research done on topical formulation efficacy comparisons. Nonetheless, diclofenac has been the subject of the greatest research when it comes to musculoskeletal conditions. Topical diclofenac is thought to lessen inflammation by inhibiting the COX isoenzymes, which in turn reduces the production of prostaglandins that promote inflammation. It's unclear exactly how topical diclofenac works as an analgesic. Diclofenac may function as a sodium channel blocker to mediate local anesthetic-like effects on nociceptive afferent fibers at high tissue concentrations. Diclofenac has been available in several different topical formulations, available in different jurisdictions. These include diclofenac sodium 1% gel, diclofenac diethylamine gel 1.16%, MIKA diclofenac spray 4% gel, diclofenac DMSO lotion, and diclofenac epolamine (diclofenac hydroxyethyl-pyrrolidine) patch. Metabolism of diclofenac occurs primarily in the liver, and the majority is eliminated in the urine. In healthy volunteers, the mean terminal elimination half-life was 88.4 hours.

The diclofenac sodium patch enables transdermal absorption of the drug and therefore can be administered even in patients who have difficulty swallowing or are at risk of aspiration, and without regard to the effect of food on its absorption. This formulation allows the drug to be distributed via the systemic circulation to the location where an analgesic effect is required. Therefore, unlike locally acting formulations, the patch need not be applied to the target site, so dosing is simple and the burden is not on one area of the skin. These advantages of the diclofenac sodium patch, which are lacking in existing NSAID formulations, may make it a novel systemic NSAID option for the control of pain disorders such as low back pain [11]. The present study was undertaken to assess the efficacy of diclofenac sodium patch versus placebo using VAS score in patients with low back pain.

OBJECTIVES OF THE STUDY

The objective of the present study is to assess the efficacy and safety of diclofenac sodium patch in patients with low back pain using VAS scores.

METHODOLOGY

The present study is randomized double blinded controlled conducted in the department of Pharmacology and in association with Orthopedics in patients with low back pain after taking informed voluntary consent in the age group 30-60 years.

Study design: randomized controlled study: The study consisted of a 1-week washout period, a 1-week observation period, and a 2-week treatment period. After a 1-week washout of the prior analgesic treatment (NSAID or acetaminophen), during the observation period patients applied two placebo patches once daily for 1 week in a single-blind manner. Acceptable sites of application included the chest, abdomen, upper arm, upper and mid back, low back, and thigh. In principle, a different site from that used on the previous day was to be used. Patients assessed their low back pain daily from the start of the washout period until the end of the study by using a 100-mm VAS. The study protocol did not include the use of rescue medication for pain during the study. At the end of the observation period, each patient was assessed for eligibility by the investigator. Those confirmed to be eligible by the investigator and the participant enrolment centre were formally

enrolled and randomized by dynamic allocation in a 1:1 ratio to receive diclofenac sodium patch 75 mg, diclofenac sodium patch 150 mg, or placebo patch, respectively.
Sample size: we included a total of 100 patients with lower back pain.
Inclusion criteria: we included a total of 100 patients with lower back pain of both genders, they were randomly allocated into two groups D group and P group in the ration of 1:1. Group D received 75 mg diclofenac patch and Group P received placebo.

Assessment of analgesia

Pain was assessed by visual analogue score (VAS). VAS consists of a 10-cm line anchored at one end by a label such as" No pain'' and at the other end by a label such as the "Worst Pain Imaginable".

Linear Visual Analog Scale Score

VAS Score	**Intensity of pain**
0 – 2	No pain to slight pain
2 – 5	Mild pain.
5 – 7	Moderate pain.
7 – 9	Severe pain.
10	Worst possible pain.

Duration of complete analgesia was defined as the time from the intrathecal injection to VAS >0 - <4 and duration of effective analgesia as the time to VAS >4. Analgesics were avoided until demanded by the patient and the time taken for the first pain medication was also noted (ie, when VAS >6) VAS was also recorded 3, 6, 12 hours postoperatively.

STATISTICAL ANALYSIS

The demographic data were analyzed using either Student's t-test or Chi-square test. Quantitative data was analyzed by student's t test and qualitative data was analyzed by Chi-square test. All values were expressed as mean ± standard deviation. $P < 0.05$ was considered statistically significant.

RESULTS

Table 1: Demographic profile of the patients		
	Group D	Group P
Age	54.6±12.42	56.42±11.24
Gender		
Males	22	20
Females	28	30
3 day VAS score, mm	62.24±10.98	61.42±11.68
Patient satisfaction at the start of treatment		

Very satisfied or Satisfied	12	15
Not satisfied	38	35

Table 2: Efficacy outcomes at one week and 2 weeks		
	Group D	Group P
3 day VAS score, mm	62.24±10.98	61.42±11.68
3 day VAS score from baseline to week 1	50.24±9.88	55.6±10.23
3 day VAS score from baseline to week 2	42.64±9.78	51.23±9.86
Patient satisfaction at the start of treatment		
Very satisfied or Satisfied	32	22
Not satisfied	18	28
Global improvement rating at 2 weeks		
Improved/Much Improved	35	29
Not improved	15	21

DISCUSSION

In the present study we enrolled a total of 100 patients with low back pain, these patients were randomly allocated into two groups group D and group P consisting of 50 subjects in each group. The mean age in D group was 54.6±12.42 and in P group was 56.42±11.24 respectively. In D group 22 were males and 28 were females and in P group 20 were males and 30 were females. The 3 day VAS scores in D and P group were 62.24±10.98 and 61.42±11.68 respectively. Patient satisfaction at the start of the treatment were assessed, it is found that 12 patients were satisfied in D group and 15 were satisfied in P group. Efficacy outcome at one week and two weeks were assessed using 3 day VAS scores, it is evident that the VAS scores were decreased at one week and two weeks in both the groups, but in the D group it was statistically significant compared to the P group.

Concerning safety, no AEs were much more frequent in patients treated with the diclofenac sodium patch at either dose than in those receiving the placebo patch. All of the administration site reactions were characteristic for the use of patches and were of mild intensity. Diclofenac sodium patch is a systemically acting formulation of diclofenac sodium that need not always be applied at the target site, unlike locally acting formulations. Because it can be applied randomly to accessible skin sites, occurrence of administration site reactions is less likely to require discontinuation of its use. The other AEs reported in patients treated with diclofenac sodium patch were AEs that are known from existing formulations of diclofenac sodium. Gastrointestinal, hepatic, renal, and cardiovascular AEs that are of special concern with NSAID use [were not more frequent (i.e., not C 2% more frequent) in patients treated with diclofenac sodium patch at 75 or 150 mg/day than in those receiving placebo. Most of the reported AEs were of mild intensity, and no serious AEs occurred. These results indicate that there are no clinically significant safety concerns with daily treatment with diclofenac sodium patch for 2 weeks [12-14] . Diclofenac sodium patch, which is

designed to enable transdermal absorption of the drug, may cause fewer gastrointestinal AEs oral formulations because, unlike oral formulations, the drug is not taken up into gastrointestinal mucosa. The way in which different routes of administration affect the incidence of gastrointestinal toxicities remains to be studied in the future.

Our study has certain limitations like smaller sample size, and different doses of diclofenac sodium patch were not assessed, as this study assessed only 75 mg.

CONCLUSION

In the present study, the patients with low back pain, diclofenac sodium patch 75 mg administered once daily for 2 weeks has an adequate analgesic effect and is well tolerated. This systemically acting patch can be safely administered even to patients with trouble swallowing or who are at risk of aspiration without regard to the effect of food on drug absorption. Unlike locally acting formulations,

the patch need not always be applied to the target site, so dosing is simple and the burden is not on one area of the skin. These advantages of the diclofenac sodium patch may make it a novel systemic NSAID option for pain control in low back pain.

REFERENCES

1. Koes BW, van Tulder M, Lin CW, Macedo LG, McAuley J, Maher C. An updated overview of clinical guidelines for the management of non-specific low back pain in primary care. Eur Spine J. 2010;19(12):2075–94.
2. Oliveira CB, Maher CG, Pinto RZ, et al. Clinical practice guidelines for the management of nonspecific low back pain in primary care: an updated overview. Eur Spine J. 2018;27(11):2791–803.
3. Wong JJ, Cote P, Sutton DA, et al. Clinical practice guidelines for the noninvasive management of low back pain: a systematic review by the Ontario Protocol for Traffic Injury Management (OPTIMa) Collaboration. Eur J Pain. 2017;21(2):201–16.
4. Altman R, Bosch B, Brune K, Patrignani P, Young C. Advances in NSAID development: evolution of diclofenac products using pharmaceutical technology. Drugs. 2015;75(8):859–77.
5. Lipscomb GR, Rees WD. Gastric mucosal injury and adaptation to oral and rectal administration of naproxen. Aliment Pharmacol Ther. 1996;10(2): 133–8.
6. Leppert W, Malec-Milewska M, Zajaczkowska R, Wordliczek J. Transdermal and topical drug administration in the treatment of pain. Molecules. 2018;23(3):681.
7. Martinez MN, Amidon GL. A mechanistic approach to understanding the factors affecting drug absorption: a review of fundamentals. J Clin Pharmacol. 2002;42(6):620–43.
8. Aslam M, Vaezi MF. Dysphagia in the elderly. Gastroenterol Hepatol. 2013;9(12):784–95. esophageal dysphagia. Expert Opin Drug Deliv. 2016;13(5):645–58.
9. Kappelle WF, Siersema PD, Bogte A, Vleggaar FP.Challenges in oral drug delivery in patients with esophageal dysphagia. Expert Opin Drug Deliv. 2016;13(5):645–58.
10. De Boer AG, De Leede LG, Breimer DD. Drug absorption by sublingual and rectal routes. Br J Anaesth. 1984;56(1):69–82.
11. Ball AM, Smith KM. Optimizing transdermal drug therapy. Am J Health Syst Pharm. 2008;65(14):1337–46.

12. Marce´n B, Sostres C, Lanas A. NSAID and gastrointestinal risk. Aten Primaria. 2016;48(2):73–6.
13. Cooper C, Chapurlat R, Al-Daghri N, et al. Safety of oral non-selective non-steroidal anti-inflammatory drugs in osteoarthritis: what does the literature say? Drugs Aging. 2019;36(Suppl 1):15–24.
14. Prescott LF. Liver damage with non-narcotic analgesics. Med Toxicol. 1986;1(Suppl 1):44–56.