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Original Research Article (Clinical)

Clinical evaluation of *Vatari guggulu*, *Maharasnadi kwatha* and *Narayan taila* in the management of osteoarthritis knee

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ABSTRACT

Background: In present era, pharmacological, bio-chemical and surgical interventions are not success remedy for Osteoarthritis (OA). Ayurveda and other complementary medicine have medication for OA.
Objectives: The main aim of the study was to assess the efficacy and safety of therapeutic combination of *Vatari guggulu* along with *Maharasnadi kwatha* and *Narayan taila* with gentle massage for 15 min daily up to 12 weeks on affected knee joint pain assessed on Visual analogue scale (VAS) and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC).
Materials and methods: It was an open label, multicentre, prospective, clinical study conducted on 142 patients of OA Knee. *Vatari guggulu* 500 mg thrice in a day along with *Maharasnadi kwatha* 20 ml with equal amount of water twice daily and *Narayan taila* 20 ml twice in a day for external application with gentle massage for 15 min up to 12 weeks were used to all the study participants.
Results: VAS, WOMAC score and clinical symptoms were reduced significantly from baseline to end of the treatment ($P < 0.001$).
Conclusions: The study provides good evidence in support of the efficacy and safety of the *Vatari guggulu* along with *Maharasnadi kwatha* and *Narayan taila* in the management of Osteoarthritis knee.

1. Introduction

Osteoarthritis (OA) is a chronic degenerative disorder of multifactorial etiology characterized by loss of articular cartilage, hypertrophy of bone at the margins, subchondral sclerosis and range of biochemical and morphological alterations of the synovial membrane and joint capsule. Pathological changes in the late stage of OA include softening, ulceration and focal disintegration of the articular cartilage; synovial inflammation also may occur. Typical clinical symptoms are pain, particularly after prolonged activity and weight bearing; whereas stiffness is experienced after inactivity [1]. It is also known as degenerative arthritis, which commonly affects the hands, feet, spine, and large weight-bearing joints, such as the hips and knees. It can present as localized, generalized or as erosive osteoarthritis. Most cases of osteoarthritis have no known cause and are referred to as primary osteoarthritis. Primary osteoarthritis is mostly related to aging. Secondary osteoarthritis is caused by another disease or condition [1]. Epidemiological profile of this disease in India is not clear but it is estimated that osteoarthritis (OA) is the second most common rheumatologically problem and is most frequent joint disease with prevalence of 22%–39% in India. Eleven COPCORD (Community Oriented Program for Control of Rheumatic Disorders) reports show knee OA data: there were 3328 knee OA patients out of a total surveyed pooled sample of 41,884. The pooled prevalence of knee OA thus becomes eight percentages. Knee Osteoarthritis prevalence increases with

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age, so that about 11% of all women over the age of 60 years have symptoms due to knee OA [2].

The guidelines for treatment of the OA of the knee from the National institute of health and clinical excellence (NICE), the American college of rheumatology and the European league against rheumatism recommend non-drug treatments including the education of the patients, social support, physical exercises and weight loss [3–6]. Non-steroidal anti-inflammatory drugs (NSAIDs) are still used as the initial treatment in primary care as anti-inflammatory and analgesic agents by inhibiting the synthesis of prostaglandins [7,8]. NSAIDs are associated with a number of side effects, most importantly the increased risk of gastrointestinal (GI) bleeding and renal failure [9,10] as well as increasing risk of myocardial infarction and stroke especially in the COX-2 inhibitor category [11]. The intra-articular injections of corticosteroid and sodium hyaluronate etc. are also in practice but have limited role. Finally end stage forms of OA are treated with knee replacement therapy. This is frequently associated with pain relief but however hold a substantial post-operative risk and financial burden [12,13]. On the basis of limitations, the use of alternative therapies, such as acupuncture, medicinal herbs is on the rise and according to reports; about 60–90% of dissatisfied arthritis patients are likely to use the complementary and alternative medicine (CAM) approach for overcoming pain and associated problems. An increasing number of people in the United States are adopting complementary or alternative medicine approaches to meet their personal health problems. Arthritis (both OA and RA) is one of the foremost diseases for which patient seeks option of complementary or alternative medicine [14]. In treating osteoarthritis, glucosamine and chondroitin sulfate, two of the molecular building blocks found in articular cartilage, are the most commonly used alternative supplements [15].

Sandhivata nomenclature available in Ayurvedic literatures for this clinical entity [16], which is similar to Osteoarthritis. The cause of *sandhivata* in Ayurveda is attributed to improper diet, life style, and old age etc. leading to degeneration of body elements (*dhatu kshaya*), aggravation of *vata*; the humor responsible for all the movements and functions of the body and reduction in *shleshaka kapha;* a slimy substance present in the joints. The aggravated *vata* brings *rukshyata* (dryness), *laghutva* (lightness or porousness), *kharatva* (coarseness) in the joints causing degeneration. In *sandhivata, sandhi shula* (pain in affected joint) is the main feature. The other features are including *shotha* (swelling), *stabdata* (stiffness) and, *atopa* (crepitus) and difficulty in performing the functions of involved joint [17].

On the basis of literature and day to day clinical practice evaluate to scientifically rule out efficacy and safety this combination. Primary and secondary objective was to assess the efficacy and safety of therapeutic combination of *Vatari guggulu* along with *Maharasnadi kwatha* and *Narayan taila* in the management of osteoarthritis simultaneously.

2. Materials and methods

It was an open label, multicenter, non-comparative, prospective, pragmatic trial. The trial protocol and related documents were reviewed and approved by the Institutional Ethics committee of each participating center. The study was conducted in accordance with Schedule Y of Drugs and Cosmetics Act, India, amended in 2005 and Indian Council of Medical Research (ICMR) ethical guidelines for biomedical research on human participants, adopted from World Medical Association (WMA) – Declaration of Helsinki. Trial had registered in the clinical trial registry of India (CTRI/2014/02/004388).

2.1. Primary and secondary outcome measures

Primary outcome measure of study was to evaluate efficacy of Ayurvedic formulations *Vatari guggulu, Maharasnadi kwatha* and *Narayan taila* in the subjects suffering from OA knee by assessing change in WOMAC total Score. The secondary outcome measures were to evaluate the changes in the score of three sub scales i.e. WOMAC pain subscale, WOMAC Stiffness subscale, WOMAC physical function subscale and global assessment of disease activity by the patients and physicians by using visual analogue scale (VAS) for pain in last 48 h from the date of assessment. Laboratory parameters such as liver function tests (LFT), renal function tests (RFT), complete blood count (CBC), erythrocyte sedimentation rate (ESR), hemoglobin (Hb)%, R.A. Factor, blood sugar fasting and urine examinations were done. X-ray of affected knee joint was also performed.

2.2. Trial interventions

Therapeutic Combination of *Vatari guggulu* [18] 500 mg thrice in a day along with *Maharasnadi Kwatha* [18] 20 ml twice daily with equal amount of lukewarm water and *Narayan taila* [18] 20 ml twice in a day for external application with gentle massage for 15 min up to 12 weeks were used in this study. All the trial drugs were procured from the Ayurvedic Pharmacopoeia of India complied GMP (Good manufacturing practice) certified company.

2.3. Washout period

There was wash out period of 2 weeks only if the patient gives previous history of taking allopathic/Ayurvedic/any medicine (any oral or local application was withdrawn gradually within a week time and subject had not given any medicine for next week and then he/she was registered for the trial).

2.4. Inclusion criteria

Subjects of either sex, age between 35 and 65 years, having symptoms of OA (above 3 months and maximum 5 years confirmed by radiological changes as per grade I to III of Kellgren & Lawrence radiological scale [19] and diagnosed as per American college of Rheumatology diagnostic criteria for OA of the knee) and willing able to participate in the study for 12 weeks were included in the study.

2.5. Exclusion criteria

The subjects having grade IV Kellgren & Lawrence Radiological scale, gouty arthritis, rheumatoid arthritis and psoriatic arthritis, history of any trauma or fractured joint or surgical history to the joint in the previous 6 months before the screening visit were not included in the study. Further, patients with gross disability in performing daily normal routine i.e. bedridden subjects or confined to a wheelchair, having any deformity of knee, hip or back altering the gait and posture, uncontrolled hypertension ($\geq$160/100 mm of Hg), uncontrolled diabetes mellitus, prolonged ($\geq$6 weeks) medication with corticosteroids, antidepressants, anticholinergics, past history of atrial fibrillation, acute coronary syndrome, myocardial infarction, stroke or severe arrhythmia in the last 6 months, severe renal or hepatic disorders, Pregnant and lactating woman were also excluded from the study.

2.6. Withdrawal criteria

The subjects were free to withdrawn from the trial at any time without the permission of investigator or any reason. Further, the investigator could discontinue the subject if he/she develop any adverse effect or there is non-compliance of the treatment regimen (minimum 80% compliance was essential to continue in the study). In these cases, the actions were taken to know the reason for the withdrawal and recorded in the case report forms.

2.7. Study procedures

On screening visit, subject's voluntary written informed consent was taken. General and systemic examinations as well as biochemical and radiological procedures were done. The subjects using conventional anti-inflammatory medications prior to their enrollment were kept in 2 weeks washout period. In this period, oral or local application was withdrawn gradually within a week after enrollment and subjects were not given any medicine for next week and then he/she was registered for the trial.

Total 142 subjects who fulfilled the inclusion and exclusion criteria were enrolled in the study. All enrolled subjects were given combination of *Vatari guggulu* 500 mg thrice in a day along with *Maharasnadi kwatha* 20 ml twice in a day with equal amount of warm water orally and *Narayan taila* 20 ml twice in a day for external application with gentle massage for 15 min up to 84 days. Recruited subjects were advised to carry on their daily activities and exercises that they had been doing before the enrollment and also advised to continue the same till the end of study period. Pain was measured in a visual Analogue Scale (VAS) (subject mark the location on the 10-cm line corresponding to the amount of pain they experienced during last 48 h). VAS data of this type was recorded as the number of millimeters from the left of the line with the range 0–100. WOMAC Index (Modified – CRD Pune Version) containing 24 questions (Q) was used to grade pain (Q. 1–5), stiffness (Q. 6–7), and physical function difficulty (Q. 8–24) pertaining to the knee joint. The subject's answers were graded on a quantitative scale (0 = none, 1 = mild, 2 = moderate, 3 = severe, and 4 = extreme). The maximum possible WOMAC score was 96 (pain = 20, stiffness = 8, and Physical Function = 68). The knees were examined for the swelling/synovitis (grades: 0 = none, 1 = detectable synovial thickening without loss of bony contours, 2 = synovial thickening with loss of bony contours, and 3 = bulging synovial proliferation with cystic characteristics). Subjects were advised to return empty containers of trial medicines on every follow-up visit in order to check the drug compliance.

2.8. Follow-up assessment

Subjects were visited for follow-up visits on day 14 (Visit 1), day 28 (Visit 2), day 42 (Visit 3), day 56 (Visit 4), day 70 (Visit 5), and day 84 (Visit 6). On each follow-up visit, patient's general and systemic physical examinations were done. Assessment of the symptoms of OA was done on total WOMAC index and VAS for pain. Global assessment of disease severity score was assessed by both the investigators and subjects on every follow-up visit to know the efficacy of the treatment. Laboratory investigations i.e. CBC, Hb%, ESR, Renal Function Tests, Liver Function Test were performed at baseline and at the end of 84th day for safety evaluation of the drugs.

2.9. Adverse event or adverse drug reaction

Any adverse event or Adverse Drug Reaction observed during treatment period if any, were documented and its appropriate and timely management were done and recorded in the CRFs.

2.10. Statistical analysis

The analysis of the data using statistical software SPSS 15.0 data describing quantitative measures are expressed as median or mean ± SD or SE or the mean with range. Qualitative variables are presented as counts and percentage. Comparison of variables representing categorical data was performed using Chi-square test. All p (probability) values are reported based on two-sided significance test and all the statistical tests are interpreted as significance at 5% level ($p < 0.05$).

3. Results

The study was conducted on 142 subjects. Out of these, 126 have completed the study and 16 were dropped out due to loss to follow up and imputation technique applied on 15 cases. The data of 15 subjects were taken for analysis along with the data of completed cases by last observation carry forward method for intention-to-analysis. In this study, Age 54–59 and 60–65 were more affected 37 (26.2%) and 50 (35.4%) respectively.

Further most of the subjects (95.7%) have no addiction, 62.4% have normal sleep, 78.7% were having regular bowel habit, and 85% were not having any kind of allergy to any material. No significant changes were observed at the end of therapy from baseline in any of the vital signs i.e. pulse rate, body temperature, Respiratory rate, systolic and diastolic blood pressure, appetite, and body weight.

3.1. Effect of therapy on outcomes measures

At baseline visit, the mean knee joint pain score assessed on Visual Analogue Scale (VAS) was 41.48 ± 2.59. The mean knee joint pain score (VAS) reduced significantly from baseline to 29.77 ± 2.15 after 14th day treatment with this medicines. The mean pain score further reduced significantly from baseline to 23.11 ± 1.75; 19.87 ± 1.704; 17.88 ± 1.61; 14.76 ± 1.43 and 13.03 ± 1.50 on days 28th, 42nd, 56th, 70th and 84th respectively [Fig. 1].

At baseline visit, the mean score of total Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) was 48.87 ± 0.99, which was reduced significantly to 19.43 ± 01.25 at the end of the study. The mean WOMAC pain sub score reduced significantly from baseline 10.30 ± 0.27–3.33 ± 0.25 at the end of the study. The mean WOMAC stiffness sub score reduced significantly from baseline 03.11 ± 00.1–0.68 ± 0.1 at the end of the study. At baseline visit, the mean WOMAC Physical functioning sub score was 35.39 ± 0.71, which was reduced significantly to 15.39 ± 0.95 at the end of the study [Fig. 2].

Further, the mean of physician's global assessment of disease activity at the baseline was 30.35 ± 1.65 and 64.15 ± 1.63 was at end of the study. The mean score of patient's global assessment of disease activity at baseline was 28.83 ± 01.847; 36.84 ± 1.547; 44.36 ± 1.459; 47.62 ± 1.416; 54.79 ± 1.507; 58.48 ± 1.567; 63.72 ± 1.644 on days 14th, 28th, 42nd, 56th, 70th and 84th day respectively. The mean of laboratory parameters i.e. CBC, Hb%, ESR, Renal Function Tests, Liver Function Tests were not significantly changed at baseline and at the end of the study.

4. Discussion

The key objective of this study was to evaluate the efficacy of combination of classical Ayurvedic drugs *Vatari guggulu* along with *Maharasnadi kwatha* and gentle massage of *Narayana taila* in the management of Osteoarthritis knee. The subjects were selected as per the criteria of American college of rheumatology, and the effect of therapy was assessed by WOMAC combined score, three WOMAC sub scales, pain by Visual analogue scale, global assessment of

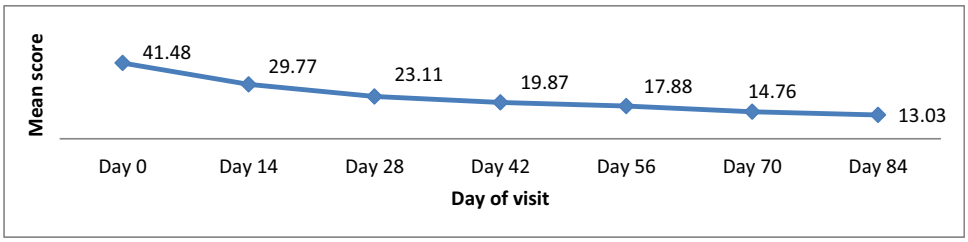

Fig. 1. Shows the effect of therapy on pain in knee joint assessed by Visual Analogue Scale.

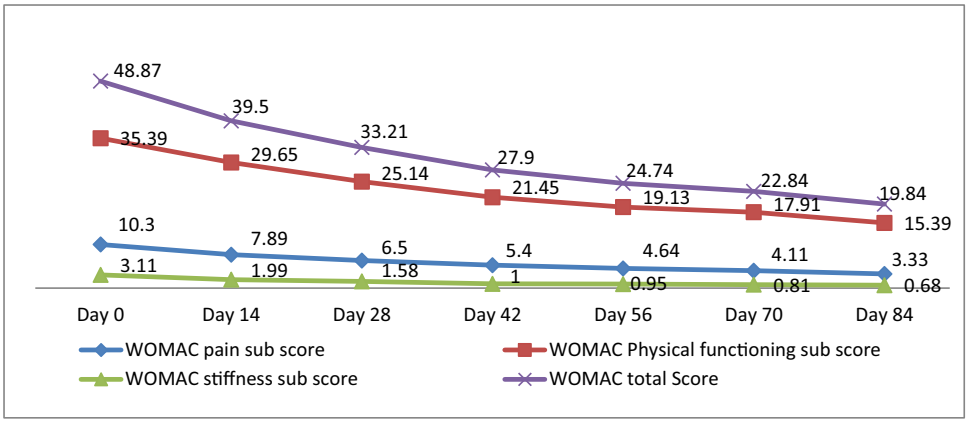

Fig. 2. Shows the effect of therapy on WOMAC parameters.

disease severity both by the physicians as well as patients. The hematological and biochemical parameters were done for the safety evaluation of the trial drugs. X-ray of knee joints was also done before the treatment.

Results of the study showed that 35.40% subjects were found in 60–65 years of age group. The results are encouraging at the end of study. Statistically results are highly significant ($p < 0.001$). Mean knee joint pain score (assessed on VAS) was decreased on every follow up visit. WOMAC sub scales (pain, stiffness, physical functioning) decreased significantly from their baseline values. The need of rescue medicine for pain management was reduced as study progressed. Findings show that combination of these Ayurvedic drugs reduced joint pain; joint stiffness and improved physical function [Table 1].

In this study, the global assessment of drug tolerability assessed by the physician, most of the subjects had feeling of good to excellent tolerability of drugs. Drawer's test, test for medial and lateral collateral ligaments and McMurray's test for meniscal tears were normal. Baseline to end of the study values were observed in safety laboratory parameters such as total leucocyte count, neutrophil, eosinophil, erythrocyte sedimentation rate, serum uric acid, serum creatinine. No changes were observed in X-ray of knee joints. Basically osteoarthritis knee or degenerative joint disease (DJD) starts at the age of 40 which is declining stage of middle age [20] Osteoarthritis or may first appear without symptoms between 20 and 30 years of age. The symptoms, such as pain and inflammation, appear in middle age. Till the age of 55 it occurs equally in both sexes; after 55 the incidence is higher in women [17]. Etiologically *sandhivata* is attributed to improper diet, life style, and old age. Aggravated *vata* brings *rukshyata* (dryness), *laghutva* (lightness or porousness), *kharatva* (coarseness) in the joints causing degeneration. *Sandhi shula* (pain in affected joint) is the predominantly feature. The other features are *shotha* (swelling), *stabdata* (stiffness) *atopa* (crepitus).

Composition of *Vatari guggulu* is collectively having *vata-shamaka*, *kaphashamaka*, *aamapachana*, *dipana*, *vedanasthapana* and *rasayana* properties. Due to *ushna virya* and *vatanulomana* properties, it normalizes the movement of *apana vaayu* and *vyana vaayu* which in turn helps to relieve pain. Furthermore, the *kaphashamaka* properties of *Eranda* (*Ricinus communis* Linn) and *Guggulu* (*Commiphora wightii* (Arn.) Bhandari) by its *laghu* (lightness), *ushna* (hot), *sukshma*, *strotoshudhikara* properties; it checks

Table 1
Effect of therapy on chief complaints in the subjects of OA knee.

Clinical symptom	No. of patients		Percentage of patients who got the relief
	Before treatment	After treatment	
Joint pain on movement	141	19	86.52
Joint pain at rest	96	107	−11.45
Restricted movement of joints	114	40	64.91
Crepitus/crunching in the joints	140	94	32.85
Weakness of affected joints	95	58	38.94
Swollen joints	84	13	84.52
Bony enlargement of the joints	13	04	69.23
Joint stiffness	126	38	69.84

blockage of path occurred due to *kapha dosha* and so helps to relieve *stambha* (stiffness) and *shotha* (inflammation) [21]. *Maharasnadhi kwatha* is a polyherbal formulation proved to be safe and nontoxic has the potential for providing relief to arthritis patients. This formulation is prepared from parts of 26 different plants that are used in traditional medicine for a variety of purposes such as reduction of pain, reduction of inflammation, and antipyretic activity [22]. *Narayan taila* is also a potent *vatashamaka* properties. It is composited by *vatashamaka* drugs like *patala* (*Stereospermum suaveolens* DC.), *ashvagandha* (*Withania somnnifera* Dunal.), *agnimantha* (*Clerodendrum phlomidis* Linn. f.), *atibala* (*Sida cordifolia* Linn.) etc. [23]. In this study we use for its massage locally on knee joints.

For safety evaluation of the drugs Laboratory investigations i.e. CBC, Hb%, ESR, Renal Function Test, Liver Function Test were performed at baseline and at the end of 84th day. No adverse reaction was noted during the study.

5. Conclusion

It is concluded that the effect is of the treatment package of trial is effective in the management of Osteoarthritis knee. This prospective study provides the evidence in support of the potential efficacy and safety of Ayurvedic medicines. It is a safe and effective treatment of OA knee.

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Support for the conduct of the trial is Central Council for Research in Ayurvedic Sciences, New-Delhi.

Conflicts of interest

All authors have no competing interest in the trial of drug.

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