Effect of Rumalaya in Rheumatoid Arthritis with Special Reference to its effect on Alpha-I-Antitrypsin Levels

Agarwal, N.K., M.B.,B.S., M.D., Ph.D.,
Lecturer in Physiology,
Goyal, R.K., M.B.,B.S., M.S.,
and
Vandana Singh, M.Sc.,
Departments of Physiology and Department of Orthopaedics,
S.N. Medical College, Agra, (U.P.)

INTRODUCTION
Rheumatoid arthritis (R.A.) is the commonest disease entity in the group of “chronic arthritis”. It has afflicted human beings since time immemorial and has even been reported in lower animals. It is a disabling disease affecting the connective tissue structure of the joint.

In recent times, the association of Alpha-I-antitrypsin (alpha-I-At) with RA has opened up many avenues of research. Sweedlund et al (1974) found elevated levels in patients with RA and degenerative arthritis. Sjabloem and Wollheim (1977) observed relatively low serum Alpha-I-AT concentration in patients with active rheumatoid arthritis. Walsh and McConkey (1977) have recently reported changes in acute phase protein profile by increased mean Alpha-I-AT.

This study was taken up with a view to observe the role of Rumalaya therapy in the management of rheumatoid arthritis and to note its effect on Alpha-I-antitrypsin levels in such cases.

MATERIAL AND METHODS
One hundred cases of rheumatoid arthritis were selected from among both in-patients and outpatients in the Department of Orthopaedics. S.N. Medical College and Hospital, Agra, between March 1979 and February 1981. Twenty age and sex-matched healthy subjects served as controls.

Diagnosis of rheumatoid arthritis was established on the basis of the criteria laid down by the American Rheumatic Association (1958) and further confirmed by histopathological examination of the synovial membrane. A detailed clinical examination was done, while routine blood and urine investigations, radiological and serological examinations were conducted in all cases. Serum Alpha-I-AT was estimated by single radial immuno-diffusion method (Manoini et al, 1965), using M-partigen immuno diffusion plates (Behring Diagnostic, Germany). With the help of three standard dilutions (1: 10, 1: 5, 1: 2), a standard graph was drawn and Alpha-I-antitrypsin was measured with the help of a calibrated graph.

The cases were divided into three groups:
Group A (n = 59) on only Rumalaya therapy
Group B (n = 31) on Rumalaya therapy + specific therapy
Group C (n = 10) on only specific therapy
Rumalaya tablets were given in a dosage of 2 tablets, t.i.d., and Rumalaya cream was applied locally at the same time. The patients were asked to attend the out-patient department at one month’s interval for clinical, biochemical and immunochemical assessment. Student’s ‘t’ test was used for statistical purposes. Alpha-I-AT deficiency was labelled, using the criteria of Lieberman (1973) as described in detail in our earlier publications (Kishore, et al 1979; Kishore, 1980).

**OBSERVATIONS**

Of the 100 cases, 48 were males and 52 were females. Their mean age as well as the mean age at which symptoms deviate are detailed in Table I.

<table>
<thead>
<tr>
<th>Sex</th>
<th>Male</th>
<th>Female</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of cases</td>
<td>48</td>
<td>52</td>
<td>—</td>
</tr>
<tr>
<td>Age mean</td>
<td>37.4 ± 7.8</td>
<td>44.4 ± 11.6</td>
<td>41.7 ± 9.2</td>
</tr>
<tr>
<td>Age at symptoms</td>
<td>35.2 ± 4.3</td>
<td>32.3 ± 3.7</td>
<td>—</td>
</tr>
</tbody>
</table>

The mean level of serum Alpha-I-AT in 20 healthy subjects was 238.2 ± 30 mg%, ranging from 162.5—290.0 mg%. In cases of rheumatoid arthritis, the value of Alpha-I-AT ranged from 45—342 mg% with a mean of 203.7 ± 37.8 mg/100 ml. The difference in the two groups was highly significant ($p<0.01$).

Seventy-six percent cases had chronic illness while 24% cases presented in the acute stage of the disease. Fifty-seven percent cases had mono-articular involvement whereas 43% had polyarticular disease. Out of 100 cases, 59 cases were kept in Group A where Rumalaya alone was given, while 31 were in Group B where specific therapy (analgesic anti-inflammatory drugs, corticosteroids and vitamins) was administered along with Rumalaya tablet/cream. Ten cases in Group C were only on specific therapy. Rumalaya tablet was given in a dosage of 2 tablets, t.i.d. and Rumalaya cream was applied locally 3-4 times a day.

All the cases presented with pain (100%). Most of them had stiffness of the joint (63%) and restriction of movement (52%). On examination, synovial thickening was noted in 93% cases, tenderness in 62%, effusion in 33%, deformity in 24% and muscular wasting in 48%. The ESR levels tended to be high in most cases (89%) and serum alkaline phosphatase levels were above 13 KA units in 56% cases.

By the end of the trial, 58 cases completed the full course: 33 cases in Group A, 19 in Group B and 6 in Group C. Rest of the cases (42%) could not report for final analysis as they discontinued the treatment. (The ratio of the dropouts was almost uniform in all groups, i.e., 40%).

<table>
<thead>
<tr>
<th>Type of subjects</th>
<th>Range</th>
<th>Average</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy</td>
<td>162.5—290.0 mg%</td>
<td>238.2 ± 30 mg%</td>
</tr>
<tr>
<td>R.A. Cases</td>
<td>45 ± 342 mg%</td>
<td>203.7 ± 37.8 mg%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Illness</th>
<th>Acute</th>
<th>76%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic</td>
<td>24%</td>
<td></td>
</tr>
<tr>
<td>Involvement of joints</td>
<td>Mono-articular</td>
<td>57%</td>
</tr>
<tr>
<td></td>
<td>Polyarticular</td>
<td>43%</td>
</tr>
<tr>
<td>Therapy A</td>
<td>Rumalaya tabs. + cream</td>
<td>59</td>
</tr>
<tr>
<td>Therapy B</td>
<td>Rumalaya tabs. + cream + specific therapy</td>
<td>31</td>
</tr>
<tr>
<td>Therapy C</td>
<td>Specific therapy</td>
<td>10</td>
</tr>
</tbody>
</table>
RESULTS
The response was the maximum in Group B (84.6%) where specific therapy and Rumalaya were both given. In Group A, 63.5% showed good response to Rumalaya alone whereas 50% were relieved on specific therapy alone in Group C.

Most of the cases got symptomatic relief of pain, stiffness and effusion of the joints, within one month on Rumalaya therapy. The range of movement in the joints increased regularly; muscular wasting, tone and power of the muscles improved very well. Synovial thickening, however, did not regress. Mean value of ESR and serum alkaline phosphatase were found to be significantly lower after therapy ($p<0.01$). Conventional therapy alone could not bring about such results in Group C (Table V).

Alpha-I-AT levels were found to have increased in all the groups. However, the increase was maximum in Group A and minimum in Group C. In Alpha-I-AT deficient cases, where the levels were below 180% mg, Rumalaya increased the levels significantly. However, no such significant effect was observed in one patient, who was having homozygous deficiency (45 mg%).

DISCUSSION
In terms of incidence and prevalence of the deformity and disability, rheumatoid arthritis constitutes the most important group of crippling disorders. The condition causes pathological changes in the structure and functions of the tissue of the joints. Many studies have been initiated for early diagnosis offers a permanent cure. They mostly provide symptomatic relief or slow down the progress of the disease.
The results of the present long-term study with Rumalaya produced significant reduction in pain, swelling, stiffness of the joint, effusion of the joint and restriction of the movements. Most important was the fact that once the patients got symptomatic relief, their condition remained stable for the remainder of the trial. This clearly indicates that drug tolerance to Rumalaya does not develop and an increasing dosage is not required to maintain the progress.

Biochemical assessment too showed significantly lower ESR and serum alkaline phosphatase values. Serum Alpha-I-AT levels showed a significant rise in all the Groups. This, it seems that Rumalaya elevates the level of antiprotease enzymes against increased proteolytic activity in such cases.

According to Weissman, lysosomal enzymes are released from synovial cells and leukocytes, which indicate the pathogenesis of the inflammatory process in joints of patients with rheumatoid arthritis. This lysosomal permeability is responsible for the destruction of cells and liberation of cytoplasmic enzymes into the joint cavity. These lysosomal enzymes inhibited by the most potent protease inhibitor i.e., Alpha-I-AT. A lack of Alpha-I-AT enables the inflammation to increase, because of uninhibited release of lysosomal enzymes. Rumalaya increases antiprotease enzymes and helps the patients in inhibiting the lysosomal enzymes which are responsible for the destruction of the joint tissue.

In conclusion, this study demonstrated that Rumalaya given on a thrice daily dosage schedule is an effective and well tolerated treatment for inflammatory arthritic conditions. The response was maximum in Group B, where conventional drugs were also given with Rumalaya therapy. However, 65.5% cases in Group A managed very well on Rumalaya alone without conventional therapy. No side-effects were associated with this therapy.

CONCLUSION
This project spanning two years was taken up for observing the role of Rumalaya in cases of rheumatoid arthritis. Out of 100 cases, 59 cases were kept in Group A (Rumalaya therapy), 31 in Group B (Rumalaya + Conventional therapy) and 10 in Group C (conventional therapy). Mean age of the patients was 41.7 ± 9.2 years. Mean levels of Alpha-I-AT in 20 healthy controls was 238.2 ± 30.0 mg% and in cases of rheumatoid arthritis it was 203.7 ± 37.8 mg%. The difference in two groups was highly significant results and the relief was permanent. No drug tolerance and side-effects were reported by any patients. Alpha-I-AT values were found to be increased by this therapy (P < .01). Thus, it seems that, Rumalaya therapy increases the levels of antiproteases against proteolytic damages.

Rumalaya therapy is well tolerated and safe.

ACKNOWLEDGEMENT
We would like to thank the Himalaya Drug Co., Bombay, for the generous supply of Rumalaya Tablets/Cream.

REFERENCES

