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RESEARCH ARTICLE

Clinical Efficacy of Classical Ayurvedic Formulations *Vatari Guggulu, Rasnasaptaka Kashaya,* and *Brihat Saindhavadya Taila* in the Management of Rheumatoid Arthritis (*Amavata*): An Open-label Prospective Randomized Multicenter Study

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ABSTRACT

Introduction: Rheumatoid arthritis (RA) is an autoimmune disease resulting in chronic inflammation of the joints and extra-articular tissues characterized by persistent inflammatory synovitis, usually involving the peripheral joints in a symmetric manner. The disease *Amavata* described in Ayurveda has similar symptomatology to that of RA.

Aims and objectives: To assess the clinical efficacy and safety of *Vatari Guggulu, Rasnasaptaka kashaya*, and *Brihat Saindhavadya taila* in patients suffering from RA.

Materials and methods: A prospective, open-label multicenter study was carried out at four peripheral centers of the Central Council for Research in Ayurvedic Sciences (CCRAS). A total of 230 patients of RA satisfying the selection criteria were enrolled from the outpatient department (OPD) of these centers and were administered *Vatari Guggulu* 1.5 gm (3 tablets of 500 mg each) twice daily after food with lukewarm water, and *Rasnasaptaka kashaya* 15 ml with 1 gm *Shunthi churna* twice daily internally before food in group I and in group II along with these two drugs, *Brihat Saindhavadya taila* 20 ml was used twice daily for external application over affected joints. The duration of the treatment was 12 weeks. Paired sample t-test was used to compare mean change in the subjective and objective parameters, Disease Activity Score (DAS-28), disability index (the Indian Health Assessment Questionnaire), change in acute phase reactants—erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and Health Questionnaire short form (SF)-36 score from baseline to the 84th day. A p-value <0.05 was considered significant.

Results: At the end of treatment (after a period of 84 days), statistically significant change (p-value <0.001) was observed in DAS-28 score, Disability index (the Indian Health Assessment Questionnaire), and Health Questionnaire SF-36 score in both the groups. Slight change in acute phase reactants—ESR, CRP—was also observed as compared with baseline; however, it was statistically insignificant.

Conclusion: *Vatari Guggulu, Rasnasaptaka kashaya* (with *Shunthi churna prakshepa*), and *Brihat Saindhavadya taila* given in the above-mentioned dose were found effective and safe in patients suffering from RA.

Keywords: *Amavata*, *Ayurveda*, *Ayurvedic formulations,* Efficacy, Rheumatoid arthritis, Safety.

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INTRODUCTION

Rheumatoid arthritis is a chronic multisystem disease, which affects joints and extra-articular tissues characterized by persistent inflammatory synovitis, usually involving the peripheral joints in a symmetric manner.[1] Rheumatoid arthritis has a worldwide prevalence of

0.5 to 1% in the adult population. The onset is most frequent during the fourth and fifth decades of life. The exact etiopathogenesis of the disease is still the subject of contention, but most theories advocate RA as an autoimmune-mediated condition.[2] Condition with similar picture has been described under the heading "*Amavata*" in *Ayurveda.* According to *Ayurveda,* the main cause of the disease *Amavata* is irregular dietary habits and sedentary lifestyle. An irregular dietary habit causes *jatharagnimandya* (diminution of digestive fire), which leads to "*Ama*" (unmetabolized or semidigested food) formation. Because of sedentary activities and irregular dietary habits "*Vata*" vitiates, carries the *Ama* to various *Kapha sthanas* (loci of *kapha dosha*) like *Sandhi* (joints), *Urah* (thorax), *Sirah* (head), *Kantha* (throat), and causes the disease *Amavata*.[3]

The exact etiology and pathogenesis of RA remain unclear. Rheumatoid arthritis requires an integrated approach that includes use of nonpharmacologic therapies and pharmacologic agents, such as nonbiologic and biologic disease-modifying antirheumatic drugs, nonsteroidal anti-inflammatory drugs, analgesics, and corticosteroids. These medicines do provide symptomatic relief and slow down the progression of the disease/development of the deformities in certain patients but have limitations owing to their adverse effects. *Ayurvedic* formulations have been in use since ages and have found to be useful in treating RA and also in improving the prognosis. *Vatari Guggulu* and *Rasnasaptaka kashaya* are formulations that are commonly used in joint diseases in Ayurveda. *Brihat Saindhavadya taila* is prescribed for external application in inflamed joints to reduce the symptoms of *Ama* in *Sandhi* (*joints*). This study was conducted to comparatively assay the clinical efficacy and safety of internal administration of *Vatari Guggulu* and *Rasnasaptaka kashaya* (*Shunthi churna prakshepa*) in one group and a combination of internal administration of the same together with external application of *Brihat Saindhavadya taila* in second group was taken up for clinical evaluation.

OBJECTIVES

To assess the clinical efficacy and safety of *Vatari Guggulu, Rasnasaptaka kashaya,* and *Brihat Saindhavadya taila* in the management of RA.

MATERIALS AND METHODS

Study Design

The study was randomized conducted as a multicenter open-labeled, prospective study executed at OPD level at four institutes centers of CCRAS, under Ministry of AYUSH. The study was approved by the Institutional Ethical Committee of all the four participating centers and was conducted according to the Declaration of Helsinki for clinical trials and existing guidelines of good clinical practice of the country and registered in the Clinical Trial Registry of India vide CTRI Reg (CTRI//2014/05/004629).

Study Participants

A total of 230 participants were enrolled in the trial from four peripheral institutes of CCRAS, viz., Regional *Ayurveda* Research Institute for Skin Disorders, Vijayawada; Central *Ayurveda* Research Institute for Cardiovascular Diseases, New Delhi; Regional *Ayurveda* Research Institute for Endocrine Diseases, Jaipur; and Achanta Lakshmipathi Research Center for *Ayurveda*, Chennai. Patients were screened in accordance with the inclusion and exclusion criteria and were recruited in the study after obtaining the written informed consent. The cases were randomly allocated to two groups and out of 230 cases, 201 cases completed the study and 29 cases dropped out in the course of study.

Inclusion Criteria

Patients of either sex with age between 20 and 60 years, willing to participate in the study for 12 weeks and presence of any four out of the seven criteria (American College of Rheumatology, 1987),[4] viz., morning stiffness: Stiffness in and around joints lasting 1 hour before maximal improvement, arthritis of three or more joints, at least three joint areas, observed by physician, having pain with soft tissue swelling or joint effusion, not just bony overgrowth, arthritis of hand joints, at least one area in wrist and hand is swollen, symmetric arthritis, presence of rheumatoid nodules, serum rheumatoid factor positive, typical radiographic changes of arthritis on posteroanterior view of hand and wrist radiograph that must include erosions or unequivocal bony decalcification, and localized in or adjacent to involved joints.

Exclusion Criteria

Patients who have developed complications of RA, e.g., deformity of joints/bones, pleura-pericardial disease, patients who are unable to walk without support and/or confined to wheelchair, those with structural deformity as the complication of RA, poorly controlled hypertension (≥160/100 mm Hg), patients suffering from diabetes mellitus [(F) > 126 mg/dL], other types of arthritis like gouty arthritis, tuberculous arthritis, patients on prolonged (>6 weeks) medication with corticosteroids, antidepressants, anticholinergics or any other drugs that

may have an influence on the outcome of the study, past history of atrial fibrillation, acute coronary syndrome, myocardial infarction, stroke or severe arrhythmia in the last 6 months, symptomatic patients with clinical evidence of heart failure, concurrent serious hepatic disorder (defined as aspartate aminotransferase and/or alanine aminotransferase, total bilirubin, alkaline phosphatase > two times upper normal limit) or renal disorders (defined as serum creatinine >1.2 mg/dL), severe pulmonary dysfunction (uncontrolled bronchial asthma and/or chronic obstructive pulmonary disease), or any other condition that may jeopardize the study, alcoholics and/or drug abusers, h/o hypersensitivity to any of the trial drugs or their ingredients, pregnant/lactating woman, and patients who have completed participation in any other clinical trial during the past 6 months were exempted from the study.

Laboratory Investigations

The laboratory investigations hemoglobin, total leukocyte count, differential leukocyte count, ESR, blood sugar, blood urea, serum uric acid, serum creatinine, liver function test (LFT), CRP, antistreptolysin O titer, RA factor (immunoturbidity test), X-ray of hand and wrist, and electrocardiography were carried out.

Outcomes

Primary Outcome Measure

- Changes in DAS-28 score[5]

Secondary Outcome Measures

- Change in Disability index (the Indian Health Assessment Questionnaire)[6]
- Change in Acute phase reactants—ESR and CRP
- Change in Health Questionnaire SF-36[7]

Study Interventions

The formulations fulfilling the physicochemical standards and quality parameters and prepared as per standard operating procedures were procured from Good Manufacturing Practice-certified companies. Patients in group I were administered *Vatari Guggulu*[8] 1.5 gm (3 tablets of 500 mg each) twice daily after food with lukewarm water and *Rasnasaptaka kashaya*[9] 15 mL with *prakshep* of 1 gm *Shunthi churna*[10] twice daily before food internally and in group II *Brihat Saindhavadya taila*[11] 20 mL was used for external application twice daily over affected joints along with internal administration of *Vatari Guggulu* and *Rasnasaptaka kashaya* with the same dosage mentioned as for group I. The duration of treatment was for 12 weeks. The drug compliance was assessed on each visit during the study.

Study Procedure

On the enrollment day at baseline (visit 1), patient's demographic profile, medical history, family history, *Sharirik Prakriti*, and vital parameters were recorded. General physical and systemic examination, assessment of DAS-28 scale, assessment of disability index, SF-36 scoring, and assessment of ayurvedic parameters were done at baseline and on 84th day. Subsequent visits were planned at an interval of 14 days [14th day (visit 2), 28th day (visit 3), 42nd day (visit 4), 56th day (visit 5), 70th day (visit 6), and 84th day (visit 7)]. Patients were assessed and given study medications at each subsequent visit till 84th day. There was also without medication follow-up after 15 days of the 90th day visit. Details of clinical assessment and study schedule are given in Flow Chart 1.

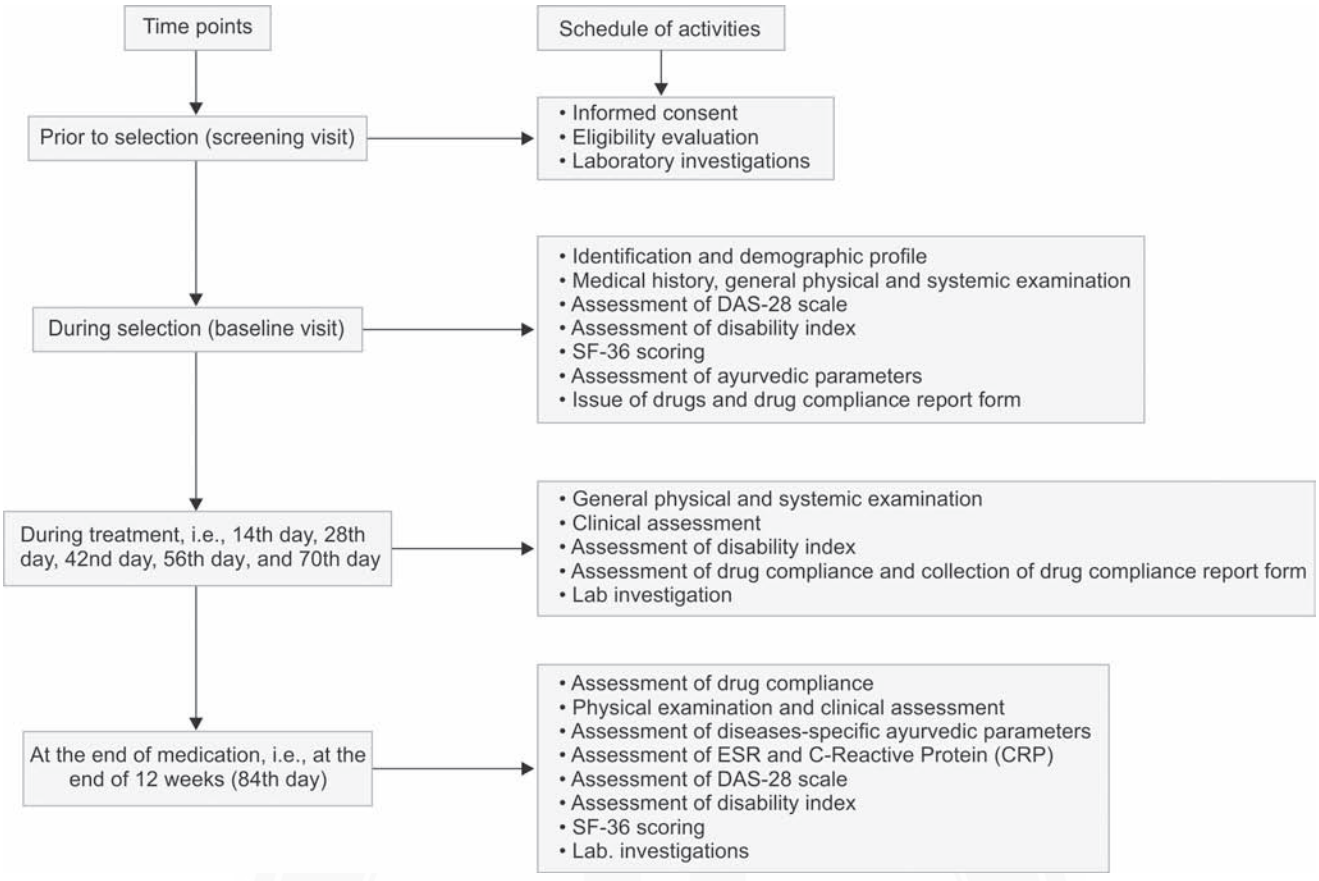
At the study site, data of all the patients were recorded in predesigned case report forms (CRFs) and were also entered in electronic formats (e-formats) designed in MS Excel with many data validation checks to ensure correct data entry. The e-formats and Xerox of the CRFs along with the laboratory investigations reports of the patients were sent by the participating centers to the council's headquarters on weekly basis for the purpose of clinical trial monitoring. A total of 230 participants were enrolled and were randomly allocated to two groups and out of 230 cases, 201 cases completed the study and 29 cases dropped out in the course of study. Last-observation-carried-forward (LOCF) was applied and a total of 225 (group I: 113 and group II: 112) cases were selected for statistical analysis. Flow Chart 2 shows the outflow of the patients in the study.

OBSERVATIONS AND RESULTS

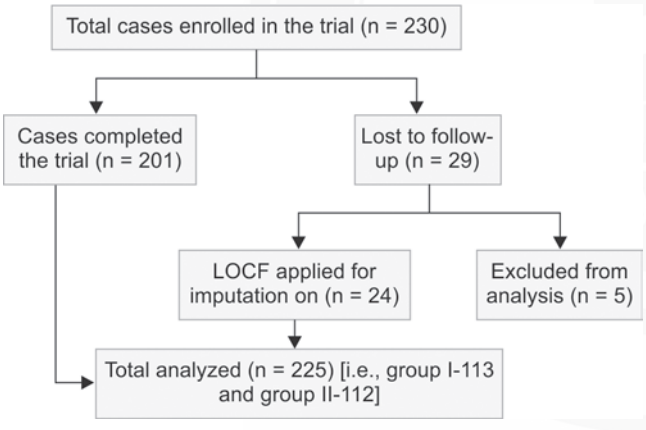
Demographic Profile

Majority of the patients were female (80.9%); 34.2% cases were in the age group of 31 to 40 years followed by 32.4% in the age group of 41 to 50 years. Maximum patients were married (87.5%) and 84.4% patients were literate (read and write) and 64.8% patients were doing only household work. About 70.6% patients were from above poverty line and 71.1% patients were from urban area. Majority of patients were followers of Hinduism (91.1%) and about 53.3% patients were nonvegetarian. Most of the patients (91.5%) were not having any type of addiction. About 60.4% patients were having regular bowel habit while remaining 39.6% were having irregular bowel habit. Maximum (99%) of the patients were having emotional stress, out of which 45.3% patients were having moderate

Flow Chart 1: Study schedule



Flow Chart 2: Outflow of the patients in the study



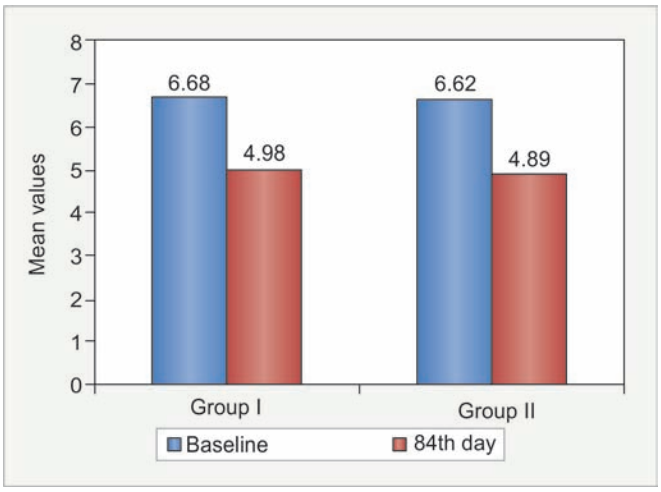
emotional stress while 18.66% patients having too much emotional stress. Most of the patients were of either *Vata-pittaja* (31.11%) or *Vata-kaphaja* (31.11%) *Prakriti* followed by *Pitta-kaphaja prakriti* (30.66%). Demographic profile of the patients is given in Table 1.

Effect of Medication

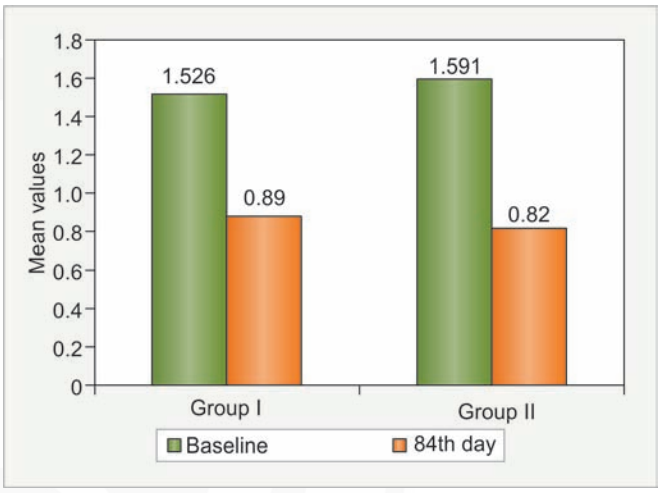
In group I, after 12 weeks of intervention, the mean DAS-28 score (primary outcome) reduced from 6.68 at baseline to 4.98 on 84th day showing statistically significant improvement ($p < 0.001$) (Graph 1). In Disability index the mean score at baseline was 1.53 and got reduced to 0.89 on 84th day showing statistically significant improvement ($p < 0.001$) (Graph 2). The acute phase reactants, ESR and CRP, did not undergo any statistically significant change. In SF-36 questionnaire, statistically significant improvement was observed in all the domains; physical functioning, role limitation due to physical health, limitations due to emotional problems, energy/fatigue, emotional well being, social functioning, pain and general health with p-value ($p < 0.001$), which is evident from Table 2 and Graph 3. Out of 72 RA factor-positive cases at baseline, total three cases converted to RA negative after 12 weeks of treatment (Tables 3 to 5). Chief complaint noticed was swelling in joints, which was present in 113 (100%) cases at baseline and after treatment, i.e., 84th day, it was present in 104 (92%) cases, morning stiffness was present in 112 (99.1%) cases at baseline, and after treatment, i.e., 84th day, it was present in 55 (48.7%) cases. Tenderness in joint was present in 109 (96.5%) cases at baseline and after treatment it was present in 102 (90.3%) cases. Fever was present in 66 (58.4%) cases at baseline and only in 5 (4.4%) cases at the end of trial period. Malaise/fatigue/weakness was present in 108 (95.6%) cases at baseline and significantly improved at the end of trial period, in 42 (37.2%) cases (Table 6).

Table 1: Demographic profile of the patients

Demographic profile	*Group I*	*Group II*
Sex		
Male	18 (15.9%)	25 (22.3%)
Female	95 (84.1%)	87 (77.3%)
Age group (years)		
20–30	23 (20.4%)	11 (9.8%)
31–40	40 (35.4%)	37 (33%)
41–50	35 (31%)	38 (33.9%)
51–60	15 (13.3%)	26 (23.2%)
Marital status		
Married	99 (87.6%)	98 (87.5%)
Unmarried	8 (7.1%)	6 (5.4%)
Widow(er)/divorcee	5 (4.4%)	7 (6.3%)
Any other	1 (0.9%)	1 (0.9%)
Educational status		
Illiterate	19 (16.8%)	16 (14.3%)
Read and write	94 (83.3%)	96 (85.7%)
Socioeconomic status		
Above poverty line	83 (73.5%)	76 (67.9%)
Below poverty line	30 (26.5%)	36 (32.1%)
Habitat		
Urban	81 (71.7%)	79 (70.5%)
Semiurban	17 (15%)	17 (15.2%)
Rural	15 (13.3%)	16 (14.3%)
Dietary habits		
Vegetarian	48 (42.5%)	57 (50.9%)
Nonvegetarian	65 (57.5%)	55 (49.1%)
Sleep		
Normal	56 (49.6%)	51 (45.5%)
Disturbed	57 (50.4%)	61 (54.5%)
Bowel habits		
Regular	66 (58.4%)	70 (62.5%)
Irregular	47 (41.6%)	42 (37.5%)
Physical exercise		
Heavy labor	5 (4.4%)	5 (4.4%)
Moderate labor	68 (60.2%)	59 (52.7%)
Office job	3 (2.7%)	05 (4.4%)
Sedentary	37 (32.7%)	43 (38.4%)
Emotional stress		
Average	36 (31.9%)	43 (38.4%)
Moderate	50 (44.2%)	52 (46.4%)
Too much	26 (23%)	16 (14.3%)
Occupation		
Desk work	11 (9.7%)	13 (11.6%)
Field work with physical labor	17 (15%)	16 (14.3%)
Field work	09 (8%)	13 (11.6%)
House work	76 (67.3%)	70 (62.5%)
Sharirik Prakriti		
Vataja	0 (0%)	3 (2.7%)
Pittaja	0 (0%)	1 (0.9%)
Kaphaja	0 (0%)	1 (0.9%)
Vata-pittaja	32 (28.3%)	38 (33.9%)
Vata-kaphaja	37 (32.7%)	33 (29.5%)
Pitta-kaphaja	37 (32.7%)	32 (28.6%)
Sannipataja	7 (6.2%)	4 (3.6%)



Graph 1: Effect of the treatment on DAS-28 score



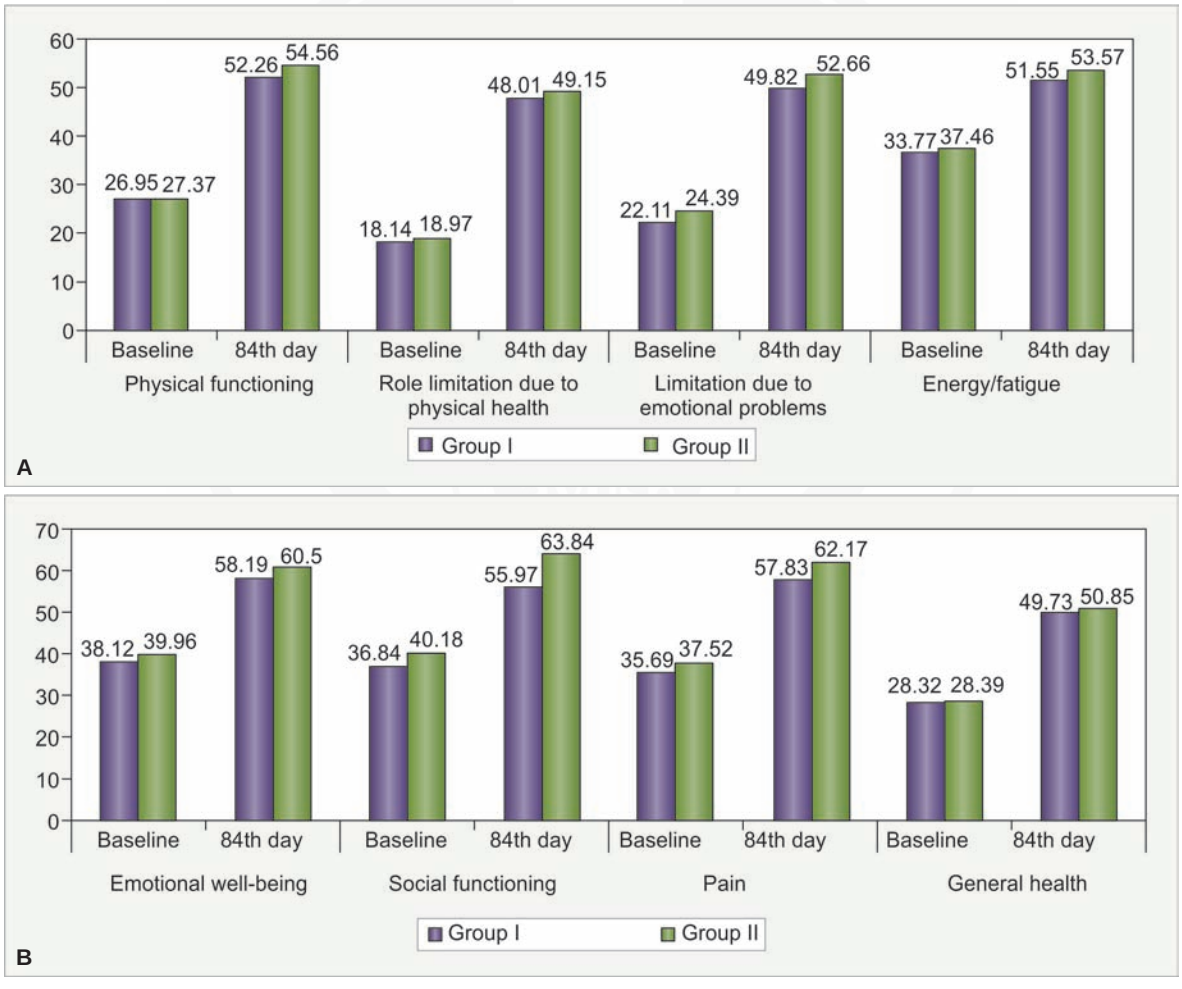
Graph 2: Effect of the treatment on disability index

In group II, after 12 weeks of trial period the mean DAS-28 score reduced from 6.62 at baseline to 4.89 on 84th day showing statistically significant improvement with ($p < 0.001$) (Graph 1). In disability index, the mean score at baseline was 1.59 and was reduced to 0.82 on 84th day showing statistically significant improvement ($p < 0.001$) (Graph 2). The acute phase reactants, ESR and CRP, did not undergo any statistically significant change. In SF-36 Questionnaire, statistically significant improvement was observed in all the domains; physical functioning, role limitation due to physical health, limitations due to emotional problems, energy/fatigue, emotional well being, social functioning, pain and general health with p-value ($p < 0.001$), which is evident from Table 2 and Graph 3. Out of 69 RA factor-positive cases at baseline, total 10 cases converted to RA negative after 12 weeks of treatment (Table 3). About objective parameters based on chief complaints, swelling in joints was present in 112 (100%) cases at baseline and after treatment, i.e., 84th day, it was present in 93 (83%) cases, morning stiffness was present in 109 (97.3%) cases at baseline and after treatment, and

Table 2: Effect of the treatment on outcome parameters

	Group I				*Group II*			
Parameters	*Baseline*	*84th day*	*t-value*[$]	*p-value**	*Baseline*	*84th day*	*t-value*[$]	*p-value*
DAS-28 score	6.68 (0.95)	4.98 (1.26)	14.927	<0.001	6.62 (1.05)	4.89 (1.3)	12.79	<0.001
Disability index	1.53 (0.42)	0.89 (0.56)	12.02	<0.001	1.59 (1.25)	0.82 (0.49)	6.16	<0.001
Health Survey Questionnaire SF-36								
1. Physical functioning	26.95 (17.62)	52.26 (20.2)	12.54	<0.001	27.37 (16.44)	54.56 (22.22)	12.56	<0.001
2. Role limitation due to physical health	18.14 (24.61)	48.01 (29.15)	9.97	<0.001	18.97 (22.57)	49.15 (29.93)	9.74	<0.001
3. Limitations due to emotional problems	22.11 (27.67)	49.82 (31.53)	8.62	<0.001	24.39 (28.98)	52.66 (29.21)	8.41	<0.001
4. Energy/fatigue	36.77 (11.53)	51.55 (14.14)	10.585	<0.001	37.46 (12.28)	53.57 (14.04)	11.78	<0.001
5. Emotional well-being	38.12 (17.33)	58.19 (15.61)	9.429	<0.001	39.96 (17.44)	60.50 (16.92)	10.12	<0.001
6. Social functioning	36.84 (20.1)	55.97 (20.46)	9.844	<0.001	40.18 (22.48)	63.84 (22.97)	10.27	<0.001
7. Pain	35.69 (17.62)	57.83 (16.32)	11.205	<0.001	37.52 (18.39)	62.17 (20.10)	11.65	<0.001
8. General health	28.32 (12.56)	49.73 (17.34)	10.650	<0.001	28.39 (13.21)	50.85 (20.61)	10.68	<0.001
ESR	42.17 (30.02)	39.6 (28.34)	1.3	0.222	41.35 (27.83)	40.15 (26.61)	0.845	0.40
CRP	10.15 (13.01)	10.60 (23.62)	0.211	0.833	10.28 (16.23)	9.92 (14.67)	0.315	0.753

Values are expressed as mean (standard deviation), [$]Compared using paired t-test at baseline and 84th day, *p-value of <0.05 has been considered as significant



Graphs 3A and B: Effect of the treatment on SF-36 health survey domains

at the end of 84th day it was present in 60 (53.6%) cases, tenderness in joint was present in 108 (96.4%) cases at baseline and after treatment, it was present in 94 (83.9%) cases, fever was present in 66 (58.9%) cases at baseline and after treatment, it was present in 2 (1.8%) cases. Malaise/fatigue/weakness was present in 105 (93.8%) cases at baseline and after treatment, i.e., 84th day, it was present in 53 (47.3%) cases (Table 6).

Table 3: Effect of treatment on RA factor

RA factor (immunoturbidity test)	*Group I*				*Group II*			
	Baseline		*84th day*		*Baseline*		*84th day*	
	No. of patients	*%*	*No. of patients*	*%*	*No. of patients*	*%*	*No. of patients*	*%*
Negative	41	36.3	44	38.9	43	38.4	53	47.3
Positive	72	63.7	69	61.1	69	61.6	59	52.7
Total	113	100.0	113	100.0	112	100.0	112	100.0

Table 4: Effect of treatment on ESR

ESR score	*Group I*				*Group II*			
	Baseline		*84th day*		*Baseline*		*84th day*	
	n	*%*	*n*	*%*	*n*	*%*	*n*	*%*
0	22	19.5	31	27.4	23	20.5	26	23.2
2	48	42.5	44	38.9	49	43.8	50	44.7
4	22	19.5	18	15.9	18	16.1	17	15.2
6	7	6.2	8	7.1	12	10.7	10	8.9
8	14	12.4	12	10.6	10	8.9	9	8.0
Total	113	100.0	113	100.0	112	100.0	112	100.0

Table 5: Effect of treatment on CRP

CRP Score	*Group I*				*Group II*			
	Baseline		*84th day*		*Baseline*		*84th day*	
	n	*%*	*n*	*%*	*n*	*%*	*n*	*%*
0	58	51.3	60	53.1	62	55.4	56	50.0
2	34	30.1	40	35.4	30	26.8	35	31.3
4	21	18.6	13	11.5	20	17.9	21	18.8
Total	113	100.0	113	100.0	112	100.0	112	100.0

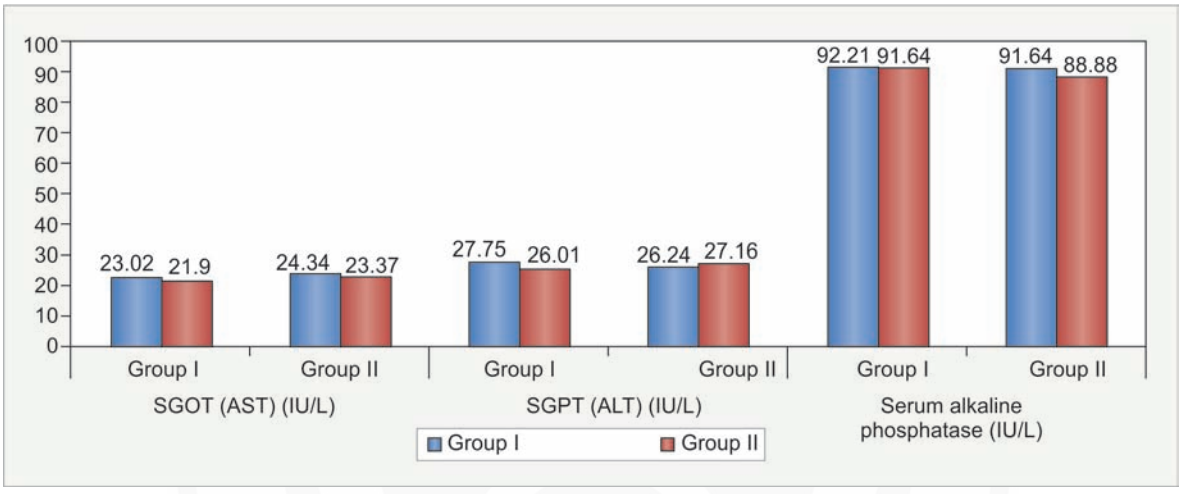
Table 6: Effect of the treatment on ayurvedic clinical parameters

Presence of chief complaints (ayurvedic parameters)	*Group I*		*Group II*	
	Baseline, n (%)	*84th day, n (%)*	*Baseline, n (%)*	*84th day, n (%)*
Angamarda (Body pain)	112 (99.1)	99 (87.6)	110 (98.2)	93 (83)
Aruchi (Anorexia)	77 (68.1)	20 (17.7)	85 (75.9)	35 (55)
Trishna (Excessive thirst)	72 (63.7)	11 (9.7)	71 (63.4)	28 (25)
Alasya (Lethargy)	98 (86.7)	63 (55.8)	101 (90.2)	65 (58)
Gaurava (Heaviness in the body)	96 (85)	61 (54)	92 (82.1)	56 (50)
Jwara (Raised body temperature)	61 (54)	9 (8)	69 (61.6)	11 (9.8)
Apaka (Indigestion)	67 (59.3)	26 (23)	72 (64.3)	25 (22.3)
Anga shunata (Body swelling)	45 (39.8)	26 (23)	42 (37.5)	21 (18.8)
Sandhi shotha (Joint swelling)	113 (100)	104 (92)	112 (100)	94 (83.9)
Sandhi ruja (Joint pain)	113 (100)	112 (99.1)	112 (100)	109 (97.3)
Bahumutrata (Polyuria)	46 (40.7)	4 (3.5)	44 (39.3)	12 (10.7)
Praseka (Excessive salivation)	24 (21.2)	4 (3.5)	26 (23.2)	8 (7.1)
Utsaha hani (Loss of interest in any activity)	75 (66.4)	48 (42.5)	82 (73.2)	49 (43.8)
Vairasya (Impairment in taste)	61 (54)	24 (21.2)	52 (46.4)	21 (18.8)
Daha (Burning sensation)	48 (42.5)	10 (8.8)	41 (36.6)	10 (8.8)
Kukshi Kathinata (Hardness of abdomen)	33 (29.2)	12 (10.6)	37 (33)	8 (7.1)
Shula (Pain abdomen)	30 (26.5)	12 (10.6)	32 (26.5)	9 (8)
Nidraviparyayam (Disturbed sleep)	65 (57.5)	12 (10.6)	71 (63.4)	27 (24.1)
Chardi (Vomiting)	15 (13.3)	4 (3.5)	20 (17.9)	4 (3.5)
Brahma(Giddiness)	50 (44.2)	21 (18.6)	49 (43.8)	19 (17)
Hridgraha (Stiffness in pericardial region)	42 (37.2)	9 (8)	42 (37.5)	14 (12.5)
Vidvibaddhata (Constipation)	52 (46)	11 (9.7)	51 (45.5)	17 (15.2)
Jadya (Stiffness of body)	100 (88.5)	44 (38.9)	102 (91.1)	52 (46.4)
Antrakujan (Excessive bowel sounds)	47 (41.6)	16 (14.3)	48 (42.9)	22 (19.6)
Vatanubandha/*Tivra ruja* (Excessive pain)	113 (100)	90 (79.6)	112 (100)	92 (82.1)
Daha (Burning sensation)	52 (46)	26 (23)	43 (38.4)	19 (17)
Raga (Redness)	59 (52.2)	42 (37.2)	55 (49.1)	38 (33.9)
Guruta (Heaviness)	109 (96.5)	81 (71.7)	105 (93.8)	75 (67)
Sthamitya (Feeling like body covered with wet cloth)	109 (96.5)	61 (54)	108 (96.4)	63 (56.3)
Kandu (Itching)	14 (12.4)	3 (2.7)	26 (11.6)	2 (1.8)

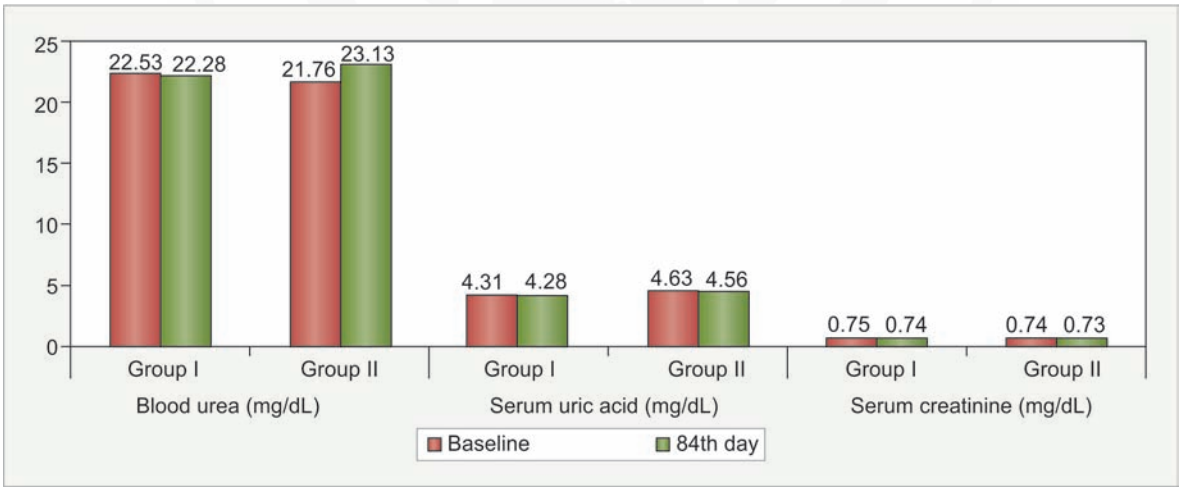
Table 7: Effect of the treatment on safety parameters—LFT and RFT

	Group I				Group II			
Parameters (n = 160)	*Baseline*	*84th day*	*t-value*[$]	*p-value**	*Baseline*	*84th day*	*t-value*[$]	*p-value*
Blood urea (mg/dL)	22.53 (7.52)	22.28 (7.88)	0.444	0.658	21.76 (7.13)	23.13 (8.11)	2.241	0.027
Serum uric acid (mg/dL)	4.31 (1.04)	4.29 (1.06)	0.413	0.680	4.64 (1.51)	8.17 (38.14)	0.983	0.328
Serum creatinine (mg/dL)	0.76 (0.20)	0.75 (0.20)	0.712	0.478	0.74 (0.2)	0.74 (0.2)	0.311	0.757
SGOT (IU/L)	23.02 (7.08)	21.9 (6.01)	1.897	0.060	24.34 (8.14)	23.37 (10.52)	1.144	0.255
SGPT (IU/L)	27.75 (15.73)	26.01 (15.7)	2.092	0.039	26.24 (12.77)	27.16 (14.83)	0.918	0.361
Total protein (gm/dL)	7.24 (0.55)	7.20 (0.54)	0.842	0.402	8 (7.56)	7.21 (0.49)	1.124	0.263
Serum albumin (gm/dL)	3.94 (0.38)	3.91 (0.39)	1.048	0.297	3.96 (0.36)	3.94 (0.32)	0.695	0.488
Serum globulin (gm/dL)	3.30 (0.58)	3.29 (0.67)	0.492	0.624	3.34 (0.6)	3.27 (0.54)	1.496	0.138
Conjugated bilirubin (mg/dL)	0.17 (0.10)	0.17 (0.08)	0.600	0.550	0.17 (0.11)	0.18 (0.11)	1.465	0.146
Unconjugated bilirubin (mg/dL)	0.45 (0.22)	1.43 (10.5)	0.990	0.324	0.42 (0.2)	0.42 (0.21)	0.197	0.844
Serum alkaline phosphatase (U/L)	92.21 (26.35)	91.64 (25.7)	0.272	0.786	92.3 (27.81)	88.9 (28.93)	2.209	0.029

Values are expressed as mean (standard deviation), [$]Compared using paired t-test at baseline and 84th day, *p-value of <0.05 has been considered as significant; SGOT: Serum glutamic oxaloacetic transaminase; SGPT: Serum glutamic pyruvic transaminase



Graph 4: Effect of the trial drug on safety parameters (LFT)



Graph 5: Effect of the trial drug on safety parameters (Kidney function test)

Safety Profile

The effect of this treatment on various safety parameters, such as LFTs and kidney function tests (KFTs) were assessed on baseline and at 84th day visit. No statistically significant change was observed in the LFT and renal function test (RFT) parameters at the end of the trial period (Table 7, Graphs 4 and 5). In both the groups no adverse drug reaction or adverse events were reported during the study period.

DISCUSSION

Rheumatoid arthritis is a chronic, progressive, inflammatory autoimmune disease associated with articular, extra-articular, and systemic effects. The exact etiopathogenesis is unclear but can be said to have multifactorial etiology ranging from infections to chromosomal factors. Ayurveda has described Amavata disease with similar symptomatology and describes the condition as a disease that occurs due to accumulation of ama (unmetabolized nonhomogeneous substance) in the joints. As per *Ayurveda*, provoked *Vata dosha* and *Ama* are the responsible factors for causation of the disease. Here, the treatment is aimed at bringing *Vata dosha* to normalcy and improving the jatharagni (digestive fire) so that to remove *Ama*. Drugs that possess *katu* (pungent taste), *tikta rasa* (bitter taste), and *deepana* (enhances digestive activity) qualities are useful for *Amapachana* (*eliminating ama*) and to increase *Agnibala* (metabolic power).

Rheumatoid arthritis is more prevalent in the middle aged and women and the results of the study are consistent with the fact. In this study, it has been observed that the maximum number of patients suffering from RA had emotional stress, which indicates that emotional stress may have a role in etiology of disease or may be an effect of the disease itself. *Angamarda* (body pain), *Aruchi* (anorexia), *Trishna* (excessive thirst), *Alasaya* (lethargy), *Gaurava* (heaviness in the body), *Apaka* (indigestion), *Jwara* (fever), *Anga shunata* (swelling in the body), *Utsahahani* (loss of interest in activities), *Bahumutrata* (polyuria), and *Vairasya* (distaste) described under the general features of *Amavata* in *Ayurveda* were reported by good number of patients in this study. Quite a good number of patients (60.44%) were having *Nidraviparyaya* (disturbed sleep pattern), which has been described as important complication of *Amavata* in *Ayurveda*.

This study revealed that the study formulations have potential role in the management of clinical features of RA. Statistical analysis report shows that there is significant improvement in primary outcome (DAS-28 score) and secondary outcome (disability index and Health Survey Questionnaire SF-36 in all the eight domains) after 12 weeks of treatment. Subjective improvement was also observed in various symptoms like morning stiffness, fever, fatigue, *Aruchi* (tastelessness), *Trishna* (thirst), *Alasya* (laziness), *Gaurava* (heaviness of body), *Apaka* (indigestion), *Bahumutrata* (polyuria), *Praseka* (salivation), *Utsahhani* (loss of enthusiasm), *vairasya* (distaste), *jadyata* (stiffness), and *Nidraviparyaya* (disturbed sleep pattern).

Above effects may be due to the *Guggulu* component of the formulation *Vatari Guggulu*. *Guggulu* contains guggulsterones, which reduce the level of proinflammatory cytokines cyclooxygenase-2 messenger ribonucleic acid level and suppress its tumor necrosis factor-αmediated induction and activation. Its antirheumatic and analgesic properties have been reported.[12] *Commiphora wightii* ethanolic extracts at the dose of 150 µg/mL and aqueous extract 50 µg/mL dissolved monosodium urate monohydrate (MSUM) crystals completely in 24 hours. Crystals of MSUM, calcium pyrophosphate dehydrates, and basic calcium phosphates are responsible for synovitis, cartilage damage, and joint destruction in gouty arthritis.[13] *Guggulu* is well known for its anti-inflammatory activity due to *Tikta* (bitter), *Katu* (pungent) *rasa, Ushna veerya* (hot potency), and *Katu vipaka* (pungent vipaka), which alleviates *Vata Kapha Dosha* and is capable of enhancing the quality of *agni* (digestive fire).

Shunthi (*Zingiber officinale*), which was given along with *Rasnasaptaka kashaya,* is considered as best *Agni Deepana* and *Amapachana* due to its *Katurasa* and *Ushna veerya*. The main ingredients of *Rasnasaptaka kashaya* are *Rasna, Guduchi, Gokshura, Eranda, Punarnava, Aragwadha,* and *Devadaru*. Rasna has been described as best *Vatahar* (capable of alleviating vata) drug in *Ayurvedic* classics. *Rasna* is reported to have immunosuppressive and anti-inflammatory activity and it helps in down regulation of T-cell surface markers ($CD8^+/CD4^+$) and intracellular T helper cell 1 (interleukin-2 and interferon gamma) cytokines.[14] *Eranda* (*Ricinus communis*) has been described as best medicine for *Amavata* in *Ayurvedic* classics and its anti-inflammatory and analgesic activity has been reported in experimental study.[15] *Punarnava* (*Boerhaavia diffusa* Linn.) has been described as best *Shothahar* drug in *Ayurveda* and its anti-inflammatory activities have been reported from experimental study.[16] More improvement in pain and tenderness was noticed in group II patients where *Brihat Saindhavadya taila* was given for local use along with other two trial medicines. *Brihat Saindhavadya taila* contains *Saindhava lavana*, *Gaja pippali*, *Rasna*, *Satapushpa*, *Yavani*, *Sarjikshara*, *Shunthi*, *Yastimadhu*, *Ajamoda*, *Jeeraka*, and *Eranda* taila. The *Lavana (*salts) has penetrating character and owing to it, it may help in eliminating the *Ama* accumulated in the joints. Majority of the drugs have *Vatashamaka* property, which might be responsible for analgesic effect and anti-inflammatory effect.

The synergistic and cumulative effect of these formulations might be responsible for improving the subjective and objective parameters and primary and secondary outcomes of *Amavata* (RA).

CONCLUSION

Based on this open-label, prospective multicenter clinical study, it can be inferred that the combination of *Ayurvedic* formulations *Vatari Guggulu*, *Rasnasaptaka kashaya* with *Shunthi churna prakshepa* internally in group I and *Vatari Guggulu*, *Rasnasaptaka kashaya* with *Shunthi churna*

prakshepa internally along with *Brihat Saindhavadya taila* externally in group II patients has good efficacy and safety profile in the management of *Amavata* (RA). Significant improvement in the clinical parameters and other assessment parameters, i.e., DAS-28 score, disability index (the Indian Health Assessment Questionnaire), Health Questionnaire SF-36 and slight change in acute phase reactants ESR and CRP, was observed in both the groups. However, more improvement in pain and tenderness of joints was observed in group II patients. No adverse drug reactions/adverse events have been reported in both the groups during study period. These drugs can be safely used for the management of RA.

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हिंदी सारांश

रुमेटायड अर्थराइटिस (आमवात) रोग के प्रबंधन में वातारि गुग्गुलु, रास्नासप्तक कषाय एवं बृहत् सैन्धवाद्य तैल का चिकित्सीय मूल्यांकन

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पृष्ठभूमिः रुमेटायड अर्थराइटिस (आमवात) एक स्वतः प्रतिरक्षी (ऑटो इमयून) व्याधि है जिसमें संधियों व संधिय अतिरिक्त ऊतकों में जीर्ण शोथ होता है। इस व्याधि में शरीर की परिधीय संधियों में दोनों और लगातार शोथ (सिनोव्हाइटिस) होता है। रुमेटायड अर्थराइटिस की तुलना आयुर्वेद में वर्णित 'आमवात' नामक व्याधि से की जाती है।

उद्देश्य एवं लक्ष्यः रुमेटायड अर्थराइटिस (आमवात) से पीड़ित रोगियों में वातारि गुग्गुलु, रास्नासप्तक कषाय एवं बृहत् सैन्धवाद्य तैल की चिकित्सीय प्रभावकारिता और सुरक्षा का आंकलन करना इस शोध अध्ययन का उद्देश्य व लक्ष्य है।

सामग्री व विधिः सी.सी.आर.ए.एस के चार परिधीय केन्द्रों पर एक संभावित, खुले स्तर पर बहुकेन्द्रीय अध्ययन किया गया। इन केन्द्रों पर बहिरंग रोगी विभाग से रोगी चयन मापदंडो को पूरा करने वाले 230 रोगियों का अध्ययन हेतु नामांकन किया गया। वर्ग I के रोगियों में वातारि गुग्गुलु 1.5 ग्राम (500 मिलीग्राम की 3 टेबलेट) दिन में दो बार गुनगुने जल से भोजनोपरांत व रास्नासप्तक कषाय 15 मिलीलीटर (1 ग्राम शुंठी चूर्ण प्रक्षेप के साथ) दिन में दो बार भोजन – पूर्व मुखमार्ग से दी गई।

वर्ग II में उपरोक्त दोनों औषधियों के साथ बृहत् सैन्धवाद्य तैल प्रभावित संधियों पर दिन में दो बार बाह्य अभ्यंग हेतु प्रयुक्त किया गया। उपचार की अवधि 12 सप्ताह थी। व्यक्तिपरक एवं वस्तुपरक मापदंड, DAS–28 स्कोर, विकलांगता सूचकांक (भारतीय स्वास्थ्य मूल्यांकन प्रश्नावली), तीव्र चरण अभिकारकों (एक्यूट फेस रियकटेंट) (ESR तथा CRP) में बदलाव एवं स्वास्थ्य प्रश्नावली SF-36 स्कोर का प्रत्येक 14 दिनों के अंतराल पर 12 सप्ताह तक आकलन किया गया। DAS –28 स्कोर, विकलांगता सूचकांक (भारतीय स्वास्थ्य मूल्यांकन प्रश्नावली), तीव्र चरण अभिकारकों (ESR तथा CRP) में बदलाव एवं स्वास्थय प्रश्नावली SF–36 स्कोर में आधारभूत दिवस से 84वें दिवस तक औसत परिवर्तन की तुलना करने के लिए युग्मित नमूना टी – परीक्षण (paired sample t-test) का उपयोग किया गया। <0.05 पी मान महत्वपूर्ण माना गया है।

परिणामः उपचार के अंत में 84वें दिन पर DAS–28 स्कोर, विकलांगता सूचकांक (भारतीय स्वास्थ्य मूल्यांकन प्रश्नावली) एवं स्वास्थ्य प्रश्नावली SF–36 स्कोर में दोनों वर्गो के रोगियों में सांख्यिकीय रूप से महत्वपूर्ण परिवर्तन (पी मान <0.001) पाया गया। आधारभूत दिवस की तुलना में 84वें दिवस पर तीव्र चरण अभिकारकों (एक्यूट फेस रियकटेंट) ESR तथा CRP में थोड़ा बदलाव देखा गया। जो कि संखिय्कीय दृष्टि से महत्वपूर्ण नहीं था।

निष्कर्षः वातारि गुग्गुलु, रास्नासप्तक कषाय (शुंठी चूर्ण प्रक्षेप के साथ) एवं बृहत् सैन्धवाद्य तैल पूर्व वर्णित मात्रा में रुमेटायड अर्थराइटिस (आमवात) से ग्रसित रोगियों में प्रभावी, सुरक्षित व निरापद पाए गए।

कुंजी शब्दः आयुर्वेद, आमवात, रुमेटायड अर्थराइटिस, वातारि गुग्गुलु, रास्नासप्तक कषाय, बृहत् सैन्धवाद्य तैल, चिकित्सीय प्रभावकारिता, सुरक्षा।