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U.R.K. Rao

Additional Professor, Dept. of Medicine, NIMS, Hyderabad

N.S. Bhatt

Medical Director (Ayu), Zandu Pharmaceutical Works Ltd., Bombay

M.U.R. Naidu

Additional Professor

T.R. Kumar

Assistant Professor.

U. Shobha

Senior Resident

CPMR, NIMS, Hyderabad

K. Venubabu

Resident, General Medicine, NIMS, Hyderabad.

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101, Lawrence Apartments II, Vidyanagari Marg, Kalina,
Santa Cruz (E), Bombay-400 098.

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Clinical Trial

Efficacy of Rhumayog and Rhumayog with Gold in Rheumatoid Arthritis - A Double Blind Study

U.R.K. Rao*, N.S. Bhatt[®], M.U.R. Naidu**, T.R. Kumar***,
U.Shobha⁺, K. Venubabu⁺⁺

SUMMARY

Thirty patients (women-22, Seropositive-21) with active rheumatoid arthritis were studied to evaluate the efficacy of Ayurvedic products Rhumayog (Rh) (n=15) and Rhumayog with Gold (Rh Au) (n=15) for a period of 6 months. Both drugs showed antiinflammatory and disease modifying activity. Patients on Rh showed improvement in articular index (AI) (p=0.001), pain index (PI) (p=0.01), walking time (WT) (p=0.05), ESR (p=0.01), CRP (p=0.01) and in Immunoglobulins (IG) (p=0.001), WT (p=0.05), ESR (p=0.001), Rheumatoid Factor (p=0.001) and Ig levels - IgG (p=0.001), IgA (p=0.05) and IgM (p=0.01). However, Rh Au was better in improving the grip strength (p=0.05) and morning stiffness (P=0.01). No side effects were encountered with the drugs during the study period. Ayurvedic preparations Rhumayog and Rhumayog with Gold have positive role in the management of Rheumatoid Arthritis due to their antiinflammatory and disease modifying activities.

KEY WORDS

Rheumatoid Arthritis, Rhumayog, DMARDS, Ayurvedic Drugs.

achieved by nonsteroidal antiinflammatory drugs (NSAIDs) and

INTRODUCTION

Rheumatoid Arthritis (RA) is a chronic disease with uncertain aetiology affecting about 1 per cent of the population. Untreated deformities and/or ankylosis of joints will ensue with marked suffering. Drug therapy forms the mainstay of the treatment which has two fundamental objectives:

1. Short term suppression of inflammation in joints which lead to lesser pain and greater mobility, generally

2. Long term suppression of inflammation which may lead to preservation of joint structure and function to lessen the likelihood of deformities which is achieved by disease modifying anti rheumatoid drugs (DMARDS)¹. The currently used drugs in relieving the symptoms are not free from untoward side effects, the major being gastrointestinal. Gold salts which belong to the group of DMARDS are not without side effects but are used in therapy of established disease².

*Additional Professor, Dept. of Medicine, NIMS, Hyderabad, [®]Medical Director (Ayu), Zandu Pharmaceutical Works Ltd., Bombay, **Additional Professor, ***Assistant Professor, *Senior Resident, CPMR, NIMS, Hyderabad, **Resident, General Medicine, NIMS, Hyderabad. Paper presented at "XVIIIth (ILAR) International League Against Rheumatism, Congress of Rheumatology held at Barcelona, Spain, July 1993".

Ayurvedic medicine widely practised in India has description of disease similar to RA and is claimed to offer treatment of the same through drug and non drug therapies^{3,4,5}. Gold preparation in a different form as Gold Bhasma - a colloidal form of metallic gold- is used in Ayurvedic treatment for variety of disease including RA⁶.

Two Ayurvedic pharmaceutical preparations Rhumayog (Rh) and Rhumayog with Gold (Rh Au) in two earlier preliminary studies were found to exhibit a moderate degree of antiarthritic activity^{7,8}. In an experimental study Rhumayog also was observed to potentiate the antiinflammatory activity of other NSAIDs when used concomitantly⁹.

A double blind study involving Rhumayog (Rh) and Rhumayog with Gold (Rh Au) was undertaken to evaluate the antiinflammatory and the disease modifying effect in patients with active RA.

MATERIAL AND METHODS

Thirty three consecutive cases with R A attending rheumatology services of Nizam's Institute of Medical Sciences were enrolled into the study. The diagnosis of R A was based on the American Rheumatology Association (ARA) criteria¹⁰. Each patient had thorough clinical, haematological, serological, biochemical, immunological and radiological evaluation. The disease was graded according to the Steinbrocker's classification¹¹.

Inclusion and Exclusion Criteria

Male or female cases with R A - seropositive or seronegative - with morning stiffness of more than 30 minutes

and E S R levels more than or equal to 30 mm/1st hr. belong to the age group from 18-60 years were included for the study.

Patients having active peptic ulcer disease or major systemic illness with renal or hepatic impairment and female patients planning for progeny or lactating mothers were excluded. Patients using steroids or disease modifying drugs such as chloroquine, auranofin, injectable gold, sulfasalazine and methotrexate were also excluded.

Evaluation Criteria

The parameters for evaluation were as follows

Clinical- Articular Index (AI), Pain Index (PI), Loop Size (LSr) right, Loop Size (LSl) left, Grip Strength (GS) mm Hg., Walking Time (WT) 15 mt in seconds and Morning Stiffness (MS) in minutes.

Laboratory- Haemoglobin (Hb), Erythrocyte Sedimentation Rate (ESR), Rheumatoid Factor (RF), C-Reactive Protein (CRP) and Immunoglobulins (IgG, IgA, IgM).

After basal evaluation the clinical evaluation was done every month, the haematological biochemical and urinalysis every two months whereas the immunological and radiological studies were done at the end of 6 month therapy. Routine parameters including liver and renal function tests were also done at regular intervals so as to notice any untoward effects.

A case record form specially designed for the study was followed.

The medicines coded as Rh-1 and Rh-2 were supplied in the identical capsules to the randomised patients in a daily dose of 4 capsules (500 mg each) three times a day in a weekly packing which was specially prepared for the study. No concomitant therapy such as aspirin, naproxen, diclofenac or ibuprofen were allowed. A provision for record of any other illness during the period of study and that of any untoward effect were in the case record form.

RESULTS

The study was designed so as to get 15 cases in each of the two groups which either will complete the study or provide specific information for the drop out. However, totally 33 cases were enrolled of which 3 were dropped, 2 due to non compliance (non reporting) and 1 due to occurrence of pregnancy. At the end of the six month trial it was known after decoding that there were 15 patients in each group of Rh-1 (Rhumayog) and Rh-2 (Rhumayog with Gold). The demographic data of the patients is given in Table-1

The analysis of results showed improvement and interestingly comparable results. All the patients except one case

in group Rh-2 belonged to functional class II or III and anatomical stage II or III.

In the Rh-1 group statistically significant improvement was observed in AI ($P<0.001$), PI ($P<0.01$) WT ($P<0.05$) with the treatment. There was significant fall of acute phase reactants namely ESR ($P<0.01$) and CRP ($P<0.01$). There was significant change in immunoglobulin levels ($P<0.001$). (Table-2a)

In the Rh-2 group statistically significant improvement was observed in AI ($P<0.001$), PI ($P<0.001$), GS ($P<0.005$), WT ($P<0.05$) and MS ($P<0.01$). There was significant fall in ESR ($P<0.001$) and RF ($P<0.01$). The change in immunoglobulin levels though variable was also significant [IgG ($P<0.001$), IgA ($P<0.05$), IgM ($P<0.01$)]. (Table-3).

Figures 1 to 6 indicate the Comparative Percentage Variation in clinical parameter with both the drugs. Figs 7 and 8 provide the same in ESR and immunological parameters respectively.

The analysis of variance though did not show any statistically significant difference between the drugs.

Parameter	(Rh-1) Rhumayog	(Rh-2) Rhumayog with Gold
No. of Patients	15	15
Female : Male	12 : 3	10 : 5
Age (years) (Mean + SD)	38.2 + 10.4 (range 22-52)	38.13 + 09.34 (range 22-50)
Duration of Disease (Months-Mean + SD)	36.73 + 26.40	25.60 + 33.13
Seropositivity	12	9

Table 2
Efficacy of Rhumayog in Rheumatoid Arthritis Treatment

No.	Parameter	Before Treat.	After Treat.	t	P
1.	Articular Index	16.13 + 5.0	9.13 + 3.0	5.3379	0.001
2.	Pain Index	24.21 + 13.58	12.26 + 4.62	3.56	0.01
3.	Loop Size (Right)	56.46 + 3.54	56.13 + 3.60	0.310	NS
4.	Loop Size (Left)	55.33 + 2.63	54.60 + 4.06	0.59	NS
5.	Grip Strength (mm Hg)	8.90 + 10.53	15.33 + 14.06	-1.67	NS
6.	Walking Time (15 mts in Sec.)	59.80 + 50.15	36.0 + 18.80	2.27	0.05
7.	Morning Stiffness (in Minutes)	67.0 + 52.84	48.66 + 59.62	1.62	NS
8.	Hb (gm%/dl)	11.47 + 1.40	11.23 + 1.87	0.5641	NS
9.	ESR (mm/l)	68.06 + 25.8	44.46 + 25.29	3.34	0.01
10.	RF (Elisa)	80.26 + 81.70	40.53 + 40.03	1.83	NS
11.	CRP (mg/l)	13.2 + 14.37	1.2 + 3.36	3.68	0.01
12.	IgG (mg/l)	1499.3 + 551.58	1195.2 + 389.65	4.72	0.001
13.	IgG (mg/l)	737.33 + 276.81	603.45 + 219.89	4.27	0.001
14.	IgG (mg/l)	307.86 + 103.94	231.46 + 47.0	5.35	0.001

DISCUSSION

Ayurvedic drugs are claimed to have beneficial effects in the treatment of Rheumatic disorders. Many of these drugs have Guggulu- gum exudate of a plant *Commiphora Mukul*, is the main ingredient. Purified, steroidal fractions of Guggulu show a marked inhibition of platelet aggregation by ADP, Adrenalin and Serotonin, the effect being comparable to that of Clofibrate¹⁴.

The steroidal component of fraction A of the petroleum ether extract has marked antiarthritic effect, comparable to that of hydrocortisone, and more potent than Phenylbutazone¹⁵.

A steroidal moiety isolated from guggulu the main component of Rhumayog was found to be more potent than hydrocortisone in inhibiting the severity of the secondary lesions in the animal model of adjuvant arthritis^{12,13}. Guggulu is always prescribed together with Maharasnadi quath in the Ayurvedic practice. The quath possess a mild anti-inflammatory activity (Sharangdhar Samhita Part 2, Chapter 2). The exact mechanism of their beneficial action is not yet fully known in terms of biochemical parameters¹⁶.

Rasnadi Quath, another component of Rhumayog, has Rasna (*Pluchea lanceolata*) as main ingredient. The anti-inflammatory potential of some

Table 3
Efficacy of Rhumayog (Rh-2) with Gold In Rheumatoid Arthritis Treatment

No.	Parameter	Before Treat.	After Treat.	t	P
1.	Articular Index	15.26 + 6.45	6.4 + 4.77	5.63	0.001
2.	Pain Index	26.93 + 16.33	9.24 + 6.85	4.50	0.001
3.	Loop Size (Right)	57.93 + 3.69	55.46 + 3.50	1.58	NS
4.	Loop Size (Left)	57.93 + 4.14	54.06 + 4.51	1.42	NS
5.	Grip Strength (mm Hg)	9.46 + 8.15	23.93 + 12.06	-2.55	0.05
6.	Walking Time (15 mts)	56.06 + 43.52	31.26 + 4.93	2.80	0.05
7.	Morning Stiffness (minutes)	74.00 + 56.54	21.33 + 35.58	3.53	0.01
8.	Hb (gm%/dl)	12.29 + 1.74	12.36 + 1.78	0.45	NS
9.	E.S.R. (mm/l)	77.00 + 21.23	38.66 + 25.81	5.52	0.001
10.	RF (Elisa)	73.66 + 91.11	62.06 + 114.61	3.2976	0.01
11.	CRP (mg/l)	14.4 + 18.81	3.6 + 7.09	2.05	NS
12.	IgG (mg/l)	1316.13 + 499.09	1100.6 + 414.59	4.48	0.001
13.	IgA (mg/l)	582.26 + 291.47	484.86 + 292.46	2.46	0.05
14.	IgM (mg/l)	267.2 + 84.64	185.46 + 56.18	5.9	0.01

Ayurvedic formulations containing but the *Pluchea lanceolata* extract was tested on experimental Arthritis and granuloma pouch. This showed marked antiinflammatory activity in both models¹⁷.

Although remission induced by gold therapy may be associated with better immuno regulation and suppression of inflammatory activity, it is unclear whether this reflects direct action of gold on the disease itself or epiphenomena. Gold has been shown to alter the humoral immunity, complement systems, lymphocyte, monocyte and neutrophil activities¹⁸.

Rhumayog is considered to be analgesic and antiinflammatory drug^{7,8,9} where as Rhumayog with gold has both antiinflammatory activity and disease modifying property. Antiinflammatory activity is measured by the reduction of pain and swelling of joints, reduction of severity and duration of morning stiffness and improvement in grip strength and walking time. The disease modifying property is gauged by reduction of acute phase reactants as well. They include ESR and CRP¹⁹. Progressively decreasing acute phase reactants with improvement in clinical parameters denote regression of rheumatoid disease activity. This was observed in both groups

taking Rhumayog or Rhumayog with gold. Though the latter was better in improving morning stiffness and grip strength and reducing RF titres there was no statistically significant difference in both groups.

Treatment complications are well known with established DMARDs such as gold salts²⁰ and NSAIDs such as aspirin, ibuprofen and indomethacin²¹. In the present study both the drugs did not elicit any side effects.

CONCLUSION

Both ayurvedic preparations Rhumayog and Rhumayog with gold were found to be efficacious and safe in the management of RA. It requires further studies involving larger group for longer periods.

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