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Research Article

EFFICACY AND TOLERABILITY OF AN ESSENTIAL OIL FORMULATION CONTAINING OIL OF *BOSWELLIA SERRATA* AND *CURCUMA LONGA* IN PATIENTS WITH ACUTE SOFT TISSUE INJURIES: A RANDOMIZED, OPEN LABEL, PILOT STUDY

REJI KIZHAKKEDATH*

Anugraha Medical Centre, Kochi, Kerala 682030, India. E-mail: drrejikiz@gmail.com

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ABSTRACT

Objective: The present study evaluates the efficacy and tolerability of an essential oil formulation containing oil of *Boswellia serrata* and *Curcuma longa* in patients with acute soft tissue injuries.

Methods: The Essential oil formulation containing oil of *Boswellia serrata* and *Curcuma longa* was evaluated by topical application. The subjects were divided into two groups. Subjects of one group received Essential oil formulation whereas other group of subjects received Diclofenac sodium spray (1% w/w). The formulations were applied thrice daily over the affected part for 7 days. Evaluation was based on validated Visual Analogue Score (VAS) and Verbal Rating Scale (VRS).

Results: The average pain scores by VAS at the end of seven days of treatment showed that Diclofenac sodium Spray reduced the average pain score by 72.13% whereas Essential oil formulation reduced it by 92.06 %. Essential oil formulation was comparable with Diclofenac Spray in reducing pain at rest, upon movement and pressure. No adverse events related to the study medication were noticed in the 13 patients given Essential oil formulation.

Conclusion: The results confirm the excellent efficacy, safety and tolerability profile of Essential oil formulation comparable to the commercially available Diclofenac sodium Spray. In view of its efficacy and safety, Essential oil formulation can be recommended for the treatment of acute soft tissue injuries.

Keywords: Curcumin, Boswellia, Topical spray, Anti-inflammatory, Pain, NSAID's

INTRODUCTION

Soft tissue injuries include bumps and bruises (contusions) and small tears of muscles (minor strains) or of ligaments and tendons near joints (minor sprains). Contusions, mild strains and sprains produce mild to moderate pain and swelling. The swelling can become discolored, turning purple after a day and becoming yellow or brown days later. The person usually can continue using the body part [1]. People with more severe symptoms, such as deformity, an inability to walk or use an injured part, or severe pain, may have a mild strain or sprain. However, they may also have a complete separation of bones that were attached within a joint (dislocation), partial separation of bones that were attached within a joint (subluxation), fracture, severe sprain or strain, or other severe injury. People with severe symptoms usually need medical care to determine the nature of the injury [2,3].

In general medical practice contusions, sprains and strains are frequently diagnosed, mostly as the consequences of accidents and sport injuries. The treatment applied has to alleviate the local pain and control the injury induced inflammation over several initial days, after which the proper restoration of the injured tissues should result in the healing and regaining of the full functionality. The standard therapeutic measures of the uncomplicated cases consist of ice packs, resting of the limb and pain killing medication. Traditional non-steroidal anti-inflammatory drugs (NSAID's) are known to be very effective in controlling the inflammation and reducing the pain and discomfort. Topically applied, locally active formulations of drugs offer valid therapeutic alternatives [4,5].

Boswellia is the dried gum resin of *Boswellia serrata*, which has long been used in ancient Ayurvedic medical texts of India, as a powerful anti-inflammatory agent [6]. Boswellic acids are the active constituents of gum resin of Boswellia. Studies have shown that the boswellic acids have an anti-inflammatory action much like the conventional non steroidal anti-inflammatory drugs (NSAID's) used for inflammatory conditions [7]. Boswellia inhibits pro-inflammatory mediators in the body, specifically leukotrienes via inhibition of 5-lipoxygenase, the key enzyme involved in the biosynthesis of pro-inflammatory leukotrienes. Boswellic acids are well known for its capacity to effectively reduce all signs of inflammation; pain, erythema, swelling and temperature [8-10].

Curcuma longa, commonly known as Turmeric has been used in Ayurveda for centuries. Turmeric contains an essential oil (volatile oil) containing terpenes and curcuminoids. Curcuminoids exert their anti-inflammatory action by inhibition of cyclo-oxygenase and lipo-oxygenase enzymes. This enzymatic inhibition results in diminished inflammatory products of arachidonic acid metabolism i.e. prostaglandins, leukotrienes and 5-hydroxy eicosatetraenoic acid. Curcumin selectively inhibits synthesis of inflammatory prostaglandin thromboxane (TXA_2) while not affecting the synthesis of prostacycline (PGI_2). No toxicity associated with turmeric is reported in animal or human clinical studies. The volatile oil of turmeric also possess anti inflammatory properties as evidenced from clinical studies [11-13].

Topical essential oil formulation contains essential oils of *Boswellia serrata* and *Curcuma longa*. It is clear liquid brownish-yellow in colour having characteristic odour. The present study was designed to compare the efficacy and tolerability of two topically applied formulations i.e. Essential oil formulation and Diclofenac spray based on validated Visual Analogue Score (VAS) and Verbal Rating Scale (VRS).

MATERIALS AND METHODS

Drugs and chemicals

Topical formulation containing essential oils of *Boswellia serrata* and *Curcuma longa* (Arjuna Natural Extracts Ltd., Aluva, India) and Diclofenac sodium spray 1% w/w (purchased locally) were used in the study.

Study design

The study was an open label, randomized, pilot study done at Anugraha Medical Centre, Kochi, Kerala, India. All study participants gave written informed consent to participate and the study was approved by the Ethics Committee.

Patients

Subjects of both sexes were eligible for the study if the following study criteria were fulfilled:

- Patients of both sexes aged between 19 and 70 years.

- Painful soft tissue injury (strain, sprain, contusion, distortion) within the last 24 hours.
- Pain on movement not less than 50 mm assessed by Visual Analogue Scale (VAS).
- Pain on movement not less than 30mm assessed against the Verbal Rating Scale (VRS).

Patients did not qualify if any of the exclusions were present:

- Known hypersensitivity to any component of the medications used in the study.
- Any bone injury or injuries that required treatment with NSAID within 1 week prior to the study entry.
- Presence of fractures, open wounds or skin diseases at the site of topical drug application.
- Concomitant treatment with medications that might influence the therapeutic outcomes of the study medications

After identification of a candidate who satisfied the study criteria, he/she was approached by the consenting professional regarding candidacy for the trial. Interested subjects were asked to sign the informed consent form.

Study objectives

Primary Study Endpoints

The primary study parameter was to find the difference in pain score between Day 1 and Day 7 (end of study). The pain score consists of the evaluation of pain at rest, pain on movement and pain upon pressure. The severity of each pain type was assessed against the validated visual analogue scale (VAS), a 10 cm scale with 0 at one end representing no pain and 10 at the other end representing pain as bad as it could be and expressed in mm. The average pain score was calculated by dividing the sum of the three pain severities by 3.

Secondary Endpoints

Pain at rest, movement and pressure was assessed by a 0 to 10 point verbal rating scale (VRS). Improvement in clinical signs of inflammation- swelling, redness, local temperature and functional impairment was assessed on a 5 point scale (0= no sign, 1= very mild, 2= mild, 3= moderate, 4= severe, 5= very severe). A score was built for each patient at the baseline, day1, 3, 5 and 7. The % change between the day 1 value and end of study was calculated.

Randomization

Patients were screened according to the requirements of the protocol. Patients who fulfilled the study criteria and signed the informed consent were assigned the medication according to the validated system of an ascending number randomization list. Two parallel groups were formed, group A treated with Essential oil formulation and Group B treated with a Diclofenac Sodium spray.

The study drugs (Essential oil formulation and Diclofenac sodium spray) were applied three times a day to cover the affected area entirely. The study duration for each subject was 7 days with the treatment with topical sprays starting from day 1. The selected subjects were sequentially allotted randomization numbers 101 to 130.

Study medication

Essential oil formulation was provided in 50ml bottles and a commercially available Diclofenac sodium spray in metal containers were dispensed to the patients from the pharmacy. Careful instructions were given to patients on how to use the spray. Patients were advised to apply between 2 to 5 sprays as to cover the affected area completely three times a day. Patients were requested to keep medications constant throughout the trial if possible, since any rescue medication would reduce the pain scores and cause a serious confounding of the experimental design.

Treatment of subjects

The subjects were randomized into two groups. Both groups received ice pack application and immobilization on day 0.

Group A: Subjects received Essential oil formulation applied thrice daily over the affected part from day 1 to day 7.

Group B: Subjects received Diclofenac sodium spray applied thrice daily over the affected part from day 1 to day 7.

The study assessments were made at day 0, day 1, day 3, day 5 and day 7. No concomitant application of analgesic or anti-inflammatory sprays, ointments, gels and consumption of analgesic or anti inflammatory drugs were permitted during or one week before the study. The assessments of pain at rest, pain upon movement and pressure were taken at day 0 and day 1, day 3, day 5 and day 7 on VAS and VRS. The patients were asked to report their pain intensity by indicating a point on the line. The distance between zero and the marked point was considered as the pain intensity that the patient experienced. The average pain score was calculated. The improvement in pain assessed by the VRS and improvement in the clinical signs of inflammation assessed on a 5 point scale was analyzed as secondary end points. Safety was evaluated on the basis of adverse events. In addition, patients and investigators assessed the tolerability of both the sprays using a four point scale (excellent, good, moderate, and poor) at the end of the study.

The statistical significance within a group was analyzed by using one way analysis of variance (ANOVA), followed by Dunnet's test.

RESULTS

Forty-nine patients were screened as potential participants in the study, of whom 30 were randomized into the study. Of those, 26 completed the study with average age of 38 years and an average body weight of 66 Kg. There were 9 females and 21 males. Out of 26 patients who completed the trial; 13 patients were randomized to receive Essential oil formulation and 13 patients to receive Diclofenac spray.

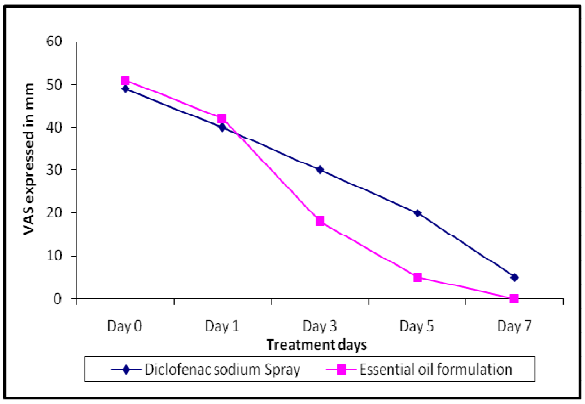

Fig. 1: Pain score at rest after 7 days treatment

No patients were taking additional oral NSAID's. The four patients who dropped out of the study did so for their own reasons.

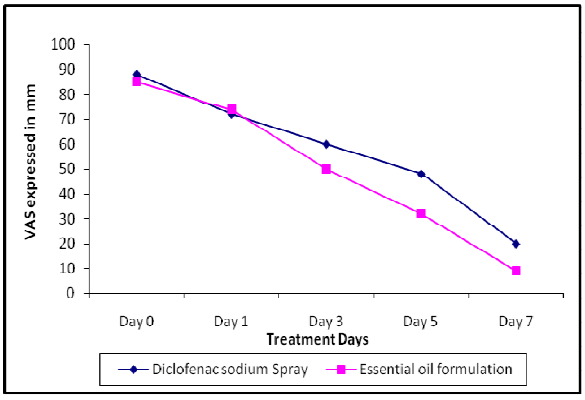

Fig. 2: Pain score upon movement after 7 days treatment

The assessment of pain scores at rest, upon movement, pressure and average pain score at different treatment days are depicted in Figure 1-4. In both the groups, there was statistically significant difference between Day 0 and Day 7 (p<0.05). There was no significant difference (p>0.05) between the two groups at any time point.

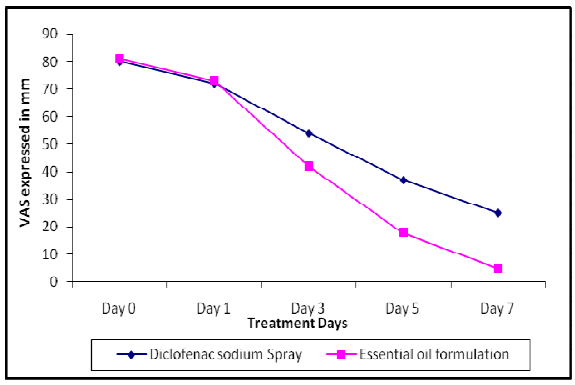

Fig. 3: Pain score upon pressure after 7 days treatment

The average pain score by VAS at the end of seven days of treatment showed that Diclofenac sodium spray reduced the average pain score by 72.13% whereas Essential oil formulation reduced it by 92.06 %. Essential oil formulation was comparable to Diclofenac spray in reducing pain at rest, upon movement and pressure.

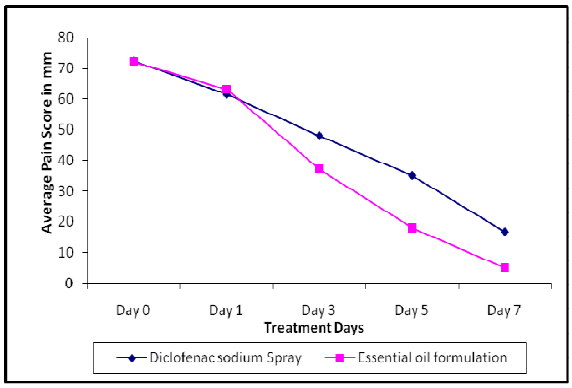

Fig. 4: Average pain score after 7 days treatment

As assessed by VRS, the Essential oil formulation decreased the average pain score by 87.30 % over a period of seven days whereas Diclofenac sodium spray decreased it only by 63 %. The average score of clinical signs of inflammation assessed on a 5 point scale at different time points showed a decrease of 70 % with Diclofenac spray and 90 % with Essential oil formulation. No extra medication was needed by the patients during the treatment period.

No adverse events related to the study medication were noticed in the 13 patients given Essential oil formulation. One patient in the Diclofenac sodium group complained of mild gastrointestinal aching and another patient complained of burning sensation at the site of application during the treatment week. Generally both treatment arms were well tolerated by the patients.

The efficacy of Essential oil formulation was rated comparable to the Diclofenac sodium spray by both the investigator and the patients and the tolerability of Essential oil formulation was excellent.

DISCUSSION

Acute soft tissue injuries require rapid and optimal treatment. The classical primary treatment with cold compresses is often supported by topical application of a variety of anti-inflammatory drugs. An effective treatment should relieve acute pain and reduce swelling in the injured area to restore normal movement. Moreover, it should be safe, well tolerated, easy to use, and accessible [14].

Although oral non steroidal anti-inflammatory drugs (NSAID's) are effective in the treatment of a variety of acute and chronic pain conditions, their use may be associated with serious systemic adverse effects particularly gastrointestinal disorders and accounts approximately one-quarter of all adverse drug reaction reports [15]. In order to minimize the incidence of systemic events related to such agents, topical NSAID's have been developed. Topical NSAID's, applied as gels, creams or sprays, penetrate the skin, subcutaneous fatty tissue and muscle in amounts that are sufficient to exert a therapeutic effect on peripheral and central mechanisms in the absence of high plasma concentrations. Data indicate that topical analgesics are effective at relieving pain in a number of acute and chronic pain indications. But even topical NSAID's have adverse effects and occur in approximately 10 to 15% of patients and are primarily cutaneous (rash and pruritus at the site of application) in nature [16-18]. Therefore, the study was an attempt to clinically establish the beneficial effects and safety of combination of two natural anti-inflammatory agents for the acute soft tissue injury.

The study shows that Essential oil formulation decreases the average pain score in patients with acute soft tissue injury 20% more efficiently than the commercially available Diclofenac sodium spray. Verbal response scale also shows a 24.3% better efficacy for the Essential oil formulation. The signs of inflammation shows a significant reduction in the swelling, redness, local temperature and functional impairment with Essential oil formulation 20% more pronounced than the Diclofenac sodium spray. No adverse events were reported with the use of Essential oil formulation and the patient compliance was excellent.

The results confirm the efficacy, safety and tolerability profile of Essential oil formulation comparable to the commercially available Diclofenac sodium spray. In view of its efficacy and safety, Essential oil formulation can be recommended for the treatment of acute soft tissue injuries.

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REFERENCES

1. Agel J, Dompier TP, Dick R, Marshall SW. Descriptive epidemiology of collegiate men's ice hockey injuries: National Collegiate Athletic Association Injury Surveillance System, 1988-1989 through 2003-2004. J Athl Train 2007; 42:241-8.
2. Arnheim D, Prentice W. Principals of Athletic Training. 14th ed. New York: McGraw Hill; 2010.
3. Campbell JD, Higgs R, Wright K, Leaver-Dunn D. Pelvis, Hip and Thigh Injuries. In: Schenck RC, editor. Athletic Training and Sports Medicine. 3rd ed. Rosemont, IL: American Academy of Orthopaedic Surgeons; 1999. p. 411-2.
4. Jackson DW, Feagin JA. Quadriceps contusions in young athletes. Relation of severity of injury to treatment and prognosis. J Bone Joint Surg Am 1973; 55:95-105.
5. Sanders B, Nemeth WC. Hip and Thigh Injuries. In: Zachazewski JE, Magee DJ, Quillen WS, editors. Athletic Injuries and Rehabilitation. 1st ed. Philadelphia, PA: WB Saunders Company; 1996. p. 611-4.
6. Ammon HP. Boswellic acids in chronic inflammatory diseases. Planta Med 2006; 72:1100–16.
7. Poeckel D, Werz O. Boswellic acids: biological actions and molecular targets. Curr Med Chem 2006; 13:3359–69.
8. Singh GB. Pharmacological profile of boswellic acids obtained from Boswellia serrata as a new type of non-steroidal anti-inflammatory drug. Phytomedicine 2008; 15:545–6.
9. Singh GB, Atal CK. Pharmacology of an extract of salai guggal ex-Boswellia serrata, a new non-steroidal anti-inflammatory agent. Agents Actions 1986; 18:407–12.
10. Sailer ER, Subramanian LR, Rall B, Hoernlein RF, Ammon HP, Safayhi H. Acetyl-11-keto-beta-boswellic acid (AKBA): structure requirements for binding and 5 lipoxygenase inhibitory activity. Br J Pharmacol 1996; 117:615–8.
11. Aggarwal BB, Kumar A, Bharti AC. Anticancer potential of curcumin: Preclinical and clinical studies. Anticancer Res 2003; 23:363-98.
12. Sharma RA, Gescher AJ, Steward WP. Curcumin: The story so far. Eur J Cancer 2005; 41:1955-68.

13. Antony B, Merina B, Iyer VS, Judy N, Lennertz K, Joyal S. A Pilot Cross-Over Study to Evaluate Human Oral Bioavailability of BCM-95CG (Biocurcumax), A Novel Bioenhanced Preparation of Curcumin. Indian J Pharm Sci 2008; 70:445-9.
14. Paolini J, Orchard J. The use of therapeutic medications for soft tissue injuries in sports medicine. Med J Aust 2005; 183:384-8.
15. Massey T, Derry S, Moore RA, McQuay HJ. Topical NSAIDs for acute pain in adults. Cochrane Database Syst Rev 2010; 16:CD007402.
16. Ivins D. Acute ankle sprain. Am Fam Physician 2006; 74:1714-20.
17. Slatyer M, Hensley M, Lopert R. A randomized controlled trial of piroxicam in the management of acute ankle sprain in Australian Regular Army recruits. The Kapooka Ankle Sprain Study. Am J Sports Med 1997; 25:544-53.
18. Dalton JD Jr, Schweinle JE. Randomized controlled non-inferiority trial to compare extended release acetaminophen and ibuprofen for the treatment of ankle sprains. Ann Emerg Med 2006; 48:615-23.