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The Effectiveness of Topical Diclofenac for Lateral Epicondylitis

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Abstract:

Introduction: Gastrointestinal upset and local pain commonly limit the use of oral nonsteroidal anti-inflammatory drugs and corticosteroid injection as treatments for lateral epicondylitis. Transdermal administration of an anti-inflammatory drug could avoid these adverse effects.

Purpose: To determine the effectiveness of topical diclofenac as a treatment of lateral epicondylitis.

Methods: A convenience sample of 14 subjects meeting clinical criteria of chronic lateral epicondylitis participated in this randomized, double blind, crossover study. Each subject applied a pluronic lecithin liposomal organo-gel (PLO) over the affected lateral elbow three times daily for 1 week, followed by a 1-week "washout" period of no gel. A second topical PLO gel was then applied similarly for 1 week. Both gels were identical, but only one gel contained 2% diclofenac. Treatment order was randomized, and both the subject and tester were blinded. Pain and isometric wrist extension strength were measured using a visual analog pain scale (VAS) and a mounted manual muscle testing dynamometer, respectively, at the following time periods: just before application of the first gel, the last day of using the first gel, the last day of the washout week, and the last day of using the second gel. Analysis was performed using repeated measures analysis of variance.

Results: When subjects used diclofenac PLO, pain was significantly less than that during the pretreatment, washout, and placebo PLO periods (mean VAS: diclofenac PLO, 2.1; pretreatment, 3.5; washout, 3.4; placebo PLO, 3.6). Average wrist extension strength was significantly greater when subjects used diclofenac PLO (8.4 kg) than it was before treatment (5.9 kg). One subject developed a local rash while using diclofenac PLO.

Conclusion: Topical 2% diclofenac in PLO appears to provide effective short-term reduction in elbow pain and wrist extensor weakness associated with chronic lateral epicondylitis.

Key Words: Epicondylitis—Tennis elbow—Diclofenac.
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Lateral epicondylitis (LE) is the most common overuse injury of the elbow in athletes and workers (3,11). Inflammation of the common extensor paratenon, tendon, or both is involved in the pathologic process particularly in the acute and subacute phases of LE (8). Accordingly, modalities such as oral nonsteroidal anti-inflammatory drugs (NSAIDs) are often used as part of the treatment. Unfortunately, gastrointestinal intolerance to NSAIDs occurs in as many as 30% of patients (10). Local injection of corticosteroids can effectively bypass the gastrointestinal tract and deliver a potent anti-inflammatory drug to the site of pathology, a method known as drug targeting. Risks of cortisone injections include infection, dermal atrophy, tendon weakening and rupture, and pain. If an anti-inflammatory drug could be bound to a vehicle that facilitates transdermal absorption after topical administration, it would act locally at sites of subcutaneous inflammation, as in the treatment of LE. It may provide a well-tolerated and safe alternative to oral NSAIDs or local corticosteroid injections.

Liposomes are vehicles that facilitate transdermal transport and subdermal residence of water soluble drugs. Liposomes are microscopic vesicles composed of membrane-like lipid layers surrounding aqueous compartments. One method of binding drugs to liposomes is a pharmaceutical compounding process called liposomal encapsulation. Once applied topically, liposomes facilitate the transdermal absorption of water soluble drugs through the lipid components of the epidermis and then help slow drug release and clearance once in the subcutaneous tissue. Diclofenac sodium is a commonly used NSAID suitable for liposomal encapsulation.

The purpose of this study was to determine whether topical diclofenac sodium in a liposome compound is an effective treatment for LE.

METHODS

Subjects

A convenience sample of 14 subjects was recruited from the patient population of the Edmonton Sport Institute. Each subject signed an informed consent before commencing the study. Inclusion criteria included the following:

LE defined clinically as lateral elbow pain plus at least one of the following: point tenderness over the lateral

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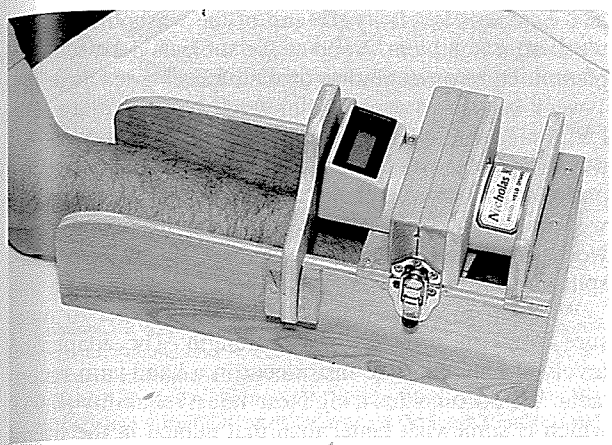

FIG. 1. Hand–arm receptacle housing a dynamometer that was used to measure isometric wrist extensor strength.

epicondyle or aggravation of lateral elbow pain by resisted wrist extension.
Symptom duration of ≥2 months.
No other treatment for LE at the time of the study (e.g., no physical therapy, ice, or NSAIDs) and no corticosteroid injections within 2 months of commencing the study.

Subjects were asked to avoid unusual arm activity for the duration of the study.

Intervention

Two percent diclofenac sodium in a pluronic lecithin liposome organo-gel (PLO) was applied three times daily over the lateral elbow. The study was administered in a double blind, randomized, crossover fashion. For the first week, subjects used PLO from jar A. This was followed by a 1-week washout period during which no PLO was used. During the third week, gel from jar B was used. The contents of each jar was identical in texture, smell, and consistency; however, one PLO contained diclofenac, whereas the other did not. Both jars were identical, and neither the subjects nor the researchers were aware of which contained the diclofenac until after the study. The content code was known by a pharmacist who established the treatment randomization schedule.

Outcome measures

Lateral epicondylitis severity was quantified by measuring isometric wrist extensor strength and the subjects' estimates of average elbow pain for the preceding 24 hours using a visual analog pain scale (6). These measurements were made on 2 consecutive days within the week before the first gel application in order to evaluate test–retest reliability of the outcome measures and to familiarize the subjects with the testing procedures. The same strength and pain measurements were also made before treatment and at the end of each of the 3 treatment weeks (jar A, washout, jar B).

Isometric wrist extension strength measurements were made using a Nicholas MMT handheld dynamometer (Lafayette Instrument, Lafayette, IN, U.S.A.) adapted by mounting it in a hand–arm receptacle (Fig. 1). This was designed to eliminate the tester component of the variability present in the previously described "make or break" tests for handheld dynamometers (1). Before the contents of the gels were revealed to the subjects, they were asked whether one gel was more effective than the other. Any adverse effects from the gel were recorded.

Analysis

Subject characteristics were summarized using descriptive statistics. Test–retest reliability was evaluated by Pearson's product moment correlation. Repeated measures analysis of variance was used to assess the efficacy of the topical diclofenac. Scheffé post hoc tests were used to assess significant differences, and alpha was set at 0.05.

RESULTS

Of the 14 subjects, 8 were men, 13 were right-handed, and 9 had LE affecting their dominant arm. The subjects' mean age was 42.5 years ± 6.8. Average symptom duration was 8.3 months (range, 2–24 months).

Preintervention test–retest reliability measures were 0.95 and 0.78 for the isometric wrist extension strength and visual analog scale, respectively.

Mean wrist extensor strength and pain at the baseline, treatment, placebo, and washout periods are illustrated in Figures 2 and 3. The main effect of strength was significant (F ratio = 3.25; p = 0.03). Strength while using topical diclofenac was significantly greater than before treatment. The main effect of pain was also significant (F

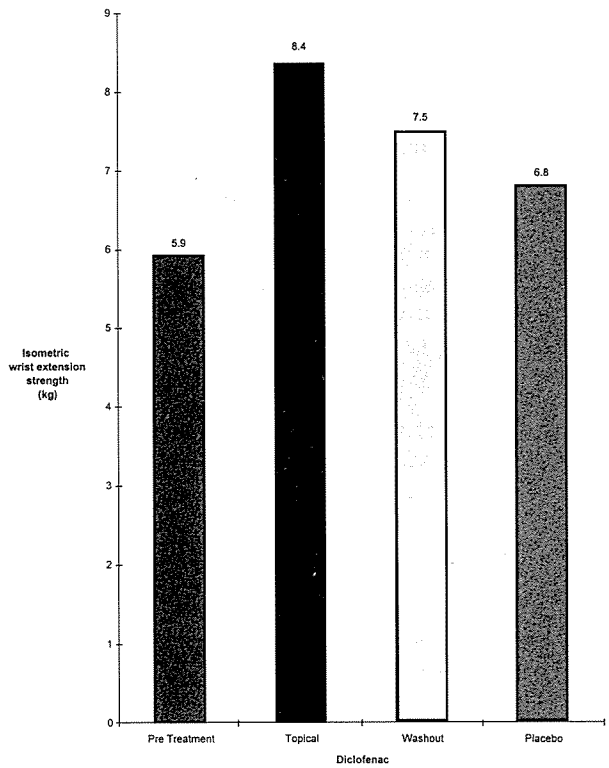

FIG. 2. Effect of topical diclofenac on isometric wrist extension strength in patients with lateral epicondylitis.

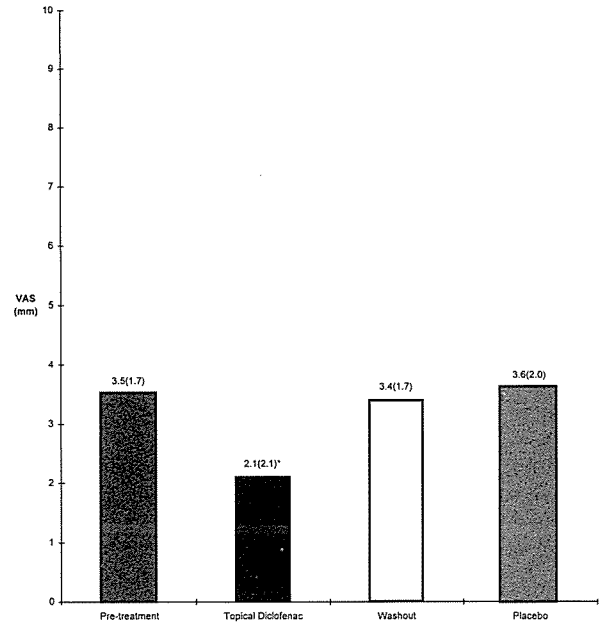

FIG. 3. Effect of topical diclofenac on visual analog pain score (VAS) in patients with lateral epicondylitis. Results are expressed as mean (standard deviation). *p < 0.05; topical diclofenac pain was significantly less than pretreatment, washout, and placebo pain.

ratio = 4.63; p = 0.007). Pain while using the topical diclofenac was significantly less than that before treatment, at the end of the washout period, and while using the placebo gel.

Eight subjects correctly identified the diclofenac gel as the therapeutic gel and thought it was helpful. One subject developed a rash at the site of application while using the diclofenac gel. This subject completed the study, and the rash cleared within 2 days of discontinuing the gel application.

DISCUSSION

The purpose of this investigation was to determine if topical diclofenac in a liposome compound is an effective treatment for LE. Our results suggest that it is effective in reducing subjective pain and associated weakness. These results are particularly impressive because of the small study sample size and that the subject sample consisted of those with chronic LE. Although active inflammation is common with acute LE, chronic LE has been characterized by angiofibroblastic hyperplasia and minimal inflammatory response (9). It therefore would be predicted that anti-inflammatory treatment is less effective for chronic LE. The advantage of using patients with chronic LE was that their condition was stable thus allowing a within-subject crossover study design. It is possible that the topical diclofenac was effective by virtue of its analgesic rather than anti-inflammatory properties. On average, pain was reduced and wrist extensor strength improved by ~one third during the period of topical diclofenac use. The effect was short lived, however, as reflected by a return to near pretreatment pain and weakness levels by the end of the washout period 1 week after treatment. None of the subjects derived complete, long-term resolution of their LE as a result of the 1-week course of topical diclofenac. For patients with LE, topical diclofenac should not be considered a curative agent, but a well-tolerated treatment adjunct that can provide partial analgesia and minimize pain-related weakness. This role would be valued by athletes and workers who are trying to continue sport and work despite chronic LE.

We used an adapted handheld dynamometer to measure isometric wrist extensor strength. The adaptation involved mounting the instrument in a hand–arm receptacle. We documented a high test–retest reliability (0.95), which is somewhat better than that quoted in the literature for handheld techniques on arms of healthy subjects (0.88) (16). It is probable that use of the hand–arm receptacle diminished the error variance by eliminating the tester contribution to that variability.

Although not commercially available in North America, topical NSAIDs are available and in common use elsewhere, particularly in Europe. Research on effectiveness has been limited but promising. Some of the prior studies have been compromised by threats to internal and external validity including ill-defined diagnostic and outcome criteria, lack of subject and assessor blinding, and lack of a control group regardless of being used to study acute musculoskeletal conditions which have a natural history of recovery (5). Despite these limitations, prior research has found that topical diclofenac compares favorably with other topical NSAIDs (2), particularly if applied as a topical plaster (7,12), and that it is effective in a variety of peri-articular and extra-articular superficial rheumatologic and sport-related conditions (4,7,12). Topical NSAIDs probably have no role in the treatment of deep soft-tissue inflammatory conditions because local penetration has been found to be a depth of only 3–4 mm below the application site (15). Only one prior study was found in the literature that specifically evaluated the effectiveness of topical diclofenac in the treatment of LE. Thirty subjects with acute LE (<4 weeks' duration) demonstrated significant reductions in rest- and activity-related elbow pain in comparison with a control group. Grip strength was unaffected (13).

One of the 14 subjects in our study developed a minor local rash while using the topical diclofenac. It cleared once the use of the agent was stopped. Other authors have reported similar experiences but did not feel discontinuation of the agent was required (5,12,13). Some investigators encountered no adverse side effects (4,7). None of the subjects in our study reported gastrointestinal symptoms while using the topical diclofenac. There is a report in the literature, however, of four cases of upper gastrointestinal hemorrhage associated with topical diclofenac use (17). Two of the patients had a history of ulcers. The topical diclofenac had been applied over a broader area than just the elbow (i.e., the back, neck, and hip). This may have resulted in increased systemic anti-inflammatory drug absorption, although blood levels of diclofenac after topical application have been docu-

mented to be <10% of those observed after parental administration (14). Caution is still advised when patients with a history of peptic ulcer disease use topical diclofenac, particularly if the application area is broad.

In summary, we evaluated the effectiveness of 2% diclofenac in PLO as a treatment for chronic LE. Elbow pain and wrist extensor weakness was reduced during the period of topical diclofenac use.

REFERENCES

1. Bohannan RW. Muscle strength testing with hand-held dynamometers. In: Amundsen LR, ed. *Muscle strength testing.* New York: Churchill Livingstone, 1990:69–88.
2. Bouchier-Hayes TA, Rotman H, Darekar BS. Comparison of the efficacy and tolerability of diclofenac gel (Voltarol Emulgel) and felbinac gel (Traxam) in the treatment of soft tissue injuries. *Br J Clin Pract* 1990;44:319–20.
3. Chard MD, Hazleman BC. Tennis elbow—a reappraisal. *Br J Rheumatol* 1989;28:186–88.
4. Galeazzi M, Marcolongo R. A placebo controlled study of the efficacy and tolerability of a nonsteroidal anti-inflammatory drug, DHEP plaster, in inflammatory peri- and extra-articular rheumatological disease. *Drugs Exp Clin Res* 1993;19:111–9.
5. Grahame R. Transdermal non-steroidal anti-inflammatory agents. *Br J Clin Pract* 1995;49:33–5.
6. Huskisson EC. Measurement of pain. *J Rheumatol* 1984;9:768–81.
7. Jenoure P, Seqesser B, Luhti U, Gremion G. A trail with diclofenac HEP plaster as topical treatment in minor sports injuries. *Drugs Exp Clin Res* 1993;19:125–31.
8. Neipal GA, Sitaj E. Enthesopathy. *Clin Rheum Dis* 1979;5:857–72.
9. Nirshl RP. Defining and treating 'tennis elbow.' *Contemporary Surg* 1977;10:13.
10. Polisson R. Nonsteroidal anti-inflammatory drugs: practical and theoretical considerations in their selection. *JAMA* 1996;100 (suppl 2A):315–36.
11. Regan WD. Lateral elbow pain in the athlete: a clinical review. *Clin J Sport Med* 1991;1:53–8.
12. Rosenthal M, Bahous I. A controlled clinical study on the new topical dosage form of DHEP plasters in patients suffering from localized inflammatory diseases. *Drugs Exp Clin Res* 1993;19: 101–12.
13. Schapira D, Linn S, Scharf Y. A placebo-controlled evaluation of diclofenac diethylamine salt in the treatment of lateral epicondylitis of the elbow. *Curr Ther Res* 1991;49:162–8.
14. Seth BL. Comparative pharmacokinetics and bioavailability study of percutaneous absorption of diclofenac from two topical formulations containing drug as a solution or as an emulsion gel. *Arzneimettelforschung* 1992;42:120–2.
15. Singh P, Roberts MS. Skin permeability and local tissue concentrations of nonsteroidal anti-inflammatory drugs after topical application. *J Pharm Exp Therap* 1994;268:144–51.
16. Wadsworth CT, Krishman R, Sear M, Harrold J, Nielson DH. Interrater reliability of manual muscle testing and hand-held dynametric muscle testing. *Phys Ther* 1987;67:1342–7.
17. Zimmerman J, Siguencia J, Tsvang E. Upper gastrointestinal hemorrhage associated with cutaneous application of diclofenac gel. *Am J Gastroenterol* 1995;90:2032–4.