Management of Musculoskeletal Disorders with Rumalaya, a Polyherbal Formulation: A Review

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ABSTRACT

Despite the availability of analgesics and anti-inflammatory drugs for centuries, satisfactory relief of chronic pain related to musculoskeletal disorders (MSD) remains an important unmet public health need. Rheumatoid arthritis (RA) and osteoarthritis (OA) are two major MSD seen in Indian middle age and elderly age groups. The management of these conditions includes varied modes to achieve desired clinical improvement. The present article reviews five clinical studies conducted on an indigenous polyherbal formulation, Rumalaya in the management of various MSD, specially arthritis. A double-blind placebo-controlled trial on arthritis on 75 patients for eight weeks showed comparable effects to Diclofenac and clearly better than the placebo group. Unlike Diclofenac group, trial group did not show adverse effects of medication namely gastritis or gastric irritation. Another double-blind study on both OA and RA in a total of 235 patients showed complete relief of symptoms in 78.65% and 84.6% of RA and OA groups, respectively. A controlled study on arthralgia of 60 athletes by Rumalaya tablet along with Rumalaya cream showed its efficacy mainly on knee pain in a total of 84% cases in two weeks, significance clearly above the control group. Another trial was conducted on OA of knee in 56 patients for four weeks to 2-month duration. Results showed a marked relief of pain in 73 of 88 knees. Another trial comparing Rumalaya tablet with ibuprofen in the management of OA of 80 patients for 2-6 weeks showed results comparable with that of standard comparator along with added advantage of cost-effectiveness.

In all the studies summarized in the review, safety profile was recorded with no adverse reactions even after long-term use and patient compliance to the trial drug was good.

Keywords: Musculoskeletal disorders, osteoarthritis, rheumatoid arthritis, Rumalaya

In 2000, the Bone and Joint Decade was proclaimed by the World Health Organization (WHO) in recognition of the significant impact of arthritis and musculoskeletal conditions on population health worldwide. This proclamation aimed to raise awareness, promote effective management, empower consumers and encourage research into these important conditions. The terms arthritis and musculoskeletal disorders (MSD) refers to a diverse group of conditions that affect muscle, joints, tendons and other parts of the musculoskeletal system. These conditions are commonly associated with pain and impaired physical function and impact on occupational and psychosocial status often resulting in a reduced quality-of-life or, for some, reduced survival.

Arthritis comprises more than 100 different rheumatic diseases and conditions. Amongst the many categories of these disorders, osteoarthritis (OA) and rheumatoid arthritis (RA) represent a significant proportion. While both diseases fall under the classification or diagnosis of arthritis and rheumatism, they are very different; each has its own distinct characteristics as well as different treatment. These two musculoskeletal conditions are the focus of this review.

An estimated 46 million US adults (about 1 in 5) report doctor-diagnosed arthritis, according to annual estimates and is projected to increase to 67 million by 2030, and more than one-third of these adults will have limited activity as a result. Although arthritis is more common among adults aged 65 years or older, people of all ages (including children) can be affected. Nearly two-thirds of people with arthritis are younger than age 65. In addition, a recent study indicated that some form of arthritis affects one in every 250 children. Arthritis is more common among women (24.4%) than men (18.1%) in every age group, and it affects members of all racial and ethnic groups.

Regardless of the type of arthritis, the common symptoms for all arthritic disorders include varied

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were selected for the study. There were 34 males and 22 females, ranging in age from 35 to 68 years.

All cases were advised Quadriceps exercises and given Rumalaya tablets; two tablets three times a day. The dosage was reduced to 1 tablet three times a day, when patients showed some improvement and was discontinued when they were asymptomatic for 4-6 weeks. Duration of treatment varied from four weeks to 2 months in 32 cases and 2 months in 32 cases and 2 months to six months in the remaining 16 cases. Total number of joints involved by OA was 88; 24 patients with unilateral involvement and 32 patients with bilateral involvement.

Study Procedure

All these cases were regularly observed, clinically examined and improvements were followed up regularly. Eight patients were lost to follow-up study (4 with bilateral involvement of knee).

Results

There was marked symptomatic and clinical relief in 73 knees. There were excellent results in 46 knees, good in 21, fair in six, poor in 3 knees. Eight cases were lost in follow-up. There were no untoward toxic effects in any of the cases.

Conclusion

It is seen that Rumalaya therapy with Quadriceps exercises gives excellent results in patients suffering from OA of knee. Rumalaya tablets can be given for longer duration without any untoward reactions, which are commonly observed with salicylates, phenylbutazone, oxyphenbutazone, indomethacin, dextropropoxyphene, naproxen, etc. From this study, it is seen that pain in OA of knee is a common symptom and one can use Rumalaya tablets for a long duration; they are effective and safe and without any toxicity.

CLINICAL TRIAL 5

Comparative Clinical Study of Indigenous Drugs with Ibuprofen in Patients of OA

Number of Patients and Method

A total number of 80 patients (age range 36-73 years) with diagnosis of OA were selected all the patients enrolled in this study had their history recorded; general physical examination and detailed joint examination was done. All patients had their X-ray of the joint, hemogram, urine examination, blood sugar and serum uric acid levels done. All the patients were asked not to take any drug without informing us. After randomization in the two groups of 40 patients each, patients were asked to take indigenous drug Rumalaya or Ibuprofen tablet (400 mg) at 8-hourly intervals after meals. All the patients were assessed for swelling, stiffness, range of joint motion and for joint pain before drug therapy and after drug therapy at two weeks and at 6 weeks time interval. Patients with any other major illness were excluded from the study.

Results

The assessment of pain relief was done on a numerical scale (1-10) before starting drug therapy and at two weeks and 6 weeks after drug therapy. On statistical analysis (two way analysis of variance) of mean pain intensity scores the results show that indigenous drug and ibuprofen provided significant pain relief at two weeks (p < 0.001) and six weeks time interval (p < 0.00), when compared to pain at the initiation of the study, at rest, on walking and squating. On statistical analysis between the two treatment groups, no significance was observed (p > 0.05) was observed at two weeks and six weeks interval. No significant changes were observed also in their swelling, stiffness and range of motion of joint. No patient reported any side effect with either the medication.

Conclusion

Though both the drugs are equally effective, the indigenous drug is cost-effective. Thus, indigenous drug may be prescribed in patients suffering from OA.

STATUS OF RUMALAYA TABLET IN MUSCULOSKELETAL DISORDERS

Arthritis is a leading cause of pain, physical disability and healthcare utilization. People living with arthritis, their families and society as a whole are affected by the outcomes of the disease. The increased burden of this disease will have a significant impact on health care resources and is also costly from an economic standpoint. Approximately two-thirds of the costs of arthritis are indirect costs due to disability, a measure of lost productivity. Current pain management is largely limited to opioids and nonsteroidal anti-inflammatory drugs, indicating a gap in the translation of new knowledge to the development of improved pain treatments. Indigenous formulation, Rumalaya tablet a polyherbal formulation was evaluated in various MSD-like arthritis and RA and review of five clinical studies are summarized in this review. To summarize, Rumalaya tablets produces beneficial effects in cases of varied types of MSD-like RA, OA, arthralgia, myalgia,
was of 28 years age and the oldest, of 85 years. The majorities were of the age group between 40 and 60 years. Rumalaya was given to 92 cases and placebo to 43 cases. Out of these 43 cases, 19 cases were again put on Rumalaya, as they had no relief with placebo. So, the total number of cases, where complete relief in Rumalaya was administered was 111. There was complete relief from symptoms in 94 cases (84.6%) on Rumalaya. The drug was partially effective in 10 cases and ineffective in 7. There were no side effects in any case. Active Quadriceps exercises against gravity and then against resistance were advised to the patients with OA of the knee. Short-wave diathermy was given to seven cases of OA of the knee. In cases of OA of the spine, hard bed and spinal exercises were advised. Five patients complained of loose motions after taking the drug. In all these patients the trial was stopped. Placebo was ineffective in all the 43 cases.

Dose: One tablet three times a day after meals was the dose prescribed to every patient except in seven cases, where two tablets t.d.s. for the first three days was prescribed.

Conclusion
A double-blind study of the therapeutic effects of Rumalaya in cases of rheumatoid and OA without deformity shows that out of 70 cases of RA-treated with Rumalaya, 78.6% had complete relief and 11.4% had partial relief. Out of 111 cases of OA on Rumalaya, 84.6% had complete relief and 9% had partial relief. These results have been arrived at by a controlled double-blind clinical trial, and could well be compared with published series and trials with other drugs. The drug acts slowly and can be given for long periods. No toxic effects of this drug were observed during the trials.

CLINICAL TRIAL 3
Role of Rumalaya Tablets and Rumalaya Cream in Arthralgia of Athletes

Number of Patients and Method
Sixty patients suffering from arthralgia of sportsmen for periods ranging between 6-24 weeks were selected for the trial. Male patients aged between 25-35 years, suffering from arthralgia and who were willing to give informed consent, were included in the trial. Patients unwilling to provide informed consent or abide by the requirements of the study were excluded from the trial.

Study Procedure
Sixty patients were selected for the trial. Two groups, control and study, consisting of 10 and 50 subjects, respectively, were selected at random for the present study. Complete medical history, general physical and local examinations were carried out and findings were recorded in a standard proforma. Two Rumalaya tablets along with local application of Rumalaya cream, thrice-daily, were given to each case of study group for a period of two weeks. In some cases, the study was carried over to third and fourth week; but, these cases have not been tabulated in the present study. The control subjects were put on placebo tablets and ordinary vaseline for a similar duration.

The results were recorded according to the degree of clinical relief. Four grades, namely ‘poor’, ‘fair’, ‘satisfactory’ and ‘good’ were formulated. Poor cases were those which did not respond to the treatment. Fair cases were those in whom there was complete disappearance of subjective feeling of pain; however, in such cases swelling and even slight tenderness were present. In satisfactory cases, there was no swelling and tenderness only on deep pressure and slight pain on extremes of active movement. Good results were recorded as complete disappearance of symptoms and signs.

Results
It was observed that the drug was most effective in cases of pain in the knee. In the first week 40% of the total number of cases of knee involvement showed good results and further, in the second week 56% more cases of knee involvement showed good results. For the remaining 4% of cases, the treatment was continued for the third and fourth week with ‘satisfactory’ to ‘good’ results. Overall success rate in terms of ‘fair’, ‘satisfactory’ and ‘good’ results of the two weeks’ trial in the study group was approximately 84%. The remaining 16% were carried to the third and fourth week of treatment with satisfactory response in 50% of these cases. The control subjects did not show any appreciable change in the two weeks’ period on placebo. No side effects were observed in any of the cases.

Conclusion
From the findings of this study, it is clearly established that Rumalaya improves the signs and symptoms of arthralgia. The drugs are most effective in relieving arthralgic manifestations of knee joint of sportsmen.

CLINICAL TRIAL 4
A Clinical Trial of Rumalaya in OA of Knee

Number of Patients and Method
Fifty-six patients suffering from OA of knee without any known local cause for the onset of the disease
tablet with that of placebo. A standard protocol of physiotherapy and heat therapy was used along with drug administration. No other drug or local analgesic application was combined during this period. Diclofenac sodium was administered as oral sustained-release tablet once-daily. The relief from joint and muscular pain, free mobility, reduction in joint swelling and tenderness with the administration of drugs were considered as the criteria of efficacy.

Results
Clinical efficacy of Rumalaya tablet was comparable to that of Diclofenac. Both the groups showed significant relief in joint pain and muscular pain. Eighty-eight percent of patients in Rumalaya-treated and 93% of patients in Diclofenac-treated group showed relief from joint pain. All the patients in the Rumalaya-treated group had relief from muscular pain symptoms, whereas in the Diclofenac group, 80% of patients showed relief from muscular pain. Sixty-three percent patients in the Rumalaya group had free mobility of joints, whereas in the Diclofenac group it was only 47%. Seventy-five percent and 90% of patients in the Rumalaya- and Diclofenac-treated groups, respectively had a significant inhibition in joint swelling. A significant reduction of 57% and 75% in joint tenderness was noticed in the Rumalaya and Diclofenac treated groups, respectively. There was significant difference in the drug intolerance in two groups - Rumalaya tablet resulted in no gastritis or gastric intolerance. In the Diclofenac group, 12 patients had to discontinue the drug due to gastritis and gastric intolerance. Rumalaya tablet was completely free from any side effects.

Conclusion
From the above findings it can be concluded that, Rumalaya tablet is suitable for patients with arthritis and nonarticular rheumatic conditions associated with pain and restricted movements, especially for elderly patients and patients with a history of hypersensitivity to Diclofenac.

CLINICAL TRIAL 2
Rumalaya in RA and OA (A Double-blind Trial)\textsuperscript{55}

Number of Subjects and Method
A total of 223 patients were included in the study (88 - RA and 135 - OA).

Patients of mild RA, i.e. without contractures and OA were picked up for study. After essential investigations to confirm the diagnosis patients were put on Rumalaya or placebo. Patients with odd outpatient numbers were given Rumalaya and those with even outpatient numbers were given placebo. The research worker did not know whether he was giving Rumalaya/placebo. Erythrocyte sedimentation rate (ESR), hemoglobin (Hb), total and differential leukocyte count, complete urine examination and stool examination for occult blood were carried out before and after the trial. After 15 days’ treatment, if the patient was having partial relief, then the treatment was continued, till there was complete relief. In cases where there was no relief either the trial was stopped or willing patients were put on the other drug of this trial.

Study Procedure
Cases with RA: In this trial 67 females and 21 males were treated with this drug for RA. Eight cases were of monoarticular arthritis (5 of ankle, 2 of knee and 1 of hip joint). In the remaining 80 cases, there were multiple joint involvements. Swelling of the joints was present in 55 cases, none had contractures.

Cases with OA: Out of 135 cases, 115 cases were of the OA of the knee (70 bilateral and 45 unilateral), 17 were of OA of the spine, two of the ankle and 1 of the carpo-metacarpal joint of thumb. Swelling of the joint concerned was present in 54 cases only. The illness in the majority of patients was chronic.

Results
Cases with RA: Twenty-nine patients were in placebo group and the results were not favorable in any of them. Eleven out of these and 59 other cases (total 70) were given trial drug. In 55 cases response was complete (78.6%). In the majority of patients response was complete in the third week. Out of the remaining, in eight cases there was partial relief from pain and tenderness, but spasm persisted. Seven cases did not respond to this drug.

Aspiration of the joint was done in 10 cases. Novocaine with hydrocortisone was injected after aspiration in all these cases. The process was not repeated afterwards in anyone of them. Patients with involvement of small joints of hands were encouraged to do active movements of fingers in warm saline. Restriction of movements due to spasm and swelling disappeared in all cases with the disappearance of pain. Fall of ESR after the trial was not consistent in all the cases. There was general feeling of well-being and increased appetite. There was actual increase in weight in three cases. Six patients volunteered the statement that their constipation was relieved. No side effect was seen in any of these cases.

Cases with OA: Out of 135 cases, 69 were males and 66 were females. The youngest patient of this series
Dosage: Initially, two tablets twice-daily, followed by 1 tablet twice-daily. Treatment may be continued till pain and inflammation subside.

Adverse effects: No adverse effects have been reported.

Contraindications: Not recommended in pregnancy.

Special precautions: None.

Pharmacological Actions of Individual Ingredients

Anti-inflammatory Activity
Shilajeet (purified),28 E. alba,29 W. somnifera30 and Moringa pterygosperma31 have strong anti-inflammatory activity. V. negundo exhibits anti-inflammatory activity mediated via prostaglandin (PG) synthesis-inhibitory and membrane-stabilizing activities.32 O. sanctum33-35 and Tribulus terrestris36 have cyclooxygenase (COX)-inhibitory activity, and control acute and chronic inflammation. Z. officinale acts as a potent anti-inflammatory agent due to its COX-1, COX-2 and PG biosynthesizing protein-inhibitory actions. Its inhibition of the biotransformation of arachidonic acid is comparable to indomethacin.37-42 Mahayograj guggul has a well-established anti-inflammatory effect in joint disorders.43

Analgesic Activity
V. negundo32 and E. alba44 exhibit analgesic activities. O. sanctum exerts analgesic action both centrally as well as peripherally, which involves interplay between various neurotransmitter systems.45 Shilajeet (purified) acts as prospective modifier of analgesic tolerance.36 Mahayograj guggul has a well-established analgesic effect in joint disorders.43

Antioxidant Activity
M. pterygosperma47 and O. sanctum33 have potent antioxidant activity. T. terrestris acts as an antioxidant due to its inducible nitric oxide synthase (iNOS)-inhibitory activity.36 Z. officinale has antioxidant effect comparable to ascorbic acid. It lowers lipid peroxidation while maintaining the activities of other antioxidant enzymes (superoxide dismutase, catalase and glutathione peroxidase).48 Swarnamakshika bhasma, well-known for its antioxidant action, has a rejuvenating effect.49 Shankha bhasma has antioxidant action due to its cytoprotective activity in the gastrointestinal tract, and reduces gastric irritation.50

Immunomodulatory Activity
O. sanctum modulates both humoral and cell-mediated immune responsiveness, and its immunomodulatory effect may be mediated by GABAergic pathways.31 W. somnifera has immunomodulatory activity.30 Z. officinale raises the thymus and spleen indices, phagocytosis, rate of alpha-naphthyl acetate esterase and titer of IgM, which indicate its immunostimulatory actions.52,53

In order to evaluate the safety and efficacy of Rumalaya tablet, several clinical trials have been conducted.

CLINICAL TRIAL 1

Efficacy of Rumalaya Tablets in Arthritis: A Double-blind Placebo-controlled Trial54

Number of Patients and Method
A total of 75 patients with pain, swelling, early morning stiffness and joint immobility were selected for the trial. Patients in the age group of 40-70 years, having chronic arthritis with pain and with restricted movement for minimum one year duration and who were willing to give informed consent, were included in the trial. Patients receiving steroids or sedatives, which would influence the analgesic effects of the trial drug and unwilling to provide informed consent or abide by the requirements of the study were excluded from the trial.

Study Procedure
The study was a double-blind placebo-controlled trial comparing its efficacy with that of the conventional anti-inflammatory drug, Diclofenac sodium. The patients were divided into three groups. Rumalaya was administered at a dose of two tablets twice-daily for eight weeks. One group of patients also received a placebo to compare the efficacy of Rumalaya tablet.
levels of pain, swelling, joint stiffness and sometimes a constant ache around the joint(s). RA has 19th century roots and a 20th century pedigree. Although its name was introduced in the 1850s, classification criteria were only developed 50 years ago. Observational studies using these criteria portray RA as a serious long-term disease with dominant extra-articular features, limited treatment options and poor outcomes.

Findings of population-based studies show that RA affects 0.5-1.0% of adults in developed countries. The disease is three times more frequent in women than men. Prevalence rises with age and is highest in women older than 65 years, suggesting hormonal factors could have a pathogenic role. Estimates of the frequency of RA vary depending on the methods used to ascertain its presence. RA is best considered a clinical syndrome spanning several disease subsets. These different subsets entail several inflammatory cascades, which all lead towards a final common pathway in which persistent synovial inflammation and associated damage to articular cartilage and underlying bone are present.

Genetic factors contribute 50% of risk of developing RA. Identification of genetic regions tagged by structural variation (single nucleotide polymorphisms) show that more than 30 genetic regions are associated with RA. At present, apart from protein tyrosine phosphatase, nonreceptor type 22 -lymphoid (PTPN22) and human leukocyte antigen (HLA) genes, no major pathogenic insights have come from these genetic associations. However, progress is shown by the realization that from a putative 2 mM of DNA harboring candidate variants, these 30 regions are all contained within 2 mM of DNA. Smoking is the dominant environmental risk factor and doubles risk of developing RA. Its effect is restricted to patients with anti citrullinated protein antibody (ACPA)-positive disease.

Pharmacologic agents are the cornerstone to the management of all patients with RA and are an important treatment option for moderate-to-severe OA. The goals of pharmacologic treatment include pain control, reduction of inflammation and, increasingly, disease modification. Disease-modifying antirheumatic drugs (DMARD) along with short-term treatment with glucocorticoids (oral, intramuscular or intra-articular) is generally considered to rapidly improve symptoms in people with newly diagnosed RA.

Pharmacologic interventions for people with OA and RA must be prescribed in conjunction with nonpharmacologic interventions including patient education, exercise, rehabilitation modalities and referral to specialty services if necessary.

Tumour necrosis factor (TNF) inhibitors and other biological agents have heralded a so-called therapeutic revolution, transforming the outlook for patients with RA. However, improved disease outcomes preceded biological agents, reflecting early use of conventional drugs, ambitious treatment goals, and better management of comorbidities on par with an historic parallel is the 1950s revolution in tuberculosis care. New biological agents in development include drugs that target proximal effects on the immune response and growth factors for T-cell subsets (such as interleukin-17). New conventional drugs with DMARD-like properties might also have important future roles. Clinical trials of inhibitors of the kinases JAK (Janus kinase) and SYK (Spleen tyrosine kinase) have provided promising data, and other targets are under investigation.

ROLE OF RUMALAYA TABLET IN THE MANAGEMENT OF MUSCULOSKELETAL DISORDERS

Rumalaya tablet, a polyherbal formulation is claimed to be effective in various MSD and indicated in rheumatism and RA, cervical and lumbar spondylosis, OA, arthralgia, gout, Frozen shoulder, sprains, traumatic inflammatory conditions like fibrosis, bursitis, synovitis, capsulitis, tenosynovitis, myositis and sciatica. Rumalaya tablet is safe in chronic conditions necessitating long-term use.

Rumalaya tablet has anti-inflammatory and analgesic properties, reduces swelling, inflammation. Muscle relaxant properties of Rumalaya helps restore mobility of the joints. Rumalaya tablets indicated in long-term therapy for conditions like RA showed improvement in stiffness of joints, circumference of joint, joint tenderness and range of movements.

Processed in Nirgundi (Vitex negundo), Guduchi (Tinospora cordifolia), Tulasi (Ocimum sanctum), Bhringaraja (Eclipta alba), Ashvagandha (Withania somnifera), Sunthi (Zingiber officinale) and Dashamoola.

Clinical Pharmacology

Rumalaya tablet has potent anti-inflammatory, analgesic, antioxidant, antiarthritic and immunomodulatory actions.

Indications: Rheumatism/RA; cervical and lumbar spondylitis; OA; arthralgia; gout; frozen shoulder; traumatic inflammatory conditions like fibrosis, bursitis, synovitis, capsulitis, tenosynovitis, myositis and sciatica.
sports injuries and others. The natural ingredients in the product act synergistically to provide multiple benefits like anti-inflammatory, analgesic, antioxidant, antiarthritic and immunomodulatory actions. By regulating the mediators of inflammation, Rumalaya tablet exerts a significant anti-inflammatory action. Muscle relaxant properties of Rumalaya help restore mobility of the joints and reduce muscle pain. Studies have confirmed the safety profile of the product without any toxic or adverse effects with long-term use and also showing good patient compliance in all the studies. To conclude the review, Rumalaya tablet is found to be effective and safe in chronic conditions necessitating long-term use.

REFERENCES