

Clinical Study to Establish Efficacy and Safety of Contodol Gel as Topical Pain Relieving Agent

S Satam^{1*}, R Jain², J Dagaonkar², C Chotalia², A Suthar², R Joshi³

¹ BSES MG Hospital, S.V.Road, Opp . Rly. Station, Andheri (West), Mumbai, Maharashtra, India

² Piramal Life Sciences Ltd., 1, Nirlon Complex, Off. Western Express Highway, Goregaon (East), Mumbai – 400 063. Maharashtra, India

³ Om Clinical Research Private Limited, 14, Shiv Shanti, Juhu Versova Link Road, Andheri (west), Mumbai 400053, India

*e-mail: s_stm@rediffmail.com

Summary

This study was planned to evaluate the efficacy and safety of Herbal Gel (Contudol Gel) in the management of pain and inflammation associated with the musculoskeletal inflammatory disorders. Forty five patients of either sex in the age group of 32 to 63 years were enrolled in the study after they fulfilled the inclusion and exclusion criteria. Patients applied Herbal gel over the affected area, twice daily with gentle rubbing for a period of three weeks. This study indicated that there was a significant reduction in pain, joint tenderness, joint swelling, mobility restriction and early morning joint stiffness. In patients with periartthritis shoulder joint, osteoarthritis knee joints, and nonspecific arthritis, there was moderate reduction of pain. There were no adverse events reported or observed during the entire period.

Keywords: Herbal Gel, Contudol, Pain, Rheumatoid arthritis, Morning stiffness.

Introduction

The international association for the study of pain has defined pain as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage”. According to the World Health Organization (WHO), pain is the most common reason for which patients visit their physician.¹ Pain can be divided into two basic categories, acute and chronic. A common definition of acute pain is “the normal, predicted physiological response to an adverse chemical, thermal or mechanical stimulus associated with surgery, trauma and acute illness”.

Chronic pain refers to pain that persists after an injury, pain related to a persistent or degenerative disease, and long-term pain from an unidentifiable cause. Chronic pain may be caused by the body's response to acute pain. One of the frustrating aspects of chronic pain is that the stimulus may be unknown. For example, the stimulus cannot be identified in as many as 85% of individuals suffering lower back pain.

The common causes of joint pain are osteoarthritis (OA), rheumatoid arthritis (RA), post-traumatic arthritis, and avascular necrosis. Joint pain can also be caused by deformity or direct injury to the joint. In some cases, joint pain is made worse by the fact that a person will avoid using a painful joint, weakening the muscles and making the joint even more difficult to move. Conservatively, analgesics, muscle relaxant gel, and pain relieving liniments are some of the simplest external application methods for relieving pain. One of the most commonly prescribed types of drugs are the non-steroidal anti-inflammatory agents or NSAIDs, which has to be taken for long-term to reduce both the pain and swelling caused by arthritis. NSAIDs are among the most widely used medications, but the side effects of these drugs frequently include gastrointestinal (GI) ulceration, indigestion, burning, and bleeding.² In rare cases, serious stomach problems, such as bleeding, can occur without warning. NSAIDs and COX-2 inhibitors should not be taken by people who are allergic to aspirin.^{3,4} Another type of medication prescribed to reduce severe pain and swelling are corticosteroids. Corticosteroid injections offer quick, effective pain relief. However, they can be used only few times a year because they weaken bone and cartilage.⁵⁻⁸ Also, as corticosteroids can cause other potentially serious side effects,^{9,10} their use must be monitored by a physician.

The use of herbal medicine is a popular healthcare approach across India as well as globe, and there are signs that the use of such products is continuing to increase. Patients use herbal medicines for health maintenance, for the treatment or prevention of minor ailments as well as also for serious, chronic illnesses.^{11,12} Herbal medicines are complex mixtures of minimally processed medicinal plants (e.g., plant parts that are boiled to make a tea). In conjunction with other components of traditional healing philosophies, such as acupuncture or massage, herbal medicines are used to treat a large range of symptoms and ailments.¹² Nowadays, it is still considered a useful and natural way to treat several medical conditions, including chronic disorders like arthritis, cancer, diabetes etc.

Herbal Gel – Contudol Gel (A product of Piramal Life Sciences Ltd, which is Department of Science and Technology, Govt. of India recognized institute focused on pharmaceutical and clinical research and development) is a polyherbal formulation and it contains Methyl salicylate, *Cedrus deodara* oil, *Boswellia serrata* oil, Eucalyptus oil, Menthol, Camphor and Capsicum oleoresin. This study was planned to evaluate the efficacy and safety of Herbal Gel in management of pain and inflammation associated with the musculoskeletal inflammatory disorders.

Application of Herbal Gel as a treatment modality has been evaluated in 45 patients attending Dr. Shubhangi Satam's Clinic of Ayurveda and Research, Mumbai, Maharashtra, India.

Methodology

Aim of the study

The present study was aimed to evaluate the clinical efficacy and long-term safety of Herbal Gel (Contudol Gel) in management of pain and inflammation associated with the musculoskeletal inflammatory disorders.

Study design

This study was an open clinical study conducted by Dr. S. Satam's Clinic of Ayurveda and Research, Mumbai, Maharashtra, India.

Inclusion criteria

Forty-five patients of either sex in the age group of 18-63 years were enrolled in the study. A written informed consent was obtained from all these patients. All included patients had clinical symptoms of either of the following:

Rheumatoid arthritis (RA),
Osteoarthritis (OA) knee joints,
Spondylosis,
Post-traumatic stiffness
Non specific arthritis
and
Peri-shoulder arthritis

Exclusion criteria

Patients with clinically active renal, hepatic or peptic ulcer disease, history of alcohol or drug abuse, concomitant skin disease or abrasions at the application site and those patients who were using any other topical product at the application site were excluded from the study. Pregnant women were also excluded from the study.

Study procedures

The study was conducted in 45 patients with a mean age of 47.5 ± 15.3 years with 27 male and 18 female patients. Duration of illness ranged between 6 months to 7 years. Out of 27 male patients, 7 were smokers and 2 were alcoholics. In the present study, 10 patients suffering from OA, 12 patients suffering from RA, 8 patients suffering from lumber/cervical spondylosis, 6 patients suffering from acute sprains, 4 patients suffering from post-traumatic stiffness and 5 patients suffering from peri-shoulder arthritis were recruited. The diagnosis of the concerned disease was confirmed by clinical examination. The study duration was three weeks. All the patients were assessed for symptomatic parameters like relief in pain intensity, swelling, tenderness, early morning stiffness, joint mobility and muscle cramps. Score for pain intensity, swelling, and tenderness was done using 0-3 scale where 0: no pain, 1: mild, 2: moderate, and 3: severe. In case of joint mobility, the scoring was 0: no restriction, 1: mild restriction, 2: moderate restriction, and 3: severe restriction. All patients were advised to apply Herbal Gel over the affected area, twice daily for the period of three weeks.

Follow-up and assessment

The patients were followed-up at weekly interval during, which evaluation of the clinical parameters was recorded. A complete clinical and orthopedic evaluation was carried out at the end of the study.

Primary and secondary outcome measures

The predefined primary outcome measures for efficacy were relief of pain, swelling and tenderness. Secondary outcome measures were short and long-term and patient compliance to therapy.

Results

A total of 45 patients were enrolled and completed the study. They were in the age group ranging between 30-63 years.

45 patients were included in the study. Symptoms such as joint pain, tenderness, swelling, joint mobility and stiffness were measured in terms of score from 0 to 3 (asymptomatic to severe) before and after treatment.

Out of 45 patients in all categories, 31 patients had joint pain before treatment. Among them 6 had mild (score 1), 11 patients had moderate (score 2), 14 patient had severe (score 3). After treatment with Herbal Gel 25 patients rendered asymptomatic (score 0), in 2 patients mild (score 1), in 3 patients moderate (score 2) and in 1 patient, the symptoms persisted as severe (score 3).

45 patients had tenderness before treatment. Among them 2 had mild (score 1), 5 patient had moderate (score 2), 38 patients had severe (score 3). After treatment with Herbal Gel 41 patients rendered asymptomatic (score 0), in 1 patients mild (score 1), in 2 patients moderate (score 2) and in 1 patients the symptoms persisted as severe (score 3).

In 30 patients who presented with swelling, 1 had mild (score 1), 8 patients had moderate (score 2), 21 patients had severe (score 3). After treatment with Herbal Gel 29 patients rendered asymptomatic (score 0), in 1 patient symptom was mild (score 1). None of them have moderate or severe symptoms.

38 patients had problem in joint mobility before treatment. Among them 6 had mild (score 1), 8 patients had moderate (score 2), 24 patients had severe (score 3). After treatment with Contudol Gel 33 patients rendered asymptomatic (score 0), in 3 patients mild (score 1), in 2 patients moderate (score 2) . None of them had severe problem in joint mobility. In 12 patients who presented with Early morning joint stiffness, 3 had mild (score 1), 4 patients had moderate (score 2), 5 patients had severe (score 3). After treatment with Contudol Gel 11 patients rendered asymptomatic (score 0), in 1 patient symptom was mild (score 1). None of them have moderate or severe symptoms. The results and the statistical significance for various parameters are shown in Tables 1 and 2.

Table 1: Symptomatic score in patients before the treatment

Parameters	Number of patients	Score			
		0	1	2	3
Joint pain	31	-	6	11	14
Tenderness	45	-	2	5	38
Swelling	30	-	1	8	21
Joint mobility	38	-	6	8	24
Early morning joint stiffness	12	-	3	4	5

Table 2: Symptomatic score in patients after the treatment

Parameters	Number of patients	Score			
		0	1	2	3
Joint pain	31	25	2	3	1
Tenderness	45	41	1	2	1
Swelling	30	29	1	0	0
Joint mobility	38	33	3	2	0
Early morning joint stiffness	12	11	1	0	0

The patients with muscle sprain experienced substantial relief from pain. Swelling and tenderness also reduced considerably. Patients with osteoarthritis, nonspecific arthritis, and peri-arthritis shoulder joint had temporary relief from pain and required additional therapy.

Those patients who had received additional sample of Herbal Gel had considerable relief from pain. There was good compliance to the treatment and no adverse events were reported or observed in the study patients during the entire study period. None of the patients withdrew from the study.

Adverse events

Most patients under study were satisfied with the use of Herbal Gel. Three patients had experienced pain and swelling after applying Herbal gel for initial couple of days but received relief within 3-4 days of continued application of the Herbal Gel.

Discussion

Pain is an unpleasant feeling that is conveyed to the brain by sensory neurons. The discomfort signals actual or potential injury to the body. A survey conducted in approximately 26,000 patients has indicated that one adult in five suffers from chronic pain, and out of these 21.5% have experienced pain lasting for longer than 6 months. Pain is the third leading reason for absence from work in the United States, where the problem of chronic pain translates into an annual expenditure of at least \$50 billion¹. In general, musculoskeletal pain, often in the form of arthritis, non-articular rheumatism, peripheral neuropathies and low back

disorders, represents the most common cause of chronic non-malignant pain (CNMP). Exposure to low social support, low social anchorage or low social participation significantly increases the odds of a high level of pain. Most patients do not attribute chronic musculoskeletal pain to injury, but those who do report significantly higher levels of emotional distress¹

For the last few decades, orthopedic treatment modalities like analgesics and external application of muscle relaxant ointments, gels and liniments have been used to relieve pain of minor injury and certain orthopedic problems. Use of analgesic, either oral or parenteral, has many associated complications like gastritis, abdominal distension, constipation, and loose motions. Moreover, analgesics cannot be used for prolonged period considering the risk of above complications.

Therefore, the ideal method for relieving pain in minor trivial injury to muscles and ligaments is a simple method of external application of gel or liniment. There is no time limitation regarding the duration of treatment by external applications. This can be used for prolonged period.

In this study, it was observed that at the end of the study, Herbal Gel (Contudol Gel), a polyherbal topical preparation helped to manage the pain and inflammation associated with musculoskeletal inflammatory disorders. Each gram of Herbal Gel contains Methyl salicylate, *Cedrus deodara* oil, *Boswellia serrata* oil, Eucalyptus oil, Menthol, Camphor and Capsicum oleoresin. Methyl Salicylate produces warm/hot sensation, which relieves painful muscles or joints. *Cedrus deodara* oil is obtained from the aerial parts of plant *Cedrus deodara* is a proven analgesic to remove chronic muscular pain caused by arthritis and also helpful in reducing inflammation and swelling. *Boswellia serrata* oil possesses analgesic and anti-arthritis properties. By regulating the mediators of inflammation, *Boswellia* exerts a significant anti-inflammatory activity. It soothes the joints and also helps in treating levels of synovial fluid making the entire structure lubricated and easy to rotate or to move. Eucalyptus oil has analgesic, anti-inflammatory, anti-rheumatic, rubefacient properties. It has a cooling and deodorizing effect on the body. It is useful as soothing oil when used for muscular aches and pains, rheumatoid arthritis, sprains and poor circulation. Menthol and Camphor used as rubefacients to stimulate circulation and also used as counter-irritants by its cooling effect. Capsicum Oleoresin contains capsaicin, a neuropeptide releasing agent that temporarily stimulates release of various neurotransmitters from these nerves, leading to their depletion. Without the neurotransmitters, pain signals can no longer be sent. Thereby it reduces the localized pain.

This study observed significant reduction in the symptom for Rheumatoid arthritis (RA), Osteoarthritis (OA), Spondylosis, Post-traumatic stiffness and Peri-shoulder arthritis. These excellent beneficial actions of Herbal Gel might be due to synergistic actions of its ingredients, which are well documented.

A total of 45 patients with various types of pain and some orthopedics diseases having pain, swelling, and muscle spasms were treated by Herbal Gel (Contudol Gel). The experience after using Herbal Gel has confirmed that the main clinical benefits are relief from pain intensity, swelling, tenderness, early morning stiffness, joint mobility and muscle cramps. The gel was found to be effective in symptomatic relief in patients suffering from Rheumatoid arthritis (RA), Osteoarthritis (OA), Spondylosis, Post-traumatic stiffness and Peri-shoulder arthritis. No adverse reactions were reported by any of the patients.

References

1. Katz WA. Musculoskeletal Pain and its Socioeconomic Implications. *Clinical Rheumatol* 2002; 21 (1, suppl):S2-S4.
2. Wallace JL, Vong L. NSAID-induced gastrointestinal damage and the design of GI sparing NSAIDs. *Curr Opin Investig Drugs* 2008;9:1151-1156.
3. Bavbek S, Dursun AB, Dursun E, Eryilmaz A, Misirligil Z. Safety of meloxicam in aspirin-hypersensitive patients with asthma and/or nasal polyps. A challenge-proven study. *Int. Arch. Allergy Immunol* 2007;142:64-69.
4. Palmer GM. A teenager with severe asthma exacerbation following ibuprofen. *Anaesth. Intensivecare* 2005;33:261-265.
5. Silbermann M, Kadar T, Hornung G. Corticosteroid-induced changes in glucose metabolism of chondrocytes. *Histochem* 1977;50:327-335.
6. Silbermann M, Maor G. Effect of glucocorticoid hormone on the content and synthesis of nucleic acids in cartilage of growing mice. *Growth* 1979;43:273-287.
7. Silbermann M, Toister Z, Lewinson D. Glucocorticoid-induced changes in the activity of cartilage alkaline phosphatase. *Metab Bone Dis Relat Res* 1981a; 3:67-75.
8. Silbermann M, Weiss A, Raz E. Retardative effects of a corticosteroid hormone upon chondrocyte growth in the mandibular condyle of neonatal mice. *J Craniofac Genet Dev Biol* 1981b;1:109-122.
9. Benyamin RM, Vallejo R, Kramer J, Rafeyan R. Corticosteroid induced psychosis in the pain management setting. *Pain Physician* 2008;11:917-920.
10. Kubota Y, Yoneda K, Nakai K, Katsuura J, Moriue T, Matsuoka Y, Miyamoto I, Ohya Y. Effect of sequential applications of topical tacrolimus and topical corticosteroids in the treatment of pediatric atopic dermatitis: An open-label pilot study. *J Am Acad Dermatol* 2009;60:212-217.
11. Joanne B. Quality, efficacy and safety of complementary medicines: fashions, facts and the future. Part II: Efficacy and safety. *Br J Clinical Pharmacol* 2003a;55:331-40 (Pt II).
12. Joanne B. Quality, efficacy and safety of complementary medicines: Fashions, facts and the future. Part I. Regulation and quality. *Br J Clinical Pharmacol* 2003b; 55: 226-233 (Pt I).
13. Jarema M. Herbal drug treatment. *Neuro Endocrinol Lett* 2008;29 (1, Suppl):93-104.