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Original Article

A Prospective Study on Comparison of Transdermal Diclofenac Patch with Oral Diclofenac as An Analgesic Modality in the Treatment of Knee Osteoarthritis

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ABSTRACT

Background: Knee osteoarthritis is a relatively common degenerative joint disorder in the world and one of the leading reasons behind chronic pain, disability, and impaired quality of life among the elderly population. Diclofenac Non-steroidal anti-inflammatory drugs, especially diclofenac, are still a strength of pharmacological treatment because of their pain-killing effects as well as anti-inflammatory effects. **Materials and Methods:** Nevertheless, there are severe systemic side effects of oral NSAID treatment, such as gastrointestinal bleeding, cardiovascular, and renal dysfunction. The current study was meant to determine the effectiveness and safety of transdermal diclofenac patch versus oral diclofenac in patients with knee osteoarthritis. **Results:** The study was a prospective randomized controlled study that involved 100 patients with knee osteoarthritis. The main results were the decrease of the level of pain measured with the help of the Visual Analogue Scale, the functional status measured with the help of the PROMIS Physical Function scores, and the quality of life measured with the help of the SF-36 questionnaire. Adverse drug reactions, patient satisfaction and rescue medication were the secondary outcomes. Transdermal diclofenac patients did not show any difference in pain relievers or functional results as compared to oral diclofenac group. Nevertheless, the incidence of systemic adverse effects was lower in transdermal group especially gastrointestinal complaints. The transdermal treatment group also showed improved patient compliance and patient satisfaction. **Conclusion:** Transdermal diclofenac patches are just as effective in pain relieving as oral diclofenac with a more favorable safety profile. These results propose transdermal delivery system to be a safer and more sustainable treatment mode of long-term management of knee osteoarthritis, particularly in the aged.

Keywords: Diclofenac, Drug safety, Knee osteoarthritis, NSAIDs, Randomized controlled study, Transdermal patch.

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INTRODUCTION

Osteoarthritis is a highly prevalent musculoskeletal chronic disease that impacts the world population and poses one of the most significant causes of disability, especially in the elderly population. The disease is manifested by the gradual atrophy of the cartilage of the joints, the remodeling of the bone beneath the cartilage, inflammation of the synovia, and structural damage of the joint tissues.[1] Knee osteoarthritis becomes a significant health issue to the general population, which leads to high health expenditure, reduced productivity and high physical and psychological weight to the patients.[2,3]

Population aging, sedentary lifestyles, increased incidences of obesity and long-life expectancy have seen the prevalence of knee osteoarthritis rise significantly over the last decades. Besides pain, other symptoms common in patients include stiffness of the joints, dysfunction, and inability to carry out common tasks by walking, climbing up and down the stairs, standing up or standing long in a single position.[5,6] Different pharmacological substances have been employed such as acetaminophen, NSAIDs, corticosteroids, and intra-articular therapies. Diclofenac is regarded to be among the most effective NSAIDs and is commonly applied in treatment of osteoarthritis and other musculoskeletal diseases.[3-5] Pharmacological treatment is also of significant importance in the symptomatic management of knee osteoarthritis. NSAIDs are common drugs that are prescribed to treat and manage the pain of osteoarthritis because of their analgesic and anti-inflammatory

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effects. Orally taken NSAIDs are systemically absorbed, they can have an effect on many organ systems other than the affected area through inflammation.[6-8] Oral NSAID treatment, there are gastrointestinal complications like gastritis, peptic ulcer disease, and gastrointestinal bleeding. Osteoarthritis is prevalent in older adults who most likely have numerous comorbidities.[3,9,10]

Transdermal drug delivery devices offer a non-invasive drug delivery method that has the ability to release drugs on a sustained basis and deliver drugs to the area of the affected joint. This modifies the first-pass metabolism and restricts the systemic exposure of drugs hence there is a possibility of enhancing the safety profile of non-steroidal anti-inflammatory drugs in chronic musculoskeletal diseases.[10] The clinical trials and meta-analyses have proved that topical or transdermal NSAIDs help a great deal in relief of pain and better functional outcome in osteoarthritis patients.[3,9] Transdermal preparations have a number of benefits which include; local action of drug absorption, elimination of gastrointestinal reactions and less exposure of the drug to the system. The transdermal diclofenac patches can achieve localized anti-inflammatory action at the painful area with a potentially decreasing systemic adverse reaction in the case of musculoskeletal conditions like knee osteoarthritis.[11] This pharmacokinetic benefit has enabled topical NSAIDs to have a special role in older patients and patients with various comorbidities to be more prone to systemic NSAID toxicity.[12]

The current prospective randomized controlled trial was carried out to determine the effectiveness and safety of transdermal diclofenac patch when compared to oral diclofenac in individuals with knee osteoarthritis.[12,13] The sustained release characteristics of patch systems allow continuous local drug exposure at the site of inflammation, which may contribute to effective pain control in chronic musculoskeletal disorders such as knee osteoarthritis.[11] The long-term release properties of patch systems provide the ability to achieve site-targeted drug delivery continuously to the inflammatory site, which can lead to pain management during chronic musculoskeletal diseases, such as knee osteoarthritis. The perception of pain in osteoarthritis is a psychological and contextual phenomenon. This phenomenon should be considered during the interpretation of clinical outcomes of pain in randomized trials. Topical NSAIDs are recommended by the National Institute of Health and Care Excellence and American College of Rheumatology as a first-line pharmacological treatment of localized osteoarthritis pain, especially with older individuals or those who are at higher risk of systemic adverse reactions of oral NSAIDs.[14-16]

The attention of many studies has been put on topical gels or creams as opposed to transdermal patch systems. Due to differences in study design, sample size, period of treatment, and the outcome measure, it is not easy to come up with conclusive figures on the comparative effectiveness and safety of the two treatment modalities.[17-19] Even though the use of topical NSAIDs is advisable in various clinical guidelines to manage osteoarthritis, there is still limited comparative evidence between the use of transdermal diclofenac patches and oral diclofenac therapy in many clinical environments. Both efficacy and safety outcomes must therefore be evaluated directly to find out the relative clinical benefits of these treatment modalities.[19-21]

MATERIALS AND METHODS

Study Design

It was a prospective randomized controlled clinical trial that was carried out to compare the efficacy and safety of transdermal diclofenac patches and oral diclofenac tablets on patients diagnosed with knee osteoarthritis. The current study aimed to be a prospective and randomized controlled clinical trial to compare and contrast the effectiveness and safety of transdermal application of diclofenac patches and oral diclofenac in patients diagnosed of knee osteoarthritis. Randomized controlled trials are regarded as the gold standard in a clinical research study to evaluate the therapeutic interventions since they reduce the bias and enable objective differences between the treatment groups. In the given case, the participants were randomly assigned to two treatment groups to each group to compare the results that were related to the two different routes of using diclofenac.

Study Population

100 patients diagnosed with knee osteoarthritis were recruited in the study. The patients were sampled on the basis of their clinical analysis and radiographic examination of osteoarthritis using Kellgren-Lawrence grading system. It was done in the orthopedic outpatient department of a tertiary care hospital. The department continues to deal with patients who present with musculoskeletal disorders, such as osteoarthritis, rheumatoid arthritis, and sport related injuries. The eligibility criteria were based on pre-established inclusion and exclusion criteria through which the patients who visited outpatient clinic complaining of knee pain were screened.

Sample Size

The number of patients (100) involved in the study was 100. The chosen sample size was sufficient to represent the target population in a sufficient manner and provide statistical comparison of the two treatment groups.

Inclusion Criteria

- Adults aged above 40 years.
- Clinically diagnosed with knee osteoarthritis.
- Experiencing moderate knee pain requiring pharmacological treatment.
- Willing to provide informed consent for participation in the study.

- Baseline Blood pressure was recorded in all patients preceding the therapy and patients with Hypertension were enrolled in the study, provided that it was satisfactorily managed on medication.

Exclusion Criteria

- Known hypersensitivity or allergy to NSAIDs.
- History of severe gastrointestinal disorders such as peptic ulcer disease.
- Presence of severe systemic illnesses such as advanced renal or hepatic disease.
- Recent knee surgery or intra-articular injection therapy.
- Pregnancy or lactation.

Treatment Groups

Group A: Transdermal Patch Diclofenac

This population of patients was given diclofenac transdermal patches directly added to the knee joint which was in problem. The patch was used on a daily basis and changed as per the instructions of the manufacturer. Patients were also advised to use clean dry skin when placing the patch in order to achieve maximum drug absorption.

Group B: Tablets of Diclofenac Oral

This group taking oral diclofenac tablets was under the doctor prescription. The drug was used in the usual therapeutic doses that were suitable in treating osteoarthritis pain. Patients were advised to take the medication during the post meal times to reduce gastrointestinal discomforts.

Outcome Measures

Treatments were assessed in terms of their efficacy and safety through primary and secondary outcomes measurements.

Primary Outcome Measures

The main outcomes were aimed at measuring pain and functional status improvement in the patients.

The pain intensity was measured with the help of Visual Analog Scale (VAS) which is a popular scale of subjective pain. Patients were asked to rate their pain using a scale of 0 (no pain) to 10 (severe pain).

They used the PROMIS Physical Function scale, which is a scale that measures the functional status of the patient in performing daily physical activities like walking, standing, and climbing stairs.

The SF-36 questionnaire was the measure of quality of life. This instrument is used to determine various dimensions of health-related quality of life such as physical functioning, pain, perception of overall health, and emotional well-being.

Secondary Outcome Measures

Secondary outcomes were aimed at assessing the safety and tolerability of treatments.

Monitoring was done on adverse drug reactions during the period of the study. Patients were advised to report any form of the symptoms like gastrointestinal discomfort, skin irritation, dizziness, or any other unexpected effects. The satisfaction of the patients with the treatment was also measured to identify the acceptability and the convenience of the therapy. Moreover, the rescue medication was also used to treat uncontrolled pain in order to determine the effectiveness of the pain treatment in each group.

Statistical Analysis

The study data were inputted in a structured database and analyzed with the help of statistical software (SPSS and Microsoft Excel). Demographic and baseline characteristics of the participants were summarized using the descriptive statistics. Accordingly, relevant statistical tests were used to compare both the treatment groups. The independent t-test was used to analyze the continuous variables like pain scores and functional scores. The Chi-square test was used to test categorical variables like the occurrence of adverse events. The p-value of below 0.05 was taken to be significant. The statistical test was to find out whether there existed any significant difference between the transdermal diclofenac patch and the oral diclofenac tablet groups on the efficacy and safety outcomes.

RESULTS

One hundred patients diagnosed with knee osteoarthritis were enrolled in the current study and were randomly assigned to the two treatment groups according to the study protocol. All registered participants had fulfilled the protocol of the study and were incorporated in the final analysis. The study period was used to assess treatment efficacy and safety outcomes through the assessment of the patients at baseline and at selected predetermined intervals. Clinical assessment involved the evaluation of the intensity of pain, functional mobility, quality of life, and adverse drug reactions. Such parameters were estimated by use of validated clinical measures including the Visual Analog Scale (VAS) of pain, PROMIS Physical Function scale of mobility and the Short Form-36 (SF-36) questionnaire of health-related quality of life. Standardized assessment tools were used, which provided an objective comparison of the results of the two treatment groups.

In baseline, the treatment groups had similar demographic and clinical features Table 1. This guaranteed that the disparities noted

in the course of the follow-up were as a result of the treatment interventions and not existing disparities.

The findings revealed that the demographic pattern of the patients was not different in Group A (transdermal diclofenac patch) and Group B (oral diclofenac tablets). The average of the participants was in the normal age group that is related to knee osteoarthritis. The sample size of the majority of patients was in the middle-aged and aged group of patients, and this indicates the long-standing association between aging and the excess prevalence of osteoarthritis. Loss of Reparative ability of the tissues of the joints and degenerative alterations in the articular cartilage, prolonged mechanical strain leads to the development of osteoarthritis among the elderly population. Both male and female subjects were involved in the research but a somewhat larger percentage of patients were females. There was also an analysis of the BMI of the participants undertaken as a form of baseline. The percentage of patients who were overweight or obese based on the general BMI classification standards was high. The intensity of osteoarthritis in the participants was measured with the help of the Kellgren-Lawrence (KL) grading system, which is a popular radiographic grading technique of osteoarthritis. A majority of the participants fell under Grade 2 or Grade 3, which implies mild to moderate severity of the disease. Patients who exhibit these grades normally come along with the symptoms of joint pain, stiffness, and functional limitations without having experienced severe structural joint damage.

Pain Reduction (VAS Score)

The level of pain used as a measure in the VAS scale revealed a significant improvement of both treatment groups. Transdermal diclofenac patch showed better pain relief than oral diclofenac at the follow-up evaluation. At week 2, the average of VAS score was significantly less in the patch group than oral diclofenac group (3.57±1.37 vs 5.27±0.95; $p<0.001$). This further improved the results by the week 3 when the patch group did show more pain reduction (2.12±1.51 vs 4.2±1.12; $p<0.001$) Table 2.

The treatment groups showed that VAS scores significantly decreased during the study period, which showed an improvement of pain symptoms in the patients with knee osteoarthritis. The use of transdermal diclofenac patch resulted into progressive and long-term pain score reduction in patients. Oral diclofenac tablets were also shown to have a significant decrease of the VAS pain score in the patients receiving the treatment. Decreased inflammatory mediators are within the joint and help relieve the pain and enhance the performance of the joint.

Physical Function (PROMIS-PF Scores)

The functional outcomes measured with the PROMIS scale demonstrated the transdermal patch group to have maintained higher functional status at the end of the study period and had higher scores on the PROMIS scale than the oral diclofenac group (43.92±3.94 vs 38.27±3.98; $p<0.001$) Table 3.

Table 1: Baseline Demographic and Clinical Characteristics of Study Participants.

Group	Frequency (%)
Oral	49 (49%)
Patch	51 (51%)
Sex	
Male	44 (44%)
Female	56 (56%)
KL Grade	
Mild	52 (52%)
Moderate	48 (48%)
Occupation	
Auto Driver	1 (1%)
Business	2 (2%)
Contractor	1 (1%)
Driver	5 (5%)
Farmer	17 (17%)
Homemaker	23 (23%)
Laborer	32 (32%)
Maid	1 (1%)
Shopkeeper	15 (15%)
Teacher	3 (3%)
Rescue medication use	
No	94 (94%)
Yes (Paracetamol IV)	6 (6%)
Adverse effects	
Epigastric pain	12 (12%)
GI Irritation	21 (21%)
Nausea	7 (7%)
None	46 (46%)
Pruritus	5 (5%)
Rash	6 (6%)
Vomiting	3 (3%)
HTN	
No	57 (57%)
Yes	43 (43%)
DM	
No	59 (59%)
Yes	41 (41%)
Dropout	
No	95 (95%)
Yes	5 (5%)

Table 2: Comparison of VAS Scores Between Treatment Groups.

	Baseline	Week 2	Week 3	Chi-square	*p*
VAS score					
Oral	7.08±0.89	5.27±0.95	4.2±1.12	95.696	0
Patch	7.16±0.76	3.57±1.37	2.12±1.51	100.12	0

Table 3: PROMIS Functional Scores.

	Baseline	Week 2	Week 3	Chi-square	*p*
PROMIS parameter T-score					
Oral	38.27±3.98	38.71±3.09	50.28±64.26	98	0
Patch	43.92±3.94	41.35±3.48	47.46±6.09	102	0

The functional improvement of participants was measured with the help of the PROMIS Physical Function (PROMIS-PF) scale which determines the capability of a patient to conduct usual physical activities. The study period showed improvement in functional scores in both treatment groups. The patients also indicated that they could now have more capacity to carry out activities like walking, standing in longer periods, and climbing the stairs without the serious pain and discomfort. The enhancement of functional mobility was a little more gradual in transdermal patch group perhaps because of the localized and continuous release of medication.

Quality of Life (SF-36 scores)

Quality of life outcomes measured using the SF-36 questionnaire demonstrated significant improvements in several domains among patients treated with the transdermal diclofenac patch Table 4.

Significant differences between groups were observed in:

Physical functioning:

$$(58.47 \pm 9.81 \text{ vs } 50.1 \pm 4.79;\ p < 0.001)$$

Bodily pain relief:

$$(66.08 \pm 10.27 \text{ vs } 56.1 \pm 5.32;\ p < 0.001)$$

Mental well-being:

$$(65.61 \pm 9.7 \text{ vs } 58.46 \pm 7.01;\ p < 0.001)$$

The SF-36 questionnaire was used to measure the quality of life with regard to health since it measures various aspects of health status such as physical functioning, bodily pains, emotional well-being and social functioning. The two treatment groups showed improvements in multiple domains of SF-36 especially those that touch on physical functioning and body pains. The decrease in the pain level also resulted in a more comfortable involvement of patients in everyday activities, which led to the overall improvement in the quality of life.

Safety and Adverse Effects

Patients who were on oral diclofenac had more cases of gastrointestinal adverse events such as gastric discomfort and gastrointestinal distress. These are the negative incidences that resulted in some drug discontinuation in the oral treatment group. Conversely, when patients were given the transdermal diclofenac patch, they only had mild and local skin reactions and, in most cases, the reactions were temporary and non-disruptive to treatment continuity. The current study also had the element of safety assessment. Adverse reactions were observed during the study period so as to determine the tolerability of the two treatment modalities. Oral diclofenac patients made complaints of more systemic negative effects on their bodies. The least described adverse reactions were gastrointestinal discomfort, dyspepsia, and mild gastrointestinal irritation. Conversely, the patients on transdermal diclofenac patch showed a lot of reduced systemic adverse reactions. The most frequent side effect observed in this group was localized skin irritation of minor degree at the patch location.

DISCUSSION

The current randomized controlled trial was done to find out the effectiveness and safety of transdermal diclofenac patches and oral diclofenac tablets on patients with knee osteoarthritis. The findings were that both forms of treatment were practical in decreasing pain and enhancing functional results on the patients. Nonetheless, they were found to differ in terms of their safety profiles.

The main goal in the pharmacological treatment of osteoarthritis is pain reduction. In the given study, both groups had shown a significant improvement in the VAS pain score which points to the effectiveness of diclofenac in analgesic action. The results can be compared with the prior studies indicating the analgesic and anti-inflammatory properties of diclofenac when applied in musculoskeletal diseases. The observed pain relief in the transdermal group is consistent with other studies that demonstrated that topical NSAIDs are capable of similar pain-relieving benefit compared to oral preparations with little

Table 4: SF-36 Quality of Life Scores Before and After Treatment.

	Baseline	Week 2	Week 3	Chi-square	*p*
Physical functioning					
Oral	49.7±3.72	49.14±4.77	50.1±4.79	73.788	0
Patch	51.52±6.68	57.44±10.94	58.47±9.81	87.266	0
Bodily pain					
Oral	50.36±4.84	48.98±5.55	56.1±5.32	78.074	0
Patch	51.09±8.43	59.2±10.8	66.08±10.27	97.158	0
General health					
Oral	55.96±6.02	56.42±5.97	57.56±5.35	80.723	0
Patch	53.33±10.11	60.12±8.18	65.08±9.9	91.652	0
Vitality					
Oral	56.74±5.56	57.24±7.2	57.16±5.53	75.524	0
Patch	52.42±9.83	60.67±9.55	64.68±8.79	90.876	0
Social functioning					
Oral	55.82±6.6	59.8±6.22	59.32±6.34	74.791	0
Patch	51.37±10.04	60.93±11.59	64.13±10.87	91.103	0
Role - physical					
Oral	50.84±4.6	49.58±4.98	50.44±6.01	81.183	0
Patch	50.95±9.77	55.8±9.54	61.25±10.83	89.144	0
Role - emotional					
Oral	60.66±6.65	61.56±6.65	59.76±6.24	75.843	0
Patch	54.37±11.55	61.15±10.12	66.91±9.16	89.922	0
Mental health					
Oral	60.3±7.59	60.54±6.48	58.46±7.01	77.465	0
Patch	54.45±10.51	61.99±10.79	65.61±9.7	89.922	0

systemic exposure. It is possible that the enhanced analgesia effect, seen in this paper, is because localized delivery of the drug is done using the inflamed tissues in and around the knee joint.[22,23]

Transdermal diclofenac patches may have similar therapeutic effects to oral diclofenac therapy since the pain in the similar groups of patients who received the two treatments is found to be comparable. This proves the idea that local drug delivery can result in sufficient drug concentrations to be presented at the inflamed site to produce therapeutic effects. Enhancement in physical functioning that was found in the current study also substantiates the role of pain management in treatment of osteoarthritis. Joint pain reduction enables patients to undertake their daily routines with more comfortability which promotes their mobility and functional independence. The positive change of functional outcome based on PROMIS scores also confirms the efficacy of transdermal therapy. Lower pain levels enable the patients to participate in physical activities with less difficulty hence enhancing the joint mobility and the overall functional capacity of the patient. The comparable results have been obtained in the research of the use of topical NSAIDs in the management of osteoarthritis. The results obtained in the current research are aligned with the existing clinical guidelines and other published systematic reviews that suggest the use of topical NSAIDs as an osteoarthritis management method. The NICE guidelines as well as the American college of Rheumatology guidelines underline the importance of using topical NSAIDs as a primary option to oral NSAIDs in patients experiencing localized pain in osteoarthritis, especially in older adults or individuals at risk of gastrointestinal or cardiovascular complications. The safety profile of transdermal diclofenac patch that was better in this study thus reinforce the current guideline recommendations of using topical NSAIDs as an effective and less risky treatment in managing pain in osteoarthritis.[24]

There was also an improvement in the quality-of-life assessments based on the SF-36 questionnaire. These gains indicate the overall benefit of pain management on the physical performance, mood, and social involvement. The measurement of quality-of-life outcomes and analysis of patient results provided by the SF-36 questionnaire showed that the transdermal patch had a significant positive impact on physical functioning, bodily pain,

and mental well-being. It has been known that chronic pain has negative effects on psychological health and social functioning. Thus, competent pain management may result in significant positive changes in general quality of life.

Among the most important results of the current research is associated with the safety profile of the treatments. Gastrointestinal adverse effects were more frequent in patients who were taking oral diclofenac. These results are in agreement with the existing literature that reports that, systemic NSAIDs can result into gastrointestinal complications and gastric irritation.

Transdermal diclofenac patches, on the contrary, had a better safety profile. Local delivery of drugs lowers the systemic exposure of drugs hence low chances of systemic adverse effects. Also, transdermal drug delivery does not undergo the first-pass hepatic metabolism that can lead to the further decrease of systemic drug concentrations and increase the safety of treatment. All in all, the findings hint at the possibility of transdermal diclofenac patches as a potentially useful treatment option among patients with knee osteoarthritis, especially among older patients who might be at a higher risk of systemic drug toxicity.[25,26,27]

Even though Diclofenac may influence Blood-Pressure, guarded monitoring is indicated in Hypertensive patients and Transdermal delivery may be beneficial as it reduces systemic exposure and related cardiovascular risks.

CONCLUSION

The findings of this randomized controlled trial prove the claim that the transdermal diclofenac patch is a safe and effective alternative to oral diclofenac in management of knee osteoarthritis.

Patients who were put on the transdermal patch felt:

- Greater pain reduction.
- Better functional performance.
- Enhanced quality of life.
- Less systemic adverse effects.

Conversely, oral diclofenac was linked to more gastrointestinal side effects, which could limit its use in the elders in the long run. The current prospective randomized controlled trial was a comparison of the efficacy and safety of transdermal diclofenac patches and oral diclofenac tablets in patients with knee osteoarthritis. Both modalities of treatment led to the realization of large-scale improvements in terms of pain relief, functional mobility and quality of life among the patients. Notably, transdermal diclofenac patches were reported to have the same efficacy as oral diclofenac in the analgesic effect. Nevertheless, the transdermal patch proved to have a better safety profile with less systemic involvement of adverse effects and mild localized skin reactions in few patients.

These results might indicate that transdermal diclofenac patches can be a less dangerous method of long-term knee osteoarthritis, especially in older patients whose systems are more vulnerable to NSAID systemic adverse effects. Thus, transdermal diclofenac patches can serve as a more favorable treatment of the osteoarthritis pain in long-term management especially in patients with the risk of NSAID-related systemic adverse events.

LIMITATIONS OF THE STUDY

Although the results are encouraging, there are some limitations that have to be noted.

- The research was that with a rather small sample size, which can restrict the extrapolation of the findings.
- The time of the study was rather limited, and it was impossible to assess the effectiveness and safety of the method in the long term.
- Also, the research itself was held at a single center of clinical care and, hence, there is a risk that the results cannot be transferred to other healthcare facilities.

The next step in the future research work ought to be long term multicenter clinical trials on a larger patient population to further assess the safety and long-term effectiveness of transdermal diclofenac therapy in osteoarthritis management.

ABBREVIATIONS

NSAIDs: Non-Steroidal Anti-Inflammatory Drugs; **VAS:** Visual Analogue Scale; **PROMIS:** Patient-Reported Outcomes Measurement Information System; **SF-36:** Short Form-36; KL **Grade:** Kellgren-Lawrence grading system; **HTN:** Hypertension; **DM:** Diabetes Mellitus; **BMI:** Body Mass Index; **NICE:** National Institute of Health and Care Excellence; **ACR:** American College of Rheumatology.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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