Efficacy of Seetarama Vati (A Sri Lankan traditional drug) and Vatari Guggulu in the management of Amavata (rheumatoid arthritis)-an open labeled randomized comparative clinical trial

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Abstract

Introduction: Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease caused by type III hypersensitivity reaction due to antigen antibody complexes which deposit at the joints resulting in arthritis. As per the concept of Ayurveda, it can be co-related with Amavata, the disease arising from deranged metabolism and Vata vitiation. Despite of advancement in diagnostic approach of RA, management of it remains challenge. Vatari Guggulu and Seetarama Vati are the formulations having analgesics properties due to their Ushna (metabolism enhancing) and Tikshna Guna (micro channel cleaning) and simultaneously possess anti-inflammatory properties. Aims and Objectives: To evaluate and compare the efficacy of Vatari Guggulu and Seetarama Vati in the management of Amavata w.s.r. to rheumatoid arthritis. Material and Methods: For the present study, 58 patients were selected and divided into two groups. Patients of group A and group B were given Vatari Guggulu and Seetarama Vati respectively with warm water after meal for one month. Before administration of trial drugs in both of groups’ patients were given 4-6 grams of Triphala powder depending upon the Koshtha of the patient, on empty stomach early morning for the purpose of Koshtha Shuddhi (purgation) for 3 days. In addition to assess effect on signs and symptoms of Amavata, haematological investigation, biochemical investigation including quantitative C-reactive protein (CRP) and rheumatoid factor (RA factor) and routine urinary examination were carried out before and after treatment in all the registered patients. The effect of therapy was assessed on the basis of changes in score in comparison to end point score. Discussion: All the cardinal and associate complaints were statistically significant improved after the course of the trial drug. Most of the functional parameters had statistically significant improvement after treatment except left side foot pressure and DAS 28 scale in B group. Biochemical and hematological parameters were within normal limit before and after treatment. The difference of effect of trial drug on chief complaints was statistically insignificant. The difference of effect of trial drug on associate complaints was statistically insignificant. Difference of effect of trial drugs on ESR of both the groups was statistically insignificant. The difference of effect of trial drug on RA factor and CRP between groups was statistically significant. The difference of effect of trial drug on functional parameters between groups were statistically significant. Conclusion: The study revealed that, though both the trial drugs; Vatari Guggulu and Seetarama Vati are effective in the management of Amavata, but clinically Seetarama Vati is comparatively more effective than Vatari Guggulu in the management of Amavata.

Keywords: Amavata, rheumatoid arthritis, Seetarama Vati, Vatari Guggulu

Introduction

Rheumatoid arthritis (RA) is a multisystem disease involving articular and extra articular tissue, the cause of which is still uncertain. It is characterized by persistent bilateral symmetric arthritis involving the peripheral small joints resulting in cartilage destruction and bony erosions with subsequent joint deformities.[1] This disease is seen throughout the world and affects all races. RA is a disease which is crucially affecting not only persons individually but also the society. The prevalence of RA is approximately 1% of the population. Women are affected approximately three times more often than men. Onset is most frequent during the fourth and fifth decades of life.
life with 80% of the patients developing the disease between the age of 35 and 50 years.[3] The disease Amavata mentioned in Ayurveda resembles this condition which is caused by deranged metabolism which results in the formation of Ama along with involvement of provoked Vata. Main clinical manifestations of this disease are pain and swelling in multiple joints, loss of appetite, lack of enthusiasm, heaviness in the body, fever and indigestion.

Management of rheumatoid arthritis is a difficult task as it needs continues intake of medicine along with restriction of diet with life style modifications. Though there is advancement in the diagnosis of RA, internal medicament, prescribed in modern medicine for this condition has not provided satisfactory results. Hence, research for more effective medicines is challenge for today’s physicians. Vatari Guggulu[4] and Seetarama Vati[5] contain Vedanahara (analgesics) and Shothahara (anti-inflammatory) drugs which are commonly used in management of Amavata (RA).

**Aim and objectives**

To evaluate and compare the efficacy of Seetarama Vati and Vatari Guggulu in the management of Amavata w.r.t. to rheumatoid arthritis.

**Materials and Methods**

For the clinical study, 58 patients belonging to age group of 20-60 years, of either sex, who had signs and symptoms of rheumatoid arthritis (Amavata) were selected from the O.P.D & I.P.D of Kayachikitsa department of IPGT & RA, Jamnagar, after taking written informed consent from them. Pharmacognostical and pharmaceutical study of both the drugs were carried out in Pharmacognostical Laboratory and Pharmaceutical Laboratory, I.P.G.T. & R.A., GAU, Jamnagar and both the trial drugs were found to be suitable for the administration. Ethical clearance for the clinical trial was obtained from the Institutional Ethics Committee vide letter No. PGT/7/A/Ethics/2016-17/2665 and trial was registered under CTRI/2017/12/011051.

**Criteria for diagnosis**

The patient who presented with any four out of the seven inclusive criteria[5] was diagnosed as case of rheumatoid arthritis which are as follows:-

1. Morning stiffness: Stiffness in and around joints lasting one hour before maximal improvement (more than 6 week’s duration)
2. Arthritis of three or more joints, at least three joint area, observed by physician, having pain with soft tissue swelling or joint effusion, not just bony over growth, (more than 6 weeks duration)
3. Arthritis of hand joints, at least 1 area in wrist and hand is swollen (more than 6 week’s duration)
4. Symmetric arthritis (more than 6 week’s duration)
5. Presence of rheumatoid nodules
6. Serum rheumatoid factor-positive
7. Typical radiographic changes of arthritis on PA view of hand & wrist radiograph that must include erosions or unequivocal bony decalcification, localized in or adjacent to involved joints.

**Inclusion criteria**

Patients of either sex with age between 20 and 60 years, patients willing and able to participate in the study and patients having signs and symptoms of RA as enlisted in diagnostic criteria were included for the clinical trial.

**Exclusion criteria**

Patients having severe systemic illness diseases such as uncontrolled hypertension, uncontrolled diabetes mellitus, myocardial infarction, or cancer; patients below 20 years and above 60 years; pregnant/lactating women; patients suffering from RA for more than 5 years; patients having severe deformities and complication; and patients taking steroids for long duration were not included in the study.

**Laboratory investigation**

Following investigations were done before and after completion of treatment to rule out other pathologies and assess the status of patients.

1. Routine hematological examination such as Hb%, total leukocyte count, differential leukocyte count and erythrocyte sedimentation rate
2. Physical and microscopic urine examination
3. Biochemical examination such as random blood sugar, serum uric acid, blood urea, serum creatinine, serum glutamic pyruvic transaminase (aspartate transaminase), serum alkaline phosphatase, RA factor as qualitative and quantitative and serum C-reactive protein (CRP) (quantitative)
4. X-ray of the affected joint.

**Plan of the study**

The present clinical trial was interventional open-labeled randomized comparative clinical trial with efficacy as an end point. A total of 58 patients of RA were registered for the study and were randomly divided in to two groups by simple random method. In group A, 28 patients and in group B, 30 patients were registered, of which 45 patients completed the complete course of the treatment.

**Posology**

- In group A: 3 Vati (125 mg each) of Seetarama Vati were given to the patient twice a day orally after meal with warm water for 1 month
- In group B: 2 Vati (250 mg each) of Vatari Guggulu were given to the patient thrice a day orally after meal with warm water for 1 month.

During the course of treatment, the patients were not allowed to use concomitant drugs. Patients were also advised to avoid food which is too oily, salty, fermented or heavy to digest. They were also advised to avoid day time sleep, exhaustion or exposure to strong or cold wind.
Follow-up
After the completion of the trial, follow-up study was carried out for 1 month at fortnight interval to record status of the patient.

Criteria for the assessment
Assessment was done on the basis of improvement in subjective as well as clinical parameters, i.e., changes in signs and symptoms, changes in ESR, DAS-28 scale, Disability Index (The Indian Health Assessment Questionnaire) and improvement in hand grip, foot pressure, walking time.

- Hand grip (grip strength): to find out the functional capacity of the affected upper limb, the patients were asked to squeeze the inflated cuff of the sphygmomanometer and the grip strength was recorded in mmHg
- Foot pressure: to assess the functional capacity of the legs, foot pressure was recorded by using a weighing machine
- Walking time: patients were asked to walk distance of 20 feet and time was recorded before and after treatment using stop watch.

Statistical analysis
Generated data of the clinical trial was subjected to suitable statistical analysis Wilcoxon signed-rank test for nonparametric paired data, Chi-square test for nonparametric unpaired data, paired t-test for quantitative parametric paired data and unpaired t-test for quantitative unpaired data was applied. The obtained results were interpreted as insignificant $P > 0.05$ and significant $P < 0.05$, $P < 0.01$ and $P < 0.001$.

Overall assessment of therapy
Complete remission was 100% relief in signs and symptoms, marked improvement <100 >75% relief, moderate improvement <74 >50% relief, mild improvement <49 >25% relief, slight improvement <10 >24% relief and unchanged <10% relief to patients.

Observation
A total of 58 patients were registered for the study and 45 patients completed the trial. Remaining patients dropped out due to their personal reasons. In group A, 22 patients and in group B, 23 patients completed full course of treatment.

Majority of the patients registered for present clinical trial belonged to the age group of 41–50 years, followed by 31–40 years. Sex-wise distribution of the patients showed that the maximum i.e., 84.44% of patients were females, followed by males (15.55%). The data of the present study reveals that most of the patients (86.66%) were belonging to urban habitat and 55.55% patients each had impaired state of digestion (Vishamagni), reduced bowel movement and were suffering from anorexia. The data reveals that maximum, i.e., 73.33% of patients, had gradual onset of the disease while 13.33% of patients had acute onset and remaining 13.33% patients had insidious onset of RA. Out of these, maximum numbers of patients, i.e., 57.77%, were suffering from RA from < 1 year, followed by 33.33% patients suffering from RA from 1 to 3 years and 8.88% patients from 4 to 5 years.

RA factor values wise distribution of the patients
31.03% of the patients of present study had RA factor value between 0 and 20 IU/dl, while 17.24% of the patients had RA factor range between 21 and 40 IU/dl, 0.68% of the patients had RA factor range between 41 and 60 IU/dl and 22.41% of the patients had RA value more than 60 mg/dl [Table 1].

C-reactive protein range-wise distribution of the patients
93.33% of the patients of the present study had CRP value between 0 and 20 mg/dl, while 4.44% of the patients had CRP range between 21 and 40 mg/dl, none of the patients had CRP range between 41 and 60 mg/dl, and 2.22% of the patients had CRP value more than 60 mg/dl [Table 2].

Results and Discussion
Treatment outcome
Results of the study showed that both Seetarama Vati and Vatari Guggulu provided statistically significant relief on the cardinal as well as associated symptoms in the patients of RA such as pain, swelling, tenderness and stiffness of the affected joints [Tables 3-5].

In most of the functional parameters, statistically significant improvement was provided after treatment except, left-sided foot pressure in group B and DAS 28 scale in group B [Table 6].

However, Seetarama Vati and Vatari Guggulu did not provide statistically significant reduction in ESR, RA factor, and CRP [Table 7].

On comparing the effects provided by ESR, RA factor, and CRP [Tables 6-7].

Table 1: RA factor range wise distribution of the patients

| RA          | No. of patients | Percentage |
|-------------|-----------------|------------|
| Gr. A       | Gr. B           | Gr. A      |
| 0 to 20 IU/dl | 5               | 13         | 18         | 31.03 |
| 21 to 40 IU/dl | 6               | 4          | 10         | 17.24 |
| 41 to 60 IU/dl | 3               | 1          | 4          | 0.68  |
| >60 IU/dl    | 8               | 5          | 13         | 22.41 |

Table 2: CRP range wise distribution of the patients

| CRP         | No. of patients | Percentage |
|-------------|-----------------|------------|
| Gr. A       | Gr. B           | Gr. A      |
| 0 to 20mg/dl | 21              | 21         | 42         | 93.33 |
| 21 to 40 mg/dl | 1               | 1          | 2          | 4.44  |
| 41 to 60 mg/dl | 0               | 0          | 0          | 0     |
| >60 mg/dl    | 0               | 1          | 1          | 2.22  |
Overall effect of therapy of Seetarama Vati and Vatari Guggulu on the patients of Amavata

22 patients in group A completed the course of the therapy. Among these, complete remission was observed in ten patients, significant improvement was observed in three patients, mild improvement was observed in 4 patients and 5 patients, remained unchanged.

23 patients in group B completed course of the therapy. Among them, complete remission was observed in five patients, significant improvement was observed in three patients, mild improvement was observed in 4 patients and 5 patients, remained unchanged.

### Table 3: Effect of Seetarama Vati and Vatari Guggulu on chief complaints on the patients of RA Right Side (Wilcoxon’s signed-rank test)

| Parameters          | Groups     | Mean   | Mean diff. | Percentage | W     | P    |
|---------------------|------------|--------|------------|------------|-------|------|
|                     | B.T.       | A.T.   |            |            |       |      |
| Pain in joints      | A (n=22)   | 2.77   | 0.66       | 2.09       | 75.41 | -253 | <0.001|
|                     | B (n=23)   | 2.81   | 0.81       | 1.86       | 65.90 | -276 | <0.001|
| Swelling in joints | A (n=22)   | 2.45   | 0.36       | 2.09       | 86.36 | -253 | <0.001|
|                     | B (n=23)   | 2.63   | 0.72       | 1.90       | 73.48 | -276 | <0.001|
| Stiffness in joints| A (n=22)   | 2.68   | 1.45       | 1.22       | 33.33 | -209 | <0.001|
|                     | B (n=23)   | 2.63   | 0.68       | 1.95       | 71.96 | -253 | <0.001|
| Tenderness in joints| A (n=22)  | 2.36   | 0.54       | 1.86       | 3.58  | -224 | <0.001|
|                     | B (n=23)   | 2.59   | 0.72       | 1.86       | 70.45 | -253 | <0.001|

B.T: Before treatment, A.T: After treatment

### Table 4: Effect of Seetarama Vati and Vatari Guggulu on chief complaints on the patients of RA Left Side (Wilcoxon’s signed-rank test)

| Parameters          | Groups     | Mean   | Mean diff. | Percentage | W     | P    |
|---------------------|------------|--------|------------|------------|-------|------|
|                     | B.T.       | A.T.   |            |            |       |      |
| Pain in joints      | A (n=22)   | 2.77   | 0.36       | 2.40       | 86.36 | -253 | <0.001|
|                     | B (n=23)   | 2.81   | 0.81       | 2          | 70.45 | -171 | <0.001|
| Swelling in joints | A (n=22)   | 2.27   | 0.36       | 1.90       | 86.36 | -210 | <0.001|
|                     | B (n=23)   | 2.63   | 0.81       | 1.81       | 70.45 | -276 | <0.001|
| Stiffness in joints| A (n=22)   | 2.59   | 0.40       | 1.22       | 33.33 | -231 | <0.001|
|                     | B (n=23)   | 2.63   | 0.81       | 1.90       | 67.42 | -253 | <0.001|
| Tenderness in joints| A (n=22)  | 2.54   | 0.27       | 2.27       | 88.63 | -253 | <0.001|
|                     | B (n=23)   | 2.68   | 0.72       | 1.95       | 73.48 | -276 | <0.001|

B.T: Before treatment, A.T: After treatment, W: Test Value

### Table 5: Effect of Seetarama Vati and Vatari Guggulu on associated complaints on the patients of RA (Wilcoxon’s signed-rank test)

| Parameters          | Groups     | Mean   | Mean diff. | Percentage | W     | P    |
|---------------------|------------|--------|------------|------------|-------|------|
|                     | B.T.       | A.T.   |            |            |       |      |
| Angamarda (Body ache)| A (n=22)   | 2.5    | 0.45       | 2          | 80    | -231 | <0.001|
|                     | B (n=23)   | 2.72   | 0.68       | 1.95       | 68.93 | -235 | <0.001|
| Aruchi (Loss of appetite)| A (n=22)  | 2      | 0.27       | 1.72       | 85    | -136 | <0.001|
|                     | B (n=23)   | 1.90   | 0.5        | 1.40       | 73.8  | -153 | <0.001|
| Trishna (Thirst)   | A (n=22)   | 1.81   | 0.22       | 1.59       | 86.7  | -120 | <0.001|
|                     | B (n=23)   | 2.09   | 0.45       | 1.54       | 73.9  | -190 | <0.001|
| Alasya (Lassitude) | A (n=22)   | 2.27   | 0.45       | 1.81       | 80    | -210 | <0.001|
|                     | B (n=23)   | 2.45   | 0.77       | 1.63       | 66.7  | -190 | <0.001|
| Gaurava (Heaviness)| A (n=22)   | 2.09   | 0.40       | 1.59       | 76    | -171 | <0.001|
|                     | B (n=23)   | 1.86   | 0.59       | 1.27       | 6.29  | -136 | <0.001|
| Jvara (Fever)      | A (n=22)   | 1.22   | 0.13       | 1.09       | 86.89 | -78  | <0.001|
|                     | B (n=23)   | 1.31   | 0.13       | 1.18       | 89.66 | -66  | <0.001|
| Apaka (Indigestion)| A (n=22)   | 1.13   | 0.13       | 1          | 88    | -66  | <0.001|
|                     | B (n=23)   | 1.68   | 0.45       | 1.22       | 72.9  | -91  | <0.001|
| Shunyatanganam (Oedematous)| A (n=22)  | 2.45   | 0.54       | 1.90       | 76.5151 | -231 | <0.001|
|                     | B (n=23)   | 2.18   | 0.63       | 1.54       | 70.8  | -171 | <0.001|

B.T: Before treatment, A.T: After treatment, W: Test Value
patients, significant improvement was observed in five patients, mild improvement was observed in six patients and seven patients remained unchanged [Table 11].

Discussion

The statistically significant relief was observed in all the four cardinal symptoms of RA in the both the groups. This proves that both the drugs are effective in alleviating the cardinal symptoms of RA. Both the drugs are having Vata pacifying properties due to their Ushna (digestive and metabolism stimulating) and Tikshna (penetrating) properties. It would have acted on vitiated Vata and helped to relieve in pain of the affected joints.

Stiffness and tenderness are produced due to the presence of Ama. Both the drugs have Agnidipana (enhance digestive power) and Srotoshodhaka (remove obstruction of the micro channels) properties, which stimulates digestion and checks, further Ama formation. Due to this relief was observed in the symptoms of body ache, loss of appetite, laziness, heaviness of body,
feverish sensation and numbness in the extremities. Pain in joints is the result of Vata vitiation. Both the drugs are having Vata pacifying properties due to their Ushna and Tikshna properties and thus relieved this symptom.

Changes in hematological parameters, biochemical parameters, ESR, C - reactive protein and RA factor were statistically insignificant except in RA factor in B group. At present, “early” RA is regarded as patients with symptom duration <3 months. 31% of the patients were in acute phase of the disease. In acute phase, these investigations fluctuate. But in chronic stage of the disease it becomes stable. Hence, no significant change in above investigations were reported. Eranda oil (castor oil) is a one of the ingredients of Vatari Guggulu. Recinolin acid is main chemical composition of it. It acts as laxative and helps to remove free radicals in the body.Hence, group B only provided statistically significant reduction in RA factor.

Foot pressure, grip strength, walking time, Disability Index and DAS 28 Scale score are the functional parameters, which were in low range in the registered patients due to pathology in articular joints and muscles. After treatment due to effect of the drugs, functional parameters were statistically significantly improved except DAS 28 scale in group B.

Functional impairment of joints is due to impairment of function of Vata Dosha, caused by due to obstruction by Ama. After treatment, due to resolving of inflammation due to anti-inflammatory effect of ingredients of trial drugs, it resulted in normal function of Vata Dosha. Hence, relief in pain and thus improvement in foot pressure, grip strength and walking time was observed and there was reduction of DAS 28 Scale score and disability index.

31% of patients of the present clinical trial were in acute phase of the disease. Due to that reason, 15 patients had complete remission.Remaining patients of the trial groups were suffering from disease since more than one year and thus had chronic stage of disease. With short duration of treatment significant and mild improvement was obtained. In 8.86% of the patients who were suffering from disease for more than 4 and 5 years, due to more chronicity of disease, these patients did not respond well to the treatment. As per the Ayurveda in chronic stage of disease Agni Bala (digestive capacity) of the patients and Vyadikshamatva (immunity) of the patients are reduced. Hence, it was difficult to achieve better result with short duration of therapy in such cases.

**Conclusion**

Most of the ingredients of Seetarama Vati and Vatari Guggulu have analgesic and anti-inflammatory actions, and hence, statistically significant improvement was observed in symptoms of RA and associated complaints, especially in those cases of RA who had less chronicity of the disease. Hence, it can be concluded that both Seetarama Vati and Vatari Guggulu are effective drugs to manage acute and moderate cases of RA; however, Seetarama Vati provided comparatively better effect than Vatari Guggulu in the case of RA.

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**Conflicts of interest**

There are no conflicts of interest.

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