

Efficacy and safety study of diclofenac epolamine topical patch in accelerating rehabilitation of moderate hamstring strain: A randomized controlled trial

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Abstract: Background: Moderate hamstring strain is a common sports injury impairing daily and athletic function. While topical nonsteroidal anti-inflammatory drugs (NSAIDs) offer localized pain relief with reduced systemic effects, high-quality evidence specific to hamstring injury is limited. **Objectives:** To evaluate the effect of a short-course topical diclofenac epolamine patch combined with rehabilitation on pain and functional recovery in moderate hamstring strain. **Methods:** In this single-center, double-blind, placebo-controlled trial, 120 patients were randomized to an experimental group (diclofenac patch twice daily for 14 days plus rehabilitation) or a control group (placebo patch plus identical rehabilitation). Outcomes assessed included pain measured by the Visual Analogue Scale (VAS), as the primary endpoint, muscle strength, knee range of motion (ROM), functional back-kick test, time to rehabilitation criteria and safety (adverse events, liver/renal function). **Results:** The diclofenac group demonstrated significantly greater pain reduction at days 14, 21 and 28 post-intervention (all $p < 0.01$). Muscle strength recovery was superior at days 21 and 28, knee ROM improved more at day 28 and functional back-kick performance was better at day 28 (all $p < 0.05$). Time to meet rehabilitation criteria was significantly shorter in the experimental group ($p = 0.002$). Adverse event incidence and changes in liver/renal function were similar between groups (all $p > 0.05$). **Conclusion:** A short-course topical diclofenac epolamine patch, combined with rehabilitation training, effectively alleviates pain, accelerates functional recovery, and is safe for treating moderate hamstring strain, supporting its use in clinical and sports rehabilitation.

Keywords: Diclofenac epolamine patch; Hamstring strain; Randomized controlled trial; Rehabilitation training

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INTRODUCTION

Hamstring strain is a common type of soft-tissue injury in sports medicine and orthopedic practice, especially during high-intensity running, jumping, or abrupt stop-and-go movements (Danielsson *et al.*, 2020). From recreational fitness enthusiasts to professional athletes, hamstring strain can cause pain, restricted mobility and even recurrent injury, thereby significantly affecting athletic performance and daily function (Gronwald *et al.*, 2022). Moderate hamstring strain usually involves partial tearing of muscle fibers and a marked inflammatory response; currently, clinical management mainly relies on oral non-steroidal anti-inflammatory drugs (NSAIDs), local physical therapy and progressive rehabilitation training, yet pain control and reduction of recovery time remain suboptimal (Whiteley *et al.*, 2021; Green *et al.*, 2020). Existing studies have observed the use of topical NSAID patches for treating soft-tissue sprains, contusions, or joint inflammation (Perna *et al.*, 2025); however, randomized controlled evidence evaluating short-course topical analgesic interventions for patients with moderate hamstring strain and their impact on the rehabilitation process remains

limited. Poor pain control after hamstring strain can increase the risk of secondary injury, impair the quality of rehabilitation training and reduce patient compliance, ultimately hindering muscle strength recovery and functional reconstruction (Busse *et al.*, 2020). Topical NSAID patches can deliver high local drug concentrations with low systemic absorption, which may be more suitable for alleviating localized inflammation and pain in muscular and tendinous regions (Shi *et al.*, 2023). Among them, diclofenac epolamine is an organic amine salt of diclofenac with good water solubility; after being formulated into a patch, it can enhance skin penetration and achieve sustained drug release, thereby maintaining a relatively stable drug concentration at the injury site and reducing systemic exposure. However, high-quality direct evidence supporting the efficacy and safety of the diclofenac epolamine patch combined with standard rehabilitation training for moderate hamstring strain remains lacking (Xiong *et al.*, 2025). Therefore, an intervention that can effectively control pain, promote functional recovery and produce fewer side effects is urgently needed in clinical practice to meet the demands of sports injury rehabilitation. In this study, a single-center, parallel-group, randomized controlled design was used to evaluate the efficacy and

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safety of a short-course diclofenac epolamine patch combined with basic rehabilitation training for moderate hamstring strain and systematically observe adverse reactions and changes in liver and renal function. The visual analogue scale (VAS) pain score was used as the primary outcome and hypothesized that this combined regimen would reduce pain more effectively than placebo patches in the short term and be associated with improved muscle strength and functional recovery, thereby potentially shortening the rehabilitation period.

MATERIALS AND METHODS

Study design

This study was a single-center, parallel-group, double-blind controlled trial. Recruitment began in January 2024 and follow-up with data analysis was completed by December 2024. This study was approved by the Ethics Committee of The Second Affiliated Hospital of Lanzhou University (No. 2023011) and registered with the Chinese Clinical Trial Registry (registration number: ChiCTR2600083497) on August 12th, 2026. The first participant was enrolled in January 2024, and registration was therefore retrospective. The authors confirm that ethical approval (No. 2023011) was obtained before enrollment.

Study participants

Inclusion criteria were as follows: (1) aged between 18 and 45 years (both sexes included); (2) moderate hamstring strain confirmed by physical examination combined with ultrasound or magnetic resonance imaging (MRI) findings, with imaging graded as Peetrons grade 2 (partial tear), manifested as partial tearing of muscle fibers accompanied by pain and limited motor function; (3) pain score (VAS) ≥ 4 at baseline assessment; (4) able to read and voluntarily sign the informed-consent form and willing to comply with the intervention and follow-up schedule during the study period.

Exclusion criteria were as follows: (1) severe hamstring tear or other serious lower-limb injury (fracture, complete ligament rupture, etc.) within the previous 3 months; (2) use of oral or topical corticosteroids within the past 2 weeks; (3) known allergy to diclofenac or components of the epolamine patch; (4) pregnant or breastfeeding; (5) serious hepatic or renal dysfunction, or severe psychiatric or neurological disorders that could affect trial compliance or intervention safety.

Withdrawal criteria included: (1) occurrence of severe skin allergy (erythema, blisters, exudation, etc.) or other intolerable adverse reactions; (2) participant's request to withdraw or inability to adhere to the intervention as required (multiple missed applications, refusal of follow-up); (3) any other serious event (e.g., new major trauma or complication) preventing continued participation.

Randomization and sample size

Based on previous literature and preliminary experimental data, the VAS pain score was defined as the primary outcome measure and a 1.5-point reduction in VAS in the experimental group compared with the control group at the end of the intervention was set as the minimum between-group difference of clinical significance (pain improvement magnitude perceptible to patients) (Modarresi *et al.*, 2021), with an estimated standard deviation of 2.0 points. With a significance level of $\alpha=0.05$ (two-sided) and a power of $1-\beta=0.80$, Power Analysis software was used to calculate the required sample size for the difference between two independent sample means, indicating that at least 56 participants were needed per group. Given an expected dropout rate of about 10%, 60 participants were enrolled per group, for a total of 120. Random allocation used a computer-generated simple randomization sequence, assigning participants to the experimental and control groups at a 1:1 ratio; the random sequence was placed in sequentially numbered, opaque, sealed envelopes, which were opened in order by an independent research assistant after participant enrollment to complete grouping, thereby ensuring allocation concealment.

This study used a double-masked design. Both the experimental and control groups used identical patches in appearance, odor, and packaging, differing only in whether they contained the active ingredient, diclofenac. Participants were unaware of the specific properties of the patch they used and collection and analysis of primary and secondary outcome measures (pain scores, muscle strength and functional tests) were performed by independent assessors blinded to group allocation. Allocation concealment was implemented using sequentially numbered, opaque, sealed envelopes; after participants completed baseline assessment, the research assistant opened the envelope in sequence and distributed the corresponding patch. Only the research assistant responsible for randomization and patch distribution knew the allocation scheme; the randomization list was kept independently by the assistant (locked cabinet/password-protected file) and unblinding was performed uniformly after database lock and completion of statistical analysis. All other personnel remained unaware of the intervention attributes during the trial and data analysis stages, thereby ensuring the effectiveness of the double-blind strategy. To assess blinding success, at the end of the intervention, participants and assessors were asked separately about their guesses of group allocation and their confidence.

Interventions

Experimental group

The medication was a diclofenac epolamine patch at a concentration of 1.3%, each containing about 180 mg of

diclofenac epolamine and measuring 7 cm × 10 cm. The dosing regimen was two applications per day, one patch each time, once around 09:00 and once around 21:00, ensuring 12 h of application and a 12 h interval, for 14 consecutive days. The patch covered the hamstring injury site, fitting closely and extending at least 2 cm beyond the main pain area. From day 3 of the intervention, under the guidance of a rehabilitation therapist, participants performed daily hamstring stretching and low-load strength exercises, lasting about 30 min per session, continuing until the end of treatment.

Control group

The placebo patch was identical in appearance and size to the experimental patch but contained no diclofenac; the dosing regimen was the same as in the experimental group, two applications per day, each for 12 h with a 12 h interval, for 14 consecutive days. The rehabilitation training protocol was also identical to that of the experimental group, including methods and frequency.

Intervention compliance management

All participants completed a daily patch-application log during the intervention, recording application and removal times. A research assistant verified patch use at least once a week through face-to-face visits or telephone calls, collected used patch packaging and recorded completion of rehabilitation training to ensure effective implementation of the intervention measures.

Outcome measures and assessment time points

Primary efficacy outcomes

Pain was assessed using the VAS (Garcia-Perez and Alcala-Quintana, 2023), with a range of 0–10 points, where 0 indicates no pain at all and 10 indicates the most unbearable, severe pain; higher values denote more severe pain. Assessment time points were baseline (1 day before the formal intervention), day 7 of the intervention, end of the intervention (day 14) and days 21 and 28 after the end of the intervention. For measurement, participants marked their own pain level on a 0–10 linear scale and the assessor read the corresponding value. Hamstring muscle strength was evaluated using Manual Muscle Testing (MMT) (Bittmann *et al.*, 2020), with a scale of 0–5, where 5 indicates normal muscle strength and 0 indicates no active contraction; higher scores indicate greater strength. The assessment time points were identical to those for the VAS. Measurement was conducted by independent assessors who had received standardized training. With the patient in the prone or supine position (adjusted according to specific muscle-testing procedures), resistance testing of the hamstrings was performed, and muscle-strength grade was determined by integrating subjective and objective resistance levels.

Secondary efficacy outcomes

Knee flexion range of motion was measured as the maximum angle achieved during active knee flexion with the participant in the supine position, using a standard goniometer, while noting any apparent pain limitation; the measurable range was 0°–135°, with greater values indicating better joint mobility. Assessment time points were baseline, the end of the intervention and day 28 after the end of the intervention. For the functional back-kick test, the participant stood supporting weight on the uninjured leg and kicked the injured leg backward to the maximum tolerable height; the vertical distance from the ankle to the ground (cm) was recorded, with greater distances indicating better functional recovery. The assessment time points for this test were the same as those for the knee-flexion range-of-motion measurement. Days to rehabilitation were defined as the actual number of days from the start of the intervention until the patient could walk continuously for 15 min without pain and had no obvious functional limitations in daily life. A research assistant contacted or visited the patient every 2–3 days; the date on which the above criteria were first met was recorded as the rehabilitation-criterion date.

Safety indicators

Local adverse reactions were observed to determine whether erythema, pruritus, blisters, or exudation appeared at the application site; if any abnormality occurred, the time of onset, duration and severity were recorded. Systemic adverse reactions were monitored during the treatment and follow-up periods for headache, dizziness, gastrointestinal discomfort and other symptoms and their relationship to the topical medication was assessed. For laboratory testing, venous blood samples were collected 1 day before the start of the intervention and at the end of the intervention (day 14) to measure alanine aminotransferase (ALT), aspartate aminotransferase (AST), serum creatinine (Scr) and blood urea nitrogen (BUN), thereby evaluating potential hepatic and renal function changes caused by the medication. On days 21 and 28 after the intervention ended, each participant received a telephone or face-to-face visit to assess pain recurrence or secondary injury and to record other factors that might affect the rehabilitation process (such as excessive exercise or re-injury).

Quality control

Before study initiation, all clinicians, rehabilitation therapists, assessors and research assistants received uniform protocol training to ensure consistency in examinations and assessments; assessors for the primary and secondary outcomes (VAS, MMT, ROM and functional tests) completed standardized training and participated in assessment only after passing consistency testing; during the study, assistants contacted participants by telephone or face-to-face at least once per week to verify

medication use and to encourage completion of rehabilitation training; if a serious adverse event occurred, the intervention was stopped immediately and medical treatment was provided, with prompt reporting to the ethics committee; the project leader held meetings every 2 weeks to summarize participant recruitment, compliance and adverse events and after the trial ended, data were centrally checked and blind analysis was performed, with group allocation unblinded only after statistical analysis was complete. The functional back-kick test used a standardized procedure and standardized verbal instructions, and each measurement was performed twice, with the mean value taken. During the baseline period, 32 cases were randomly selected for reliability assessment: intra-rater ICC = 0.93 and inter-rater ICC = 0.91, with corresponding MDC95 of 2.38 cm and 2.59 cm, respectively. This test showed good reliability in this study. In the same sampled population, inter-rater agreement for MMT (weighted κ) = 0.86 and inter-rater ICC for knee-flexion ROM was 0.94.

Statistical analysis

All scale data, test results, and adverse reaction information were double-entered independently into an electronic database with weekly data backups. Statistical analysis was performed using SPSS 25.0. Normality was tested first; normally distributed data are presented as mean $\pm$ standard deviation, whereas non-normally distributed data are presented as median and interquartile range. For normally distributed data with homogeneity of variance, intergroup comparisons used the independent-samples *t*-test; for non-normally distributed data or data with heterogeneity of variance, the Mann-Whitney U test was applied. Categorical variables are expressed as counts and percentages and the χ^2 test or Fisher's exact test was used. Repeated-measures analysis of variance was applied to multiple time-point measurements. If the group $\times$ time interaction was significant, the Bonferroni method was used for multiple-comparison correction, yielding a corrected significance level of $\alpha' = 0.05/k$, where *k* is the number of comparisons. All hypothesis tests were two-sided and differences were considered statistically significant when $p < 0.05$. Missing data were not imputed; all analyses were performed on the intention-to-treat (ITT) population, which included all randomized participants.

RESULTS

Participant enrollment and baseline characteristics

A total of 178 cases were assessed and finally 120 cases were randomly assigned to the experimental group and the control group (60 cases in each group) and all randomized participants were included in the ITT analysis (Fig. 1). A total of 120 patients were enrolled in the study. There were no statistically significant differences between the two

groups in age, sex, BMI, injury duration, baseline VAS score, baseline MMT score or activity level (*t*-test and χ^2 test, all $p > 0.05$), indicating comparability of baseline characteristics (Table 1).

Primary efficacy outcomes

Repeated-measures analysis of variance showed a significant group-by-time interaction for pain scores ($F = 4.832$, $p = 0.002$). After Bonferroni correction ($\alpha = 0.01$), the experimental group had significantly lower pain scores than the control group at 14, 21 and 28 days of intervention (all $p < 0.01$; Cohen's *d* = 0.68, 0.81 and 0.96, respectively) (Table 2). Repeated-measures analysis also demonstrated a significant group-by-time interaction for muscle-strength scores ($F = 4.120$; $p = 0.004$). After Bonferroni correction ($\alpha = 0.01$), muscle-strength improvement in the experimental group was superior to that in the control group on days 21 and 28 (both $p < 0.01$; Cohen's *d* = 0.59 and 0.77); the difference on day 14 was not significant but showed a medium effect ($p = 0.011$; Cohen's *d* = 0.46) (Table 3).

Secondary efficacy outcomes

Repeated-measures analysis of variance showed significant time-by-group differences in knee-joint range of motion and functional back-kick height ($p < 0.05$). After Bonferroni correction ($\alpha = 0.0167$), the experimental group showed a significant improvement in range of motion at day 28 (*t*-test, $p = 0.002$), while the improvement at day 14 ($p = 0.018$) did not reach statistical significance after the correction. The functional back-kick test showed a significant improvement only at day 28 (*t*-test, $p = 0.011$; Table 4). Comparison of rehabilitation days using the Mann-Whitney U test revealed that the experimental group reached the rehabilitation criterion significantly sooner than the control group ($Z = -3.153$; $p = 0.002$; Fig. 2).

Safety analysis

χ^2 tests or Fisher's exact tests showed no statistically significant differences between the experimental and control groups in local skin reactions (erythema, pruritus, blisters) or systemic discomfort (gastrointestinal symptoms, headache/dizziness, other rare reactions) (all $p > 0.05$) (Table 5). Independent-samples *t*-tests revealed no significant inter-group differences in ALT, AST, Scr, or BUN before and after the intervention (all $p > 0.05$). Within-group paired *t*-tests showed no significant changes in AST, Scr, or BUN in either group (all $p > 0.05$); the within-group increase in ALT reached statistical significance only in the control group ($p = 0.046$), although the change was small in magnitude (24.26 ± 3.28 to 24.82 ± 3.37 U/L) and was not considered clinically meaningful, indicating that the medication did not markedly affect hepatic or renal function (Table 6).

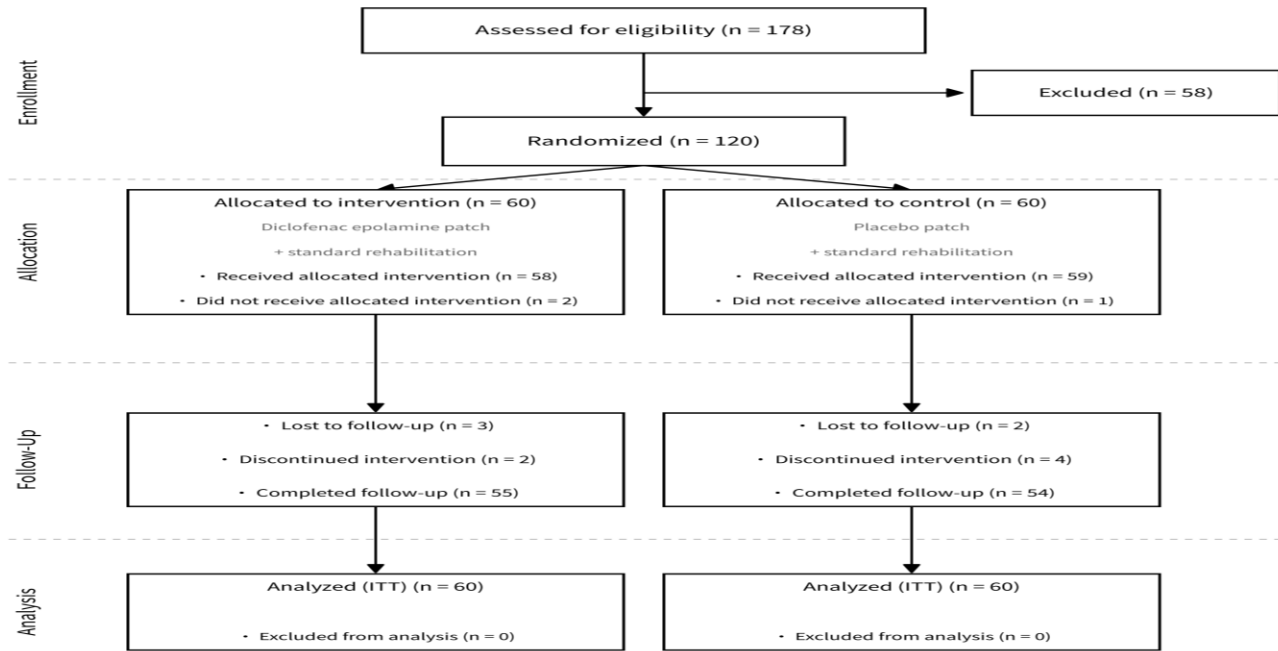


Fig. 1: CONSORT participant flow diagram

Table 1: Baseline demographic and clinical characteristics of the two groups ($\bar{x} \pm s$) or (n, %)

Variable	Experimental group (n = 60)	Control group (n = 60)	Test value	p-value
Age (years)	32.78 $\pm$ 4.23	33.62 $\pm$ 4.70	$t = -0.940$	0.349
Sex (male / female)	32 (53.33 %) / 28 (46.67 %)	35 (58.33 %) / 25 (41.67 %)	$\chi^2 = 0.404$	0.524
BMI (kg/m ²)	23.62 $\pm$ 2.72	23.85 $\pm$ 2.63	$t = -0.370$	0.713
Duration of moderate hamstring strain (days)	6.10 $\pm$ 0.84	5.92 $\pm$ 0.81	$t = 0.485$	0.629
Baseline pain score VAS	6.82 $\pm$ 0.89	6.90 $\pm$ 0.95	$t = -0.762$	0.447
Baseline muscle strength score MMT	3.17 $\pm$ 0.41	3.11 $\pm$ 0.38	$t = 0.443$	0.659
Activity level (athletes / recreational exercisers / sedentary individuals)	19 (31.67%) / 32 (53.33%) / 9 (15.00%)	22 (36.67%) / 28 (46.67%) / 10 (16.67%)	$\chi^2 = 0.539$	0.764

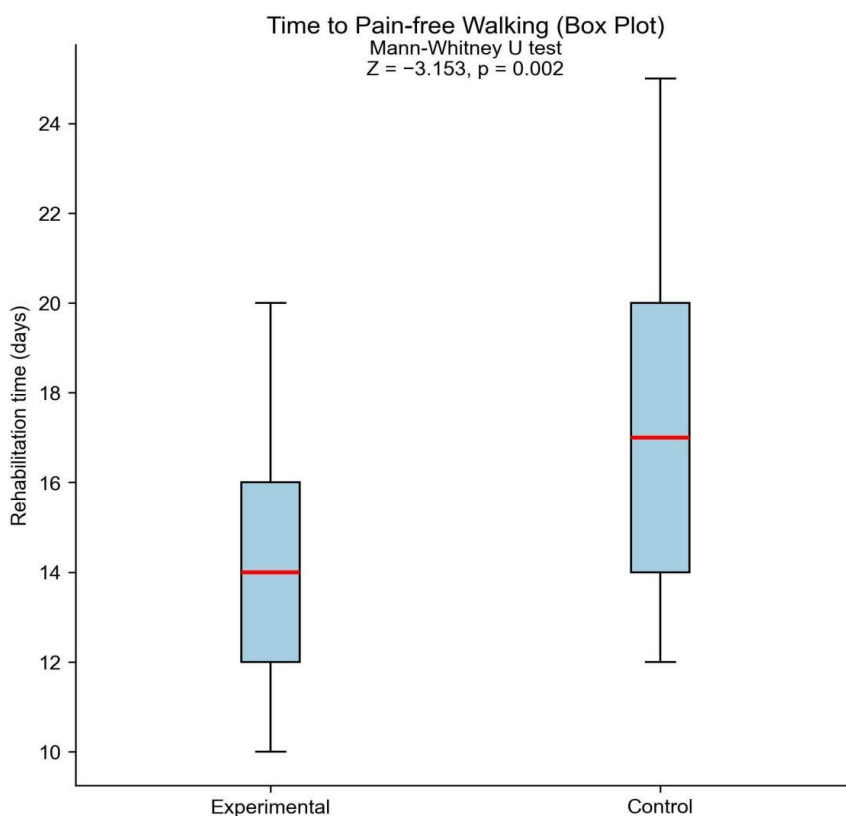
Table 2: Changes in visual analogue scale (VAS) scores at different time points in the two groups ($\bar{x} \pm s$)

Time point	Experimental group VAS	Control group VAS	t-value	p-value	Cohen's d
Baseline (before intervention)	6.82 $\pm$ 0.89	6.90 $\pm$ 0.95	-0.762	0.447	0.09
Day 7 of intervention	5.03 $\pm$ 0.72	5.36 $\pm$ 0.77	-2.201	0.032	0.43
Day 14 (end of intervention)	3.64 $\pm$ 0.65	4.18 $\pm$ 0.69	-3.618	0.001	0.68
Day 21 after intervention	2.90 $\pm$ 0.57	3.46 $\pm$ 0.62	-4.275	< 0.001	0.81
Day 28 after intervention	2.18 $\pm$ 0.56	2.94 $\pm$ 0.60	-5.012	< 0.001	0.96
Group $\times$ time interaction: $F = 4.832$, $p = 0.002$					

Table 3: Changes in manual muscle testing (MMT) scores at different time points in the two groups ($\bar{x} \pm s$)

Time point	Experimental group MMT	Control group MMT	<i>t</i> -value	<i>p</i> -value	Cohen's <i>d</i>
Baseline (before intervention)	3.17 ± 0.41	3.11 ± 0.38	0.443	0.659	0.13
Day 7 of intervention	3.59 ± 0.45	3.45 ± 0.42	1.787	0.077	0.25
Day 14 (end of intervention)	4.13 ± 0.51	3.89 ± 0.49	2.518	0.011	0.46
Day 21 after intervention	4.39 ± 0.55	4.05 ± 0.53	3.033	0.003	0.59
Day 28 after intervention	4.61 ± 0.49	4.23 ± 0.48	3.908	< 0.001	0.77
Group × time interaction: $F = 4.120, p = 0.004$					

Note: The effect sizes originally used the non-parametric index Cliff's Δ ; for consistency of comparison, they were converted to Cohen's *d* using a formula.

**Fig. 2:** Comparison of rehabilitation days between the two groups.**Table 4:** Knee-flexion range of motion and functional back-kick test results for the two groups ($\bar{x} \pm s$)

Time point	Experimental group	Control group	<i>t</i> -value	<i>p</i> -value
Knee-joint range of motion (°)				
Baseline (before intervention)	102.45 ± 6.79	101.87 ± 6.72	0.469	0.64
Day 14 (end of intervention)	117.36 ± 7.11	114.28 ± 6.85	2.401	0.018
Day 28 after intervention	126.81 ± 6.94	123.67 ± 6.44	3.164	0.002
Group × time interaction: $F = 4.520, p = 0.003$				
Functional back-kick height (cm)				
Baseline (before intervention)	28.39 ± 3.42	28.10 ± 3.27	0.473	0.637
Day 14 (end of intervention)	34.92 ± 3.88	33.67 ± 3.74	1.802	0.074
Day 28 after intervention	40.45 ± 4.02	38.39 ± 3.99	2.572	0.011
Group × time interaction: $F = 3.905, p = 0.022$				

Table 5: Incidence of local and systemic adverse reactions in the two groups (n, %)

Adverse reaction type	Experimental group(n = 60)	Control group(n = 60)	Test value	p-value
Local reactions				
Skin erythema	5 (8.33)	3 (5.00)	$\chi^2 = 0.459$	0.498
Pruritus	4 (6.67)	7 (11.67)	$\chi^2 = 1.206$	0.272
Blister/ulcer	1 (1.67)	2 (3.33)	Fisher	0.782
Systemic reactions				
Gastrointestinal discomfort (nausea, abdominal pain, etc.)	2 (3.33)	4 (6.67)	$\chi^2 = 1.061$	0.303
Headache/dizziness	3 (5.00)	2 (3.33)	$\chi^2 = 0.213$	0.645
Other rare adverse reactions	1 (1.67)	3 (5.00)	Fisher	0.436

Table 6: Hepatic and renal function test results in the two groups ($\bar{x} \pm s$)

Indicator	Time	Experimental group	Control group	t-value	p-value
ALT (U/L)	Baseline	23.74 $\pm$ 3.12	24.26 $\pm$ 3.28	-0.904	0.368
	End of intervention	24.06 $\pm$ 3.15	24.82 $\pm$ 3.37	-1.230	0.221
	t-value	-1.282	-1.303	—	—
	p-value	0.241	0.046	—	—
AST (U/L)	Baseline	26.31 $\pm$ 3.46	25.85 $\pm$ 3.55	0.722	0.472
	End of intervention	27.02 $\pm$ 3.69	26.77 $\pm$ 3.42	0.384	0.702
	t-value	-1.282	-1.617	—	—
	p-value	0.205	0.11	—	—
Scr (μ mol/L)	Baseline	76.85 $\pm$ 9.50	79.12 $\pm$ 9.44	-1.275	0.205
	End of intervention	75.41 $\pm$ 9.16	77.98 $\pm$ 9.73	-1.490	0.139
	t-value	1.428	1.667	—	—
	p-value	0.159	0.103	—	—
BUN (mmol/L)	Baseline	4.68 $\pm$ 0.58	4.81 $\pm$ 0.55	-1.226	0.222
	End of intervention	4.62 $\pm$ 0.57	4.79 $\pm$ 0.60	-1.651	0.101
	t-value	0.763	0.252	—	—
	p-value	0.448	0.802	—	—

DISCUSSION

A short-course topical diclofenac epolamine patch combined with standard rehabilitation training consistently showed an analgesic advantage during the 14- to 28-day follow-up, and the difference persisted after discontinuation. Taking day 28 as an example, the VAS score in the experimental group was 0.76 points lower than that in the control group (95% CI 0.55 to 0.97). The direction of this difference was consistent with the minimum clinically meaningful between-group difference prespecified in the sample size estimation, but the magnitude was relatively smaller, suggesting that topical analgesia may provide a perceptible benefit but still needs to be interpreted in conjunction with functional outcomes. The direction of this pain improvement is consistent with the pharmacological effects of NSAIDs for local anti-inflammatory analgesia (Jones *et al.*, 2022). From the perspective of effect size, this study showed a moderate-to-large effect of pain improvement at multiple follow-up time points and between-group differences could still be observed after discontinuation, suggesting that short-

course patch application may provide a more stable pain management window for rehabilitation training; this result is consistent with the overall trend observed in previous randomized controlled trials of topical NSAIDs for acute soft tissue injury (Dubois and Esculier, 2020). Previous studies have emphasized that early inflammation control and pain relief are beneficial for preventing secondary injury and promoting subsequent training, thereby improving the efficiency of muscle functional recovery (Sohail *et al.*, 2023). Previous literature has mostly reported the application value of oral NSAIDs in soft tissue injury; however, oral drugs may cause gastrointestinal irritation or systemic discomfort (Arnstein *et al.*, 2023). This trial provides direct randomized controlled evidence in the context of moderate hamstring strain and extends the efficacy observation to two weeks after discontinuation, making the clinical pathway of "short-course topical analgesia combined with standard rehabilitation" more targeted.

Differences in muscle strength outcomes were mainly observed at days 21 and 28, indicating that measurable

improvements in muscle strength tended to emerge later than reductions in pain. At day 28, the experimental group demonstrated a 0.38-point higher MMT score than the control group (95% CI 0.20 to 0.56). Although muscle strength showed an improving trend at day 14, it did not reach statistical significance after multiple-comparison correction, consistent with the time-dependent nature of muscle tissue repair and neuromuscular reorganization, and may also reflect the limited sensitivity of MMT for detecting subtle strength changes (Tazreean *et al.*, 2022). Importantly, the parallel improvements observed in pain and muscle strength should be interpreted as associative rather than indicative of a direct causal relationship, as training load, movement quality and neuromuscular activation were not directly quantified in this study. Accordingly, a definitive causal pathway linking pain reduction to subsequent strength recovery cannot be established based on the present data.

Randomized controlled evidence examining the effects of topical NSAIDs on muscle strength and functional outcomes remains limited, with most prior studies focusing on populations with arthritis or joint sprains rather than acute muscle injuries (Wang *et al.*, 2022). Existing literature has reported inconsistent findings regarding the influence of NSAIDs on muscle repair, particularly in the context of systemic administration (Chen *et al.*, 2024). Within the framework of short-term, localized dosing and stable laboratory indices observed in this trial, the present findings support topical diclofenac primarily as an adjunctive pain management strategy that may facilitate participation in rehabilitation. At the same time, the potential long-term effects on muscle adaptation and recovery require confirmation through studies with extended follow-up and more detailed assessment of training exposure.

Improvements in range of motion, the functional back-kick test, and time to the rehabilitation criterion were consistent with changes in pain and muscle strength, suggesting that functional recovery benefits were not limited to the symptom level. Long-term or persistent pain can lead to fear-avoidant behaviors, further impairing joint and muscle mobility and slowing recovery. In contrast, efficient local analgesia provides the necessary conditions for early stretching and strength training (Chen *et al.*, 2025). The baseline distribution of activity levels was similar between the two groups, which can to some extent reduce confounding caused by differences in sports participation, but individual differences in baseline physical fitness, previous injury history and training execution intensity may still affect functional recovery trajectories (Ambegaonkar *et al.*, 2024). Despite standardized rehabilitation guidance, differences in exercise execution and intensity could not be fully controlled, potentially

contributing to variability in functional outcomes. With respect to safety, no significant between-group differences were observed in adverse reactions or liver and renal function indices, supporting the short-term tolerability of topical diclofenac epolamine patches when used in conjunction with rehabilitation training (Bhat *et al.*, 2023). Numerous studies have identified pain as the central obstacle hindering rehabilitation progress in acute soft-tissue injuries; timely and safe analgesia can markedly enhance rehabilitation outcomes and patient adherence (Viscusi *et al.*, 2024). Given the single-center design, limited follow-up duration and restricted age range, the applicability of these findings should be confined to adults with moderate hamstring strain undergoing short-term rehabilitation and extrapolation to other injury types, severities, or populations should be undertaken with caution.

Limitations

This study has certain limitations. The single-center design, which recruited adult patients aged 18–45 years, restricts the generalizability of the results; the 4-week follow-up is short, allowing only a preliminary assessment of short-term efficacy and making it difficult to determine the risk of long-term recurrence or sustained functional impairment. Individual differences in training intensity, baseline physical fitness and comorbidities were not thoroughly analyzed, which may affect accurate evaluation of rehabilitation outcomes. No stratified analysis by sport type or occupational background was conducted, possibly overlooking the influence of specific loading patterns on hamstring recovery. The optimal patch concentration and duration for topical NSAIDs have not been precisely studied; multicenter, large-sample trials are required to clarify dosage, treatment course and long-term cutaneous or systemic adverse-effect risks. Current data reflect the effect of this short-course analgesic regimen only in adults, so extension to elderly or underage populations should be cautious. Extending the follow-up period and conducting multicenter studies will help provide more comprehensive data on recurrence and long-term functional recovery, and will also help explore the synergistic effects of the drug combined with progressive neuromuscular training or other physical therapies. Although the short-course topical patch demonstrated good safety and adherence, individualized dosing and long-term efficacy require further investigation. The results should be interpreted in light of the specific age group, limited follow-up, and potential confounding factors.

CONCLUSION

This single-center randomized controlled trial enrolled adults aged 18–45 years with moderate hamstring strain (Peetrons grade 2). When added to a standard rehabilitation

program, a 14-day course of a topical diclofenac epolamine patch, compared with placebo patches plus the same rehabilitation, was associated with greater pain relief over the 14–28-day follow-up and additional improvements in muscle strength and functional measures at selected time points, with a favorable short-term safety profile and no evidence of clinically meaningful changes in liver or renal function indices. These findings suggest that, in this population and within this time frame, this topical NSAID patch may serve as an adjunct for early pain management to support participation in rehabilitation and potentially shorten the time to meet recovery criteria. Given the restricted population and setting (18–45 years, single center, Peetrans grade 2, 4-week follow-up), the results should not be extrapolated to other sports injuries, severe tears, chronic or recurrent courses, or older or pediatric populations. Further multicenter trials with longer follow-up, return-to-sport and re-injury outcomes and objective quantification of rehabilitation load are warranted.

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Authors' contribution

Xiaomei NIU: Contributed to data collection, analysis and interpretation of data and drafted the manuscript. Zhi Zhang*: Conceived and designed the study, supervised the research process, revised the manuscript critically for important intellectual content and gave final approval of the version to be published. All authors have read and agreed to the published version of the manuscript.

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Data availability statement

All datasets generated or analyzed during this study are available from the corresponding author upon reasonable request.

Ethical approval

This study was approved by the Ethics Committee of The Second Affiliated Hospital of Lanzhou University (No. 2023011). Written informed consent was obtained from all participants prior to enrollment. This study was conducted and reported in accordance with the Consolidated Standards of Reporting Trials (CONSORT) statement. This study was performed in adherence with the CONSORT guidelines. See supplementary file for the CONSORT checklist.

Trial registration

This trial was registered with the Chinese Clinical Trial Registry (registration number: ChiCTR2600083497) on August 12th, 2026. The first participant was enrolled in January 2024, and registration was therefore retrospective. The authors confirm that ethical approval (No. 2023011) was obtained before enrollment.

Conflict of interest

The authors declare no conflicts of interest.

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