

A double blind controlled trial of R. Compound in 115 cases of Rheumatoid Arthritis & Osteo Arthritis

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Osteoarthritis is probably as old as mankind. Evidence has been seen in apeman and Egyptian mummies. It is also seen in reptiles and mammals. On the other hand, rheumatoid arthritis seems to be a new corner. It is seen in human beings and some primates only.

The textbooks of medicine and rheumatology are replete with various drugs for degenerative and rheumatoid affections of joints that held their sway from time to time. The enthusiasm that came with the discovery of cortisone dwindled rapidly when the side effects of the drug posed greater problems.

Gold preparations have been used for arthritic conditions from Vedic times. While gold salts are not without side effects, gold as Gold Bhasma is non-toxic. Guggul, an oleoresin extracted from Balsamodendron Mukul has been in use in Ayurveda for rheumatism and allied diseases. Similarly Rasna, the chief ingredient of Maha Rasnadi Quath has anti-inflammatory and antipyretic effects.

THE DRUG R. COMPOUND

A combination of Maha Yograj Guggul, Maha Rasnadi Quath and Gold Bhasma has been prepared by Alarsin Pharmaceuticals, Bombay, about two decades ago. Encouraged by reports of patients with degenerative arthritis and rheumatoid arthritis who have had this drug, it was decided to undertake a controlled trial of this drug.

MATERIALS AND METHOD

One hundred and fifteen consecutive patients attending the Arthritis Clinic of the Department of Orthopaedic Surgery, Government Stanley Hospital, Madras, in the year 1970-71 were included in the study. 60 patients with rheumatoid arthritis and 55 patients with osteoarthritis of knee joint formed the basis of this study.

A double-blind controlled trial of the drug and a placebo in identical capsules was tried on twenty four cases of rheumatoid arthritis and twenty six cases of osteoarthritis of knee. The capsules were marked X and Y and their composition was not revealed by the manufacturers till the end of the study.

The diagnosis of rheumatoid arthritis was based on the criteria laid down by the American Rheumatism Association namely

- (a) Morning stiffness.
- (b) Pain on motion or tenderness at least in one of the joints.
- (c) Swelling (soft tissue thickening or fluid, not bony over growth alone) in one joint continuously for not less than 6 weeks.
- (d) Swelling of at least one other joint.
- (e) Symmetrical joint swelling with simultaneous involvements of the same joints on both sides of the body.
- (f) Subcutaneous nodules over bony prominences on extensor surface or in juxta articular regions.
- (g) X-Ray changes typical of rheumatoid arthritis (which must include atleast bony decalcification localised to or greatest around the involved joints and not just degenerative changes) that do not exclude the diagnosis of Rheumatoid arthritis.
- (h) Positive sheep cell agglutination test (Rose-Waaler).
- (i) Poor mucin precipitate synovial fluid-fragmented or thin.
- (j) Characteristic synovial changes in nodules.
- (k) Characteristic histological changes in nodules.

Based on the above criteria the cases are grouped as follows

I	Classical	7 of the above criteria
II	Definite	5 of the above criteria
III	Probable	3 of the above criteria
IV	Possible	2 of the above criteria

The diagnosis of the osteoarthritis of knee was based on clinical and radiological findings as well as by a process of elimination of inflammatory and rheumatoid lesions.

INVESTIGATIONS

The following investigations were done for all cases (a) Radiographs; (b) Erythrocyte sedimentation rate; (c) Serum uric acid level and (d) Rose-Waaler Test. The mucin precipitation test by addition of acetic acid to joint aspirates was done whenever aspirates were available for study.

THE DRUG AND THE PLACEBO

R. Compound contains Mahayograj Guggul with Gold Bhasma 200 milligrammes and Maha Rasnadi Quath 67 milli-grammes. The placebo capsules contained calcium lactate powder.

RHEUMATOID ARTHRITIS

Classification : On the basis of the criteria laid down by the American Rheumatism Association, sixty cases of rheumatoid arthritis were classified as follows :

I	Classical	(7 criteria)	19 cases
II	Definite	(5 criteria)	58 cases
III	Probable	(3 criteria)	11 cases
IV	Possible	(2 criteria)	2 cases

Sex incidence : There were seventeen males and forty three females, almost a three-fold increase in women.

Age incidence : The age ranged from eight years to seventy years with an average age of thirty three years. The second, third, fourth and fifth decades contributed almost equal number of cases. No correlation was seen between the sex and age incidence because of the small numbers and female preponderance.

Type of manifestations : Cases with history of four weeks and less were considered acute rheumatoid arthritis and those with histories over four weeks as chronic rheumatoid arthritis. There were three cases in acute phase and remaining fifty seven were in chronic phase.

There were nineteen cases with mono articular involvement and fortyone cases with polyarticular involvement. All the three cases in the acute phase of the disease had polyarticular involvement.

ANALYSIS OF INVESTIGATIONS

Rose-Waaler Test : Rose-Waaler test was positive in forty one cases and negative in nineteen cases.

Erythrocyte Sedimentation Rate : The rates of 4 to 6 millimetres in one hour for men and 6 to 8 millimetres in one hour for women were taken as normal. On this basis, forty eight cases had elevated E. S. R. and twelve cases had E. S. R. within normal limits.

Serum Uric Acid Estimation : The levels of six milligrammes percent for men and five milligrammes percent for women were considered as normal. It was not elevated in men and it was over 2 mgm% in two cases among women.

Mucin Precipitation Test : The aspirated fluid from the knee joints of eight cases showed thin or fragmented mucin clots suggestive of rheumatoid pathology.

Radiographs : Osteoporosis of the adjoining bone was seen in nine cases. Bilateral calcaneal spurs were seen in four cases. No significant radiological changes were seen in four cases.

Synovial biopsy was not done on any of the cases.

REGIMEN

On analysis, the cases had one of the following three regimens (i) Controlled trial by double blind method; (ii) Treatment with R. Compound only; and (iii) R. Compound and physical treatment.

CONTROLLED TRIAL BY DOUBLE-BLIND METHOD

Twenty four cases were put on X or Y capsules in this study. The capsules were identical in all respects namely the size, colour of the cachet and weight. The composition of the respective capsules was not revealed by the manufacturers at this stage of trial.

One of the capsules was given to all new cases seen in a fortnight to avoid any possible error and for ease of distribution. Where there was no response to the drug, the second drug was given for the next fortnight or longer. Two capsules given thrice daily after food was the standard dose.

Eleven cases had "Y" capsules initially; except for one patient, a female of thirty years with polyarticular rheumatoid arthritis (case 40) who had slight relief of pain, all other cases had no relief. They were, therefore given "X" capsules. Four cases (case 9, 23, 35 and 59) did not improve with "X" capsules also. Six cases were enthusiastic about the change in the regimen and had relief of symptoms.

Thirteen cases had "X" capsules initially. Two cases (case 23 and 36) did not show any improvement while 11 cases had varying degree of improvement. Joint pain had decreased to a great extent; the morning stiffness disappeared and range of movements had increased.

There was no response to Y capsules in the two cases which did not improve with X capsules.

The cases that responded to X capsules were continued on this drug for three to seven weeks (average of five weeks). The improvement was maintained in almost all cases. The drug was well tolerated without any side effects. Therefore seventeen out of twenty four cases had relief with X capsules while only one case had relief with Y capsules.

Drug trial of R. Compound only : Twenty five cases were given R.Compound tablets only for varying periods of times. Six tablets were given in three divided doses. Rose-Waaler test was positive in sixteen out of twenty five cases. Five cases did not show any improvement. Two of these cases were referred to a medical unit for inclusion in Brufen trial. One patient was given aspirin without much relief.

Twenty cases out of twenty five cases showed improvement in symptoms. Morning stiffness when present was relieved in most of the cases. Patient's assessment of improvement in pain could be graded as follows: Slight relief : 2 cases; Satisfactory relief : 3 cases, and Good relief : 15 cases.

The reduction of the joint swelling and the increase in the range of movements were seen in all the twenty cases. These could not be assessed more accurately in a polyarticular disease like rheumatoid arthritis.

(iii) R. Compound and physical therapy : Eleven cases of rheumatoid arthritis of knee were put on R. Compound and were given wax bath to the knee in an attempt to expedite the recovery Wax bath was preferred to ultra short wave diathermy as the emollient action gave a soothing feeling to the region and encouraged the patients to move the joints. There was definite decrease of the swelling while the relief of pain and increase in the range of movements were not any different from the other series.

Eight of the eleven cases had intra-articular hydrocortisone injections into the knee joint. The aspirate, where available was examined for mucin precipitation by acetic acid. Not more than two injections of hydrocortisone acetate was given into any one joint. While the response to the intra-articular injection was gratifying in a few cases, the long term results are probably doubtful.

OSTEO ARTHRITIS OF KNEE JOINT

Fifty five cases of osteo arthritis of the knee joint were included in the study.

Side affected : The right knee joint was affected in twenty three cases and the left knee joint in thirteen cases while both knee joints were affected in nineteen cases. Therefore, forty two right knee joints and thirty two left knee joints were involved in fifty five patients.

Sex incidence : Females predominated with thirty eight cases for seventeen males, a ratio of 2 : 1.

Age incidence : The age ranged from nineteen years to seventy one years with an average age of forty eight years. Thirty three cases were in fourth and fifth decades of life.

ANALYSIS OF INVESTIGATIONS

Rose-Waaler test : Twenty four cases showed a positive Rose Waaler test while the test was negative in thirty one cases. Such high incidence of positivity for a degenerative arthritis raises doubts about the diagnosis. This fact probably emphasizes the difficulty met within clinical practice in the differentiation of rheumatoid and degenerative arthritis of the knee joints.

Erythrocyte Sedimentation Rate : Based on the normal levels of 4 to 6 millimetres in one hour for men and 6 to 8 millimeters for women, E.S. R. was elevated in forty three cases and normal in twelve cases.

Serum Uric Acid Estimation : The level did not exceed 5 milli-grammes, percent in any of the cases.

Radiographs : Of the seventy four knees, a patellofemoral articulation was involved in forty three knees, tibio-femoral joint was involved in eighteen cases and both components were involved in thirteen cases.

Synovial biopsy and analysis of synovial fluid was not done in any of the cases.

REGIMEN

The cases had one of the following two regimens :

- (i) Controlled trial by double-blind method ;
- (ii) Treatment with R. Compound.

(i) Controlled trial by double-blind method :

Twenty six cases were given X or Y capsules. Eight cases had Y capsules, two capsules t.i.d. for two weeks. Excepting for one case (case 21) who had slight relief of symptoms, rest of the cases did not improve. They were switched over to X capsules in the same dosage. Two cases (case 28 and 29) did not have any relief while one case (case 36) had slight relief (10%) according to her own assessment. Four cases had good relief with X capsules.

Eighteen cases had X capsules initially. All the patients had varying degrees relief of pain in two weeks. The treatment was continued for five to eleven weeks, with gratifying relief of pain, decrease of swelling and increase in the range of movements.

Twenty two cases out of twenty six cases had relief with X capsules compared to only one case with Y capsules.

(ii) Treatment with R. Compound :

Twenty nine cases were given R Compound two tablets t.i.d. for periods lasting from 2 to 15 weeks. Three cases (cases 17,51 and 52) were not relieved of pain even though the joint swelling had decreased slightly. One case (case 50) had only 25% improvement in pain. The remaining twenty five cases were enthusiastic about the relief of symptoms.

While accurate assessment was not possible, pain subsided in more than half the cases and decreased in the rest, swelling subsided in varying degrees and the movements returned in the majority of the cases.

(iii) R. Compound and physical therapy :

Physical treatment in the form of wax bath to the knee, static quadriceps exercises and graduated knee exercises was given to twenty one cases in addition to the one or the other regimen. As with rheumatoid arthritis, physical treatment had expedited the recovery and helped to consolidate the improvement in nineteen cases. There was no improvement in two cases.

As the composition of X capsules and R. Compound were identical, fifty four cases of osteoarthritis had this composition. There was no relief in four cases (including one case with minimal relief). Forty seven cases out of fifty four cases had varying degrees of relief of symptoms.

SIDE EFFECTS

It was observed that there were no untoward side effects to any of the drugs, R. Compound, X or Y capsules used in the study. Even in cases which did not respond to the drugs, there was no intolerance to them, No gastrointestinal or renal complications were seen in this study.

Summary and Conclusions

1. Sixty cases of rheumatoid arthritis were studied. Females preponderated by three to one. The second to fifth decades contributed almost equal number of cases. The average age was thirty three years. Three cases were in acute stage and fifty seven cases were in chronic stage of disease. Nineteen cases had monoarticular disease and forty one cases had polyarticular involvement.
2. In the double-blind trial, seventeen out of twenty four cases of rheumatoid arthritis were relieved of their symptoms with X capsules containing the ingredients found in R.Compound, while only one case had relief with the placebo.
3. Twenty out of twenty five cases of rheumatoid arthritis showed improvement with R. Compound tablets.
4. Physical treatment with wax-bath seems to be a worthwhile adjunct.
5. Fifty five cases of osteoarthritis of the knee joint were included in this study. There was a two to one preponderance among women. Majority of the cases were in their fourth' and fifth decades of life. The average age was forty eight years. Forty two right knees and thirty two left knees were affected in fifty five patients. Patello-femoral articulation was involved in fifty six knees while tibio-femoral articulation was affected in thirty one knees.

6. In the double-blind trial, twenty two out of twenty six cases had relief with X capsules while only one case had relief with the placebo.
7. Twenty five out of twenty nine cases had relief with R. Compound tablets.
8. Physical treatment expedited the recovery in nineteen out of twenty one cases on the drug trial for osteoarthritis of knee joint.
9. No untoward side effects were observed in the study.
10. R. Compound seems to have a place in the management of rheumatoid arthritis and osteoarthritis of the knee joint.

ACKNOWLEDGEMENT

We wish to offer our sincere thanks to the Government of Tamil Nadu for permitting this study at the Government Stanley Hospital, Madras. We are thankful to M/s. Alarsin Pharmaceuticals, Bombay and their representative Mr. K.M.S. Chetty for their help.

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