Research Article

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EVALUATION OF CLINICAL EFFICACY AND SAFETY OF STIFAIN TABLET IN THE MANAGEMENT OF RHEUMATOID ARTHRITIS (AMAVATA)

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ABSTRACT

Rheumatoid arthritis (RA) is an inflammatory arthritis that affects nearly 1% of the world's adults and is one of the most distressing irreversible arthritis which runs a chronic course with a very poor response to medicines. Ayurveda offers large number of single and poly herbal or herbo-mineral drugs for the management of Rheumatoid arthritis (Amavata) and some of these potent drugs were selected and Stifain tablet formulated. The present trial was carried out on the cases of Rheumatoid arthritis who satisfied the diagnostic and inclusion criteria. Detailed medical history to find out the causative factors like diet and lifestyle and status of disease was recorded and examination of affected joints was done. Patients willing to participate were given Stifain tablets in the dose of one tablet (500 mg) each thrice daily with lukewarm water after meal for the duration of two months with weekly follow-up. The primary end points were assessed on basis of improvement in sign and symptoms, Disease Activity score in 28 joints (DAS-28) and Disability index (The Indian Health Assessment Questionnaire). Safety assessment was hepatic function (SGPT and alkaline phosphatase (ALP) and renal function (B. urea and S. creatinine) tests. The finding of the present study suggest that Stifain tablets can be safely used as a single drug therapy in the management of mild to moderate cases of rheumatoid arthritis.

Keywords: Rheumatoid arthritis, efficacy and safety, Stifain tablet

INTRODUCTION

Rheumatoid arthritis (R.A.) one of the most distressing among arthritis is a chronic systematic inflammatory disorder of unknown cause, characterized by pain, swelling, stiffness and loss of function affected joints. The scope of therapeutic measure of R.A. is limited, even though there is extreme advancement in diagnostic approach of modern medical science. Conventional medicine prescribed for the patients of Rheumatoid arthritis provides symptomatic relief, but underlined pathology goes on unchecked. Hence, People in India have started resorting to alternative medicines with the hope of permanent solution or to reduce the dose of conventional drugs or to avoid their side effects. In this Scenario, to find out an Ayurveda formulation which is potent, easily palatable and has minimum side effects is challenge and need of the time. Classic is full of references of such drugs which can be utilized for the management of Rheumatoid arthritis which due to their Deepana, Pachana, Vedanaharr and Shothahara actions can help to break the pathogenesis of the disease as well as control inflammatory changes of the affected joints. Considering these facts, a clinical trial to establish clinical efficacy and safety of Stifain tablets was planned. The ingredients of Stifain tablet are Maharasnadi kvatha, Yograj guggul and herbo mineral formulations like Mahavatvidhwans rasa, Ekangvir rasa and Sameerpannag rasa. Further these formulations are processed with herbs viz. Brahmi (*Bacopa monnieri*), Eranda (*Ricinus communis*), Gaduchi (*Tinospora cordifolia*), Shatavari (*Asparagus racemosus*), Yavani (*Trachyspermum ammi*).

MATERIALS AND METHODS

Drug preparation

Table 1: Ingredients of Stifain tablets: Each film coated tablet contains

No.	Ingredient Name	Part used	Quantity
1.	Maharasnadi kvatha[1]	Formulation	150 mg
2.	Yograj guggul[2]	Formulation	100 mg
3.	Mahavatvidhwans ras[3]	Formulation	50 mg
4.	Ekangvir ras[4]		50 mg
5.	Sameer pannag ras[13]		25 mg
	Processed with (Bhavna Dravya)		
6.	Brahmi *(Bacopa monneri)*[5]	Whole plant	QS
7.	Eranda *(Ricinus communis)*[6]	Root	QS
8.	Guduchi *(Tinospora cordifolia)*[7]	Stem	QS
9.	Shatavari *(Asparagus racemosus)*[8]	Root tuber	QS
10.	Yavani *(Trachyspermum ammi)*[9]	fruit	QS

Plan of clinical study

The present study was a Prospective, Open label, outpatients based Single arm single centered clinical trial conducted in the department of Kayachikitsa, IPGT and RA, Gujarat Ayurved University, Jamnagar. It was conducted during November 2015 to August 2016 after obtaining approval from the Institutional Ethics Committee (Letter: no. PGT/7/-A/Ethics 2014 – 2015/1470 dated 15/08/2015). The trial is also registered under Clinical Trial Registry of India (CTRI/2018/02/012142). Single batch Stifain tablet was provided by Ayurchem Products Dombivli which was supplied in strip pack form to the patients under trial.

Selection of patients for clinical study

For the purpose patients suffering from Rheumatoid arthritis and fulfilling the criteria of diagnosis (revised criteria of American college of Rheumatology, 1987) of either sex with age between 20 and 60 years and willing to give their consent to participate in the clinical trial, were selected irrespective of their caste, religion, habitat from OPD and IPD of Kayachikitsa I.P.G.T and R.A. Hospital, Gujarat Ayurved University, Jamnagar. After preliminary registration diagnostic medical history was taken according to both Ayurveda and modern clinical methods which was recorded in detailed Performa.

Criteria for diagnosis

Presence of any four out of the following seven (jone's) criteria (1987.revised criteria of American college of Rheumatology)[10]

a) Morning stiffness: stiffness in and around joints lasting one hour before maximal improvement (more than 6-week duration).
b) Arthritis of three or more joints, at least three joint area, observed by scholar, having pain with soft tissue swelling or joint effusion, not just bony overgrowth, (more than 6-week duration).
c) Arthritis of hand joints, at least 1 area in wrist and hand is swollen (more than 6 weeks' duration).
d) Symmetric arthritis, (more than 6 weeks' duration).
e) Presence of Rheumatoid Nodules
f) Serum Rheumatoid factor-positive
g) Typical radiographic changes of arthritis on PA view of hand and wrist radiography that must include erosions or unequivocal bony decalcification, localized in or adjacent to involved joints.

Inclusion criteria

1. Patient of either sex of age group between 20 to 60 years.
2. Patients presenting with any four out of the seven (jone's) criteria (1987.revised criteria of American college of Rheumatology)
3. Patients who are willing to participate in the clinical trial.

Exclusion criteria

1. Patient who have developed complications of Rheumatoid arthritis e.g. severe deformity of joints/ bones, Pleura – pericardial disease or else.
2. Patients with poorly controlled Hypertension or with uncontrolled Diabetes Mellitus and having a past history of atrial fibrillation, Acute coronary syndrome, Myocardial infarction, Stroke or serve arrhythmia in the last 6 months.
3. Patients on prolonged medication with corticosteroids, antidepressants, anti-cholinergic, etc. or any other drugs that may have an influence on the outcome of the study.
4. H/o hypersensitivity to any of the trial drugs or their ingredients.
5. Pregnant /lactating women.
6. Patients having chronicity > 10 years.

Investigation

1. Hematology: Hemoglobin, RBC, WBC, DLC, E.S.R., (Westergren method)
2. Bio-chemistry: FBS, Serum uric acid, B. Urea, Serum Creatinine, S.G.P.T (A.S.T), Serum Alkaline Phosphate, RA factor (Quantitative) and CRP.
3. Urine Analysis: Routine and microscopic test.
4. Radiology: X-Ray of affected joints.

These investigations will be carried out before initiating the administration of trial drug and after completion of course of the treatment to confirm the diagnosis and rule out other pathogenesis. However, FBS, Serum Uric Acid and B. Urea were done only before initiating of the treatment.

Dose and Duration

Stifain tablet was given to the enrolled patients in the dose of 1 tablet thrice daily (each of 500 mg), after meal with warm orally for 2 months. Records of the dispensed medicine were maintained in drug inventory form. Concurrent analgesics in any form i.e. topical, injectable or oral was not permitted during this course of clinical trial. Patients who received rescue medicine were excluded from the trial. All subjects during the course of clinical trial were advised specific diet and lifestyle modifications which was as follow.

Do's

Consumption of Lukewarm water with light diet dominant in Tikta and Katu Rasa, yava (barley), Raktashali (red rice), Shigru (drumsticks), Karvellaka (bitter gourd), Parwar, Ardraka (ginger) and Rasona

Don'ts

Heavy dietary items such as flour of Masha (black gram), Snigdha and Amlarasa dominant diet, Virudhaahana, too much of sweets, cold water, curd, cold beverages, ice creams, day time sleeping, suppression of natural urges, exposure to cold, wind, staying in Air conditioner; Excessive of stress and excessive exertion.

Follow up

Follow up of the study was carried out of for the one month after completion of the treatment at fortnight interval to observe long term effect or any other changes reported from the patients.

Criteria for the assessment

Following parameters were adopted for the assessment of clinical efficacy of the trial drug.

Parameter for assessment to clinical features

Base line score of improvement symptoms of rheumatoid arthritis like pain, swelling, stiffness, tenderness of the involved joints was considered. For this, appropriate scoring pattern was adopted and was assessed on weekly basis. Difference between base line score

and after treatment score was taken for analysis of the effect. In addition, changes in DAS-28[11] and disability Index[12] (The Indian Health Assessment Questionnaire) before and after treatment were also assessed.

Parameter for Assessment of functional capacity

Functional capacity was assessed on the basis of three parameters viz. walking time, Grip strength and Foot pressure test. Walking time was assessed by asking the patient to walk for 100 feet. Time taken to walk this distance was recorded by stopwatch before and after treatment. Grip strength was measured by ability to compress inflated ordinary sphygmomanometer cuff under standard conditions (i.e. 20 mm Hg) and it was recorded for both hands separately before and after the treatment. Foot pressure was measured by asking patients to press the weighing machine with foot before and after the treatment)

Parameter for Assessment of bio-chemical parameters

It was done by assessing changes in ESR, RA factor (Quantitative) and CRP before and after treatment.

Overall assessment of therapy

To assess overall effect of the therapy, results were classified in four group's i.e. complete remission - 100% changes, significant Improvement – more than 50% improvement, Mild improvement – 25 to 50 % and unchanged – less than 25%.

Statistical analysis

For the analysis the effect of the trial drug and to check its statistical significance, students' 't' test was applied, and the results were interpreted as significant if p value was < 0.05 and highly significant if p value was < 0.001.

Observation

For the present clinical trial, 66 patients were registered. Out of these 60 (90.9%) patients completed the two-month treatment of Stifain tablet as per the prescribed protocol, while 6 (09.09%) patients discontinued treatment, due to various personal reasons. Maximum of these patient was from the age group of 41-60 years (71.20%) and were female (92.42%), belonging to Hindu religion (78.79%), married (84.8%), with primary school level education (46.96%) dwelling in urban area (78.78%) and from middle class strata of society (66.67%) and 62.13% of the patients were vegetarians. Among 61 registered females, 14.75 % gave the history of premature delivery.

On taking medical history all patients complain pain, swelling, stiffness and tenderness in the multiple joints associated with morning stiffness as their chief complaints. Chief joints involved in these patients were synovial joints i.e. metacarpophalangeal, proximal inter phalangeal of hand and foot, wrist, elbow, knee and ankle joints. Other complaints reported by the patients were body ache (92.42%) numbness in the extremities (78.78%), malaise (75.00%) and fever (60.60%). Onset pattern of the disease was graduating majority of the patients (92.42%) and maximum registered patients were having chronicity of less than 3 years (43.93%). The chief aggravating factors reported in patients was early morning hours (71.21%), intake of sour diet items (66.67%), winter or monsoon (72.72%) and exposure to cold wind (43.93%). The relieving factors reported in patients were noon time (59.09%), intake of warm water (50.00%), summer season (48.49%) and rest (40.91%). On examination at base line, foot pressure was in between 21-40 kg in 57.57% of patients and in between 0-20 kg in 34.84% of patients. Range of grip strength observed was 0-20 mm/Hg in 48.48% patients and was 21-40 mm/Hg in 48.48% of patients. Walking time was 10-20 seconds in 68.16% of patients and 20-30 seconds in 19.69% of patients. At baseline, DAS 28 Score in 78.77% of patients was > 5.1 with high disease activity and Disability Index Score in 33.33% of patients was 4-6 and 7-9 in 28.78% Patients. X-ray reports of patient's revealed bony ankylosing and soft tissue swelling with small joints arthritis with reduced joint space with discrete fusion in few of the cases.

Effect of treatment

Data of 60 patients who completed full two months of treatment with Stifain tablet was utilized for the analysis of the effect provided. At base line, the mean score of RA factor (Quan.) was 97.93, which was reduced to 57.70 after two months of treatment with Stifain tablet, with 47.77% reduction. Similarly, baseline score of CRP (Quantitatively) 6.18 which was reduced to 6.03 with 44.09% of changes. The level of ESR (Erythrocyte Sedimentation rate) at baseline was 36.02 which were reduced to 35.05 after the treatment with 7.23% decrease. All these changes found in these parameters were statistically significant.

There was statistically highly significant improvement in all the major symptoms of rheumatoid arthritis like pain, stiffness, swelling and tenderness. Similarly, statistically highly significant changes were reported in associated symptoms like body ache, tastelessness, excessive thirst, malaise, heaviness, fever, indigestion and numbness. On the objective parameters like walking time, Grip strength and foot pressure test also statistically highly significant changes were found.

Baseline score of DAS 28 scale was 7.14 which were 3.39 after the treatment. These changes reported in DAS 28 were statistically highly significant. Disability index score was 7.07 at the baseline which is reduced to 4.77 at the end of two the treatment with Stifain tablet. These changes were also statistically highly significant.

Overall effect of the therapy showed that significant improvement was reported in 36.67% of the patients, mild improvement in 31.67%, while complete remission was reported in 25% of the patients 6.67% patients remained unchanged after the treatment.

Safety Profile

There were no significant changes blood levels of Total and differential WBC count, Platelet count and serum levels of SGPT, Alkaline phosphate, urea and creatinine at post treatment as compared to the baseline and remained within limits before and after the treatment. In addition, during the full course of treatment with Stifain tablet and even in follow up period, none of the patient reported any untoward complaint. All these point to the fact that stifain tablet is safe.

Effect of treatment on objective criteria

Table 2: Effect of Stifain Tablet on R.A. Factor (Quan.)- n = 60

Mean value (IU/ml)		Difference	%	Paired 't' test				Significance
BT	AT			S.D. (±)	S.E. (±)	't'	P	
97.93	57.70	40.23	41.08↓	148.08	19.28	2.09	0.041	S

BT = Before treatment, AT = After treatment, % = Percentage, SD = Standard Deviation, SE= Standard Errors = Significant↓ indicates decrease

Table 3: Effect of Stifain Tablet on CRP (Quan.) n = 60

Mean value (mg/L)		Difference	%	Paired 't' test				Significance
BT	AT			S.D. (±)	S.E. (±)	't'	P	
6.18	6.03	0.15	44.09↓	5.67	0.73	0.2	< 0.84	S

BT = Before treatment, AT = After treatment, % = Percentage, SD = Standard Deviation, SE = Standard Errors = Significant↓ indicates decrease

Table 4: Effect of Stifain Tablet on ESR (Quan.): n = 60

Mean value (mm/hr.)		Difference	%	Paired 't' test				Significance
BT	AT			S.D. (±)	S.E. (±)	't'	P	
36.02	35.05	0.97	7.23↓	33.54	4.33	0.223	0.824	S

BT = Before treatment, AT = After treatment, % = Percentage, SD = Standard Deviation, SE= Standard Errors = Significant↓ indicates decrease

Table 5: Effect of Stifain Tablet on Cardinal Symptoms n = 60

Cardinal Symptoms	Mean value (mm/hr.)		Difference	%	Paired 't' test				Significance
	BT	AT			S.D. (±)	S.E. (±)	't'	P	
Pain in Joints	2.91	1.35	1.56	54.17↓	0.67	0.08	18.02	< 0.001	HS
Swelling in the Joints	1.65	0.56	1.08	62.5↓	0.65	0.08	13	< 0.001	HS
Stiffness in the joints	1.65	0.85	0.8	33.89↓	0.94	0.12	6.625	< 0.001	HS
Tenderness in the joints	1.93	0.65	1.28	66.15↓	0.74	0.10	13.45	< 0.001	HS

BT = Before treatment, AT = After treatment, % = Percentage, SD = Standard Deviation, SE= Standard Errors = Significant↓ indicates decrease

Table 6: Effect of Stifain Tablet on Associated Symptoms n = 60

Associated Symptoms	Mean value (mm/hr.)		Difference	%	Paired 't' test				Significance
	BT	AT			S.D. (±)	S.E. (±)	't'	P	
Body ache	2.08	0.77	1.25	61.49↓	0.57	0.07	16.95	< 0.001	HS
Tastelessness	0.82	0.13	0.68	87.65↓	0.89	0.12	5.93	< 0.001	HS
Excessive thirst	0.65	0.12	0.53	79.17↓	0.75	0.10	5.32	< 0.001	HS
Malaise	0.75	0.58	1.17	66.50↓	0.89	0.11	10.19	< 0.001	HS
Heaviness in the body	1.22	0.32	0.9	79.63↓	0.90	0.12	7.77	< 0.001	HS
Fever	1.12	0.32	0.80	66.67↓	0.77	0.10	6.38	< 0.001	HS
Indigestion	1.10	0.25	0.85	75.93↓	0.90	0.12	7.32	< 0.001	HS
Numbness in the extremities	1.43	0.50	0.93	62.09↓	0.82	0.11	8.81	< 0.001	HS

BT = Before treatment, AT = After treatment, % = Percentage, SD = Standard Deviation, SE= Standard Errors = Significant↓ indicates decrease

Table 7: Effect of Stifain Tablet on Functional Capacity: n = 60

Functional Symptoms	Mean value (mm/hr.)		Difference	%	Paired 't' test				Significance
	BT	AT			S.D. (±)	S.E. (±)	't'	P	
Foot Pressure (in Kg.)	50.42	63.72	-13.30	28.08↑	13.26	1.71	7.76	< 0.001	HS
Grip Strength (mm/Hg)	40.68	49.85	-8.77	23.57↑	7.35	0.95	9.26	< 0.001	HS
Walking time (seconds)	18.47	16.10	2.37	12.99↓	2.47	0.32	7.42	< 0.001	HS

BT = Before treatment, AT = After treatment, % = Percentage, SD = Standard Deviation, SE= Standard Error, HS = Highly Significant
↓ indicates decrease↑ indicates increase

Table 8: Effect of Stifain Tablet on DAS 28 Scale n = 60

Mean value (mm/hr.)		Difference	%	Paired 't' test				Significance
BT	AT			S.D. (±)	S.E. (±)	't'	P	
7.14	5.29	1.85	25.91↓	1.25	0.16	11.40	< 0.001	HS

BT = Before treatment, AT = After treatment, % = Percentage, SD = Standard Deviation, SE= Standard Error HS = Highly Significant
↓ indicates decrease

Table 9: Effect of Stifain Tablet on Disability Index n = 60

Mean value (mm/hr.)		Difference	%	Paired 't' test				Significance
BT	AT			S.D. (±)	S.E. (±)	't'	P	
7.07	3.93	4.0	44.41↓	1.59	0.21	15.27	< 0.001	HS

BT = Before treatment, AT = After treatment, % = Percentage, SD = Standard Deviation, SE= Standard Error, HS = Highly Significant
↓ indicates decrease

Table 10: Effect of Stifain Tablet on hematological parameters: n = 60

Parameter	Mean value (mm/hr.)		Difference	%	Paired 't' test				Significance
	BT	AT			S.D. (±)	S.E. (±)	't'	P	
Hb (gm%)	11.64	11.89	-0.25	2.51 ↑	0.88	0.11	-2.17	0.03	S
Total W.B.C. (/Cumm)	7328.33	7208.20	120.13	0.74↓	1508.15	194.70	0.06	0.54	IS
Neutrophils (%)	60.83	58.25	2.43	1.77↓	7.77	1.00	2.42	0.02	IS
Lymphocytes (%)	32.73	33.16	-0.43	6.00↑	6.43	0.88	-0.49	0.63	IS
Eosinophil's (%)	4.57	4.52	0.05	21.19↑	1.93	0.25	0.20	0.88	IS
Monocytes (%)	2.73	2.38	0.35	1.17↓	0.95	0.12	2.84	0.01	IS
PCV (%)	35.51	35.45	0.10	2.22↑	2.41	0.31	0.214	0.85	S
RBC (mil/cumm)	4.39	4.48	-0.08	2.73↑	0.34	0.04	-1.95	0.57	S
Platelet count (10^3/ul	321.0	342.85	-21.85	5.06↑	63.77	8.23	-2.50	0.01	IS

BT = Before treatment, AT = After treatment, % = Percentage, SD = Standard Deviation, SE= Standard Error, S = Statistically Significant, IS = Insignificant↓ indicates decrease↑ indicates increase

Table 11: Effect of Stifain Tablet on Biochemical investigations: n = 60

Parameter	Mean value (mm/hr.)		Difference	%	Paired 't' test				Significance
	BT	AT			S.D. (±)	S.E. (±)	't'	P	
RBS (mg/dL)	78.84	76.96	1.87	1.07↓	12.47	1.64	1.15	0.25	IS
Blood urea (mg/dL)	23.37	23.17	0.20	3.14	6.49	0.91	0.22	0.82	IS
S. Creatinine (mg/dL)	1.81	1.91	-0.10	1.66↓	1.03	0.13	-0.78	0.48	IS
SGPT (IU/L)	19.56	17.08	2.48	4.38↓	8.90	1.16	2.14	0.04	S
Alkaline phosphatase (IU/L)	57.02	50.75	6.27	1.98↓	21.90	2.85	2.19	0.03	IS
Uric Acid (mg/dL)	4.21	4.33	0.12	1.12↓	2.50	0.25	-0.46	0.65	IS

BT = Before treatment, AT = After treatment, % = Percentage, SD = Standard Deviation, SE= Standard Error, IS = Insignificant↓ indicates decrease

Table 12: Overall effect of therapy

Overall Effect	No. of patients	% of patients
Complete remission	15	25
Significant improvement	22	36.67
Mild improvement	19	31.67
Unchanged	04	6.67

RESULTS

Significant change in post-treatment scores of cardinal features of Rheumatoid arthritis, DAS 28 score, Disability Index score and RA factor (Quantitatively), C-reactive protein, ESR level were observed as compared to baseline scores. Treatment with Stifain tablets for two months in rheumatoid arthritis patients showed normal renal and liver function tests.

DISCUSSION

Demographic Factors

In the present study, analysis of demographic data showed that maximum patients of study were from the age group of 40-60 years, females (92.42%) coming from the urban locality of Jamnagar (78.78%) and from middle strata of the society (66. 67%). This data is supported by the finding that Rheumatoid Arthritis starts most commonly, between the third to fifth decades of life and is more common in females. The incidence of RA is typically two to three times higher in women than men. The onset of RA, in both women and men, is highest among those in their sixties[11]. Proper explanations for the male/female ratio in RA susceptibility may lie at the level of hormonal differences. Hormone influences on RA Susceptibility may be attributed to sex steroid or other hormones, such as prolactin which have well established immune regulatory effects. Oral contraceptive use increases risk of RA development following pregnancy and following breast feeding. In addition to it, many of the female also gave the history of abortions or premature delivery. In such cases, as Sootikaparicharya is not followed properly after delivery or abortion, there is higher risk for Ama and Vatavriddhi and make females more vulnerable for this condition. Occurrence of high percentage in middle class may be due to unwholesome and faulty dietetic habits, with unbalanced activity and stress.

Status of Rheumatoid arthritis

Maximum patients of this study showed chronicity of disease < 3 years (65.55%). This observation reflects the chronic and progressive nature of the disease with periods of remission and exacerbation. All the patients of the study reported pain along

stiffness with moderate swelling in multiple joints with majority of them having small joints involvement initially which is in line to the presentation of Rheumatoid arthritis. Presence of symptoms like body ache (92.42%), malaise (75%), feverish sensation (60.6%), feeling of heaviness in the body (59.06%) and indigestion (50%) indicate role of Ama in the pathogenesis of Rheumatoid arthritis. Aggravation of symptoms during winter/monsoon season (72.72%), early hours of the day (71.21%), and after taking day sleep (50%) and reporting of relief in the symptoms during noon time (59.09%), after intake of warm water (50%) and during summer season (40.91%) further supports the role of Ama and Vata vitiation in the pathogenesis of Rheumatoid arthritis. This finding are also substantiated by the facts of the investigations that maximum patients were having high disease activity (78.77%), disability index score between 4-6 (33.33%) or 7-9 (28.78%), before treatment mean RA Factor score of 97.93 IU/ml and mean ESR of 36.02 mm/indicating the presence of active phase of the disease.

Efficacy of Stifain Tablet on subjective and objective parameters and investigations: Subjective Parameters: Cardinal and Associated symptoms

It was observed that all 60 patients (100%) had presented with cardinal symptoms of the disease i.e. Pain, swelling and tenderness in affected joints with morning stiffness and were also having body ache, malaise, heaviness of the body, feverish sensation and indigestion as associated symptoms. The relief observed in all cardinal and associated symptoms were statistically highly Significant. This proves that Stifain Tablet is highly effective in alleviating the cardinal and associated symptoms of Rheumatoid arthritis. Improvement observed in the patients may be due to the contents of Stifain tablet like Maharasandi Kvatha[1], Yogaraja Guggulu[2], Mahavatvidhwansa Rasa[3], Ekangvira Rasa[4] and Sameerpannaga Rasa[13] which are known to have Shothahara, Vedanahara and Amhara activities and are indicated in the management of Vatavyadhi and Amavata.

Objective Parameters

Foot pressure, Grip strength, walking time, Disability index and DAS28 score are the functional or objective parameters, which are hampered in Rheumatoid arthritis due to inflammatory changes in joints and related muscles. As highly significant result was found in Cardinal and associated symptoms related to joints and muscles, due to effect upon underlined pathology, remarkable improvement in functional parameters were also reported. As per Ayurveda, in Amavata, Vata is obstructed due to Ama. So, these functional parameters (Normal function of Vata Dosha) are altered. After treatment, Agnideepana and Amapachana was attained which in turn leads to Sroto Sodhana. As are result, normalcy of Vata Dosha is regained, which can be understood objectively by improvement in functional parameters.

Investigations

RA factor

Presence of RA factor is not specific for RA and its value in diagnosis is poor. High titers of RA factor confirm the diagnosis in individuals with suggestive clinical presentation. However, it has prognostic significance because patients with high titers tend to have severe and progressive disease with extra- articular manifestations. Therefore, sero-positive patients have poor prognosis compared to sero-negative patients. Statistically significant reduction in RA factor after the treatment points to arrest of pathogenesis of RA of the patients who had undergone the treatment. This may be due to the presence of drugs like Eranda, Rasna, Trikatu, Guduchi, Sahachara and Guggulu which have known anti-inflammatory action and immuno modulatory effects.

CRP and ESR

ESR and CRP are acute inflammatory markers, which are found to be increased in all conditions of Sopha and Sparshaasahishnutha which are directly indicative of Amaavastha. Statistically significant decrease of ESR and CRP was observed in the present study which points out that Stifain Tablet is very effective in relieving symptoms of Rheumatoid Arthritis with special reference to its Amapachana and Agnideepana property.

Hematological, Biochemical investigations

Statistically insignificant changes were observed on almost all the hematological and Biochemical investigations except significant increases in Hb%, RBC count and PCV % were obtained. All these hematological and biochemical parameters were within normal limits and administration of trial drugs did not produce any change on hematological parameters. This factor establishes the safety profile of the drug. Reason behind increase in Hb, RBC and PCV may be due to the correction of Jatharagni ultimately Dhatvagni, which may improve status of digestion, assimilation and in the end better status of Rasa and Rakta Dhatu.

Probable Mode of Drug Action

Majority of the ingredients of Stifain Tablet are having Ushnaveerya, Agnideepana, Amapachana, Vataanulomana, Kapha Vata Shamana, Balya and Vedanaasthaapana properties. The first goal which is to be achieved in the management of Amavata is Agnideepana and Amapachana. These actions were well accomplished by the presence of Eranda, Musta, Trikatu, Chitraka and Ajamoda. The ingredients of Stifain Tablet like Eranda, Nirgundi, Shigru and Guggulu are considered as the best Vaataanulomana drugs. All these drugs also cause Srotosodhana. In addition, Guggulu has the capacity to penetrate deeply and to correct Utarothara Dhatu Dushti thus prevents or reverses Gambhiraavastha of Vataroga.

Triphala, Goshura, Kustha, Guduchi, Vishamushti and Vatsanabha, are having Agnideepana, Vedanaasthaapana and Balya properties. Along with the correction of initial pathology, it may also help to regain the normalcy of affected Dhatus, prevents further progression of the disease and complications. Maharasnadi Kvatha and Yogaraja Guggulu are very widely used drugs for Vatarogaand are specially mentioned for Amavata. Maharasnadi Kvatha is Vatashamana, Brimhana and Balya. Yogaraja Guggulu has been attributed with Agnideepana, Balya and effective for Sandhimajjagata Vataroga.

Because of the specific action of ingredients at the level of Agni, Ama, Srotasa and Dhatu, Stifain Tablet is very effective in the management of Rheumatoid Arthritis which can be assessed by improvement in subjective, objective parameters and as well as biochemical parameters. During the course of the study, none of the patients developed any untoward symptoms.

CONCLUSION

Finding of present clinical trial indicates that administration of Stifain Tablet in the patients of Rheumatoid arthritis is effective and safe. Hence, Stifain Tablet has definite role in the management of mild to moderate cases of Rheumatoid arthritis

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