Enzymatic Antioxidant Status, Malondialdehyde and Total Antioxidant Activity as Maker of Oxidative Stress in Rheumatoid Arthritis

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ABSTRACT

Background: Rheumatoid arthritis (RA) is a systemic disease characterized by progressive erosive and chronic polyarthritis. The etiology of RA is unknown, but some evidences suggest the involvement of reactive oxygen species (ROS) in pathogenesis of the disease. Objective: To evaluate enzymatic antioxidant status by measuring vitamin E, total antioxidant activity, malondialdehyde (MDA) in serum of the RA patients along with uric acid, total Thiol, C-reactive protein (CRP), rheumatoid factor (RF) and to investigate the effect of diet and hypertension in RA patients as compared to the control. Method: 300 patients with rheumatoid arthritis and 200 apparently healthy subjects were studied and serum malondialdehyde, uric acid were measured by enzymatic method, vitamin E by Netelson (1971) and total antioxidant activity according to Benzie and Strain (1999) and also Thiol by DTNB method. Results: The data obtained showed that the level of uric acid, MDA were significantly higher in the patients with RA as compared to the healthy controls, while total Thiol, vitamin E and total antioxidant were lower in RA patient as compared to the controls. Conclusion: The pathogenesis of RA contributed by antioxidant and number of hypertensive people were higher in RA compared to control.

Key-words: Rheumatoid arthritis, Reactive oxygen species, Antioxidant activity, Malondialdehyde, Rheumatoid factor, Vitamin E.

INTRODUCTION

Rheumatoid arthritis is a chronic, relapsing immuno-inflammatory multisystem disease with predominantly synovial proliferation and destruction of articular cartilage. Rheumatoid arthritis has a high prevalence worldwide, affecting about 1-2% of the general population and up to 3% of those over 60. The incidence increases with age. Women are affected more than men, although the sex difference is less in the older age group. The peak onset of the disease occurs in the fourth and fifth decades of life, so sufferers of rheumatoid arthritis are often young, active people. The progress of rheumatoid arthritis (RA) and osteoarthritis (OA) is commonly associated with inflammation and oxidative stress. Rheumatoid arthritis induces two basic recurring mechanisms of reactive oxygen species (ROS) production viz., activated polymorphonuclear cells and injury resulting from ischaemic and reperfusion in the inflamed joints. To circumvent the damage caused by ROS, multiple defense systems, collectively called as "Antioxidant defense system" are present in the serum and tissues. The role of free radicals and other oxygen-derived species in human rheumatoid disease has been illustrated by McCord. In two separate studies conducted by Gambhir et al and Taraza et
significant elevated levels of MDA were demonstrated in patients of rheumatoid arthritis, which suggests the presence of increased oxidative stress. The present study was aimed to assess the oxidative stress in the rheumatoid arthritis and the status of antioxidant defense system.

MATERIAL AND METHODS

The present prospective and observational study was conducted in the Department of Biochemistry in association with Orthopaedics and Medicine departments of RNT Medical College & MBGH, Udaipur. Total 300 diagnosed patients of rheumatoid arthritis attending the OPD of the Department of Medicine and Orthopaedics were selected for the purpose of this study. These cases formed the study group and out of them 200 healthy age and sex matched individuals formed the control group. The patients included in this study were taken according to the revised criteria of the American Rheumatism Association as per ethical norms and approved by the ethical committee of institution. Blood samples from the test and control groups were collected in plain vial and serum were obtained after centrifugation for the examination of various biochemical parameters viz., TAA (FRAP Assay by Benzie and Strain), uric acid (Uricase and POD Method; Trinder et al., 1969), Vitamin E, Glutathione, MDA (Thiobarbituric Acid method) and RF factor (Latex Slide Test). The instrument used for the estimation was ERMA colorimeter and spectrophotometer. The above parameters were recorded as the mean and standard deviation (SD). The statistical analysis of all the obtained parameters was done using student 't' test. The observations were tabulated and the conclusions were obtained from the biochemical data.

RESULTS AND DISCUSSION:

The value (mean ± SD) with statistical significance (P value) of various biochemical parameters in normal subjects (Group 1) and patients affected with rheumatoid arthritis (RA) (Group 2) are tabulated and compared in Table 1.

<table>
<thead>
<tr>
<th>Biochemical Parameters</th>
<th>Normal Subjects (Group 1) (n=200)</th>
<th>RA Subjects (Group 2) (n=300)</th>
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</thead>
<tbody>
<tr>
<td>Total thiols (nmol/L)</td>
<td>3.0±1.0</td>
<td>3.9±0.61 (P&lt;0.001)</td>
</tr>
<tr>
<td>Malondialdehyde (amoles/ml)</td>
<td>2.68±0.90</td>
<td>13.69±3.42 (P&lt;0.001)</td>
</tr>
<tr>
<td>Vitamin E (mg/dl)</td>
<td>0.70±0.12</td>
<td>0.50±0.05 (P = 0.027)</td>
</tr>
<tr>
<td>T.A.A. (amoles/dl)</td>
<td>892.04±63.33</td>
<td>788.18±111.37 (P&lt;0.01)</td>
</tr>
<tr>
<td>Uric acid (mg/dl)</td>
<td>4.12 ± 0.94</td>
<td>7.00 ± 1.98 (P&lt;0.001)</td>
</tr>
<tr>
<td>RF Factor (%)</td>
<td>94.11% (-ve)</td>
<td>96.07% (+ve)</td>
</tr>
<tr>
<td></td>
<td>58.88% (+ve)</td>
<td>3.92% (-ve) (P&lt;0.01)</td>
</tr>
</tbody>
</table>

Table 2. Hypertension between rheumatoid arthritis (case) and normal subjects (control)

<table>
<thead>
<tr>
<th></th>
<th>Hypertension</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Case</td>
<td>180 (88.2%)</td>
<td>120 (40.5%)</td>
</tr>
<tr>
<td>Control</td>
<td>24 (11.8%)</td>
<td>176 (59.5%)</td>
</tr>
<tr>
<td>Total</td>
<td>204 (100.0%)</td>
<td>296 (100.0%)</td>
</tr>
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</table>
In our study, the level of total Thiol (Table 1) in the patient of RA was found to be significantly lower (P<0.001) than those found in the controls. These results are in accordance with the results of various studies reviewed. Similar results have been observed in Taraza et al. Ambanelli in a study of 25 patients with RA also reported significantly decreased level (P<0.001) of total Thiol as compared the controls. MDA is a product of lipid peroxidation and a reliable marker of oxidative stress. MDA is a decomposition product of lipid peroxidation of polyunsaturated fatty acids, which is used as an index of oxidative damage. In our study level plasma MDA in the patient of RA was highly significant (P<0.001) in comparison to normal control (Table 1). In our study vitamin E level in the normal control range was higher than RA patients (Table 1), which is significantly lower than that of normal with P value less than 0.05 (P < 0.05). The similar results were also observed by Dwivedi et al. Sarban et al. revealed that plasma TAC levels are decreased in RA due to its inflammatory character. In our study the total antioxidant activity was significantly lower (P < 0.01) in patients with RA than in healthy controls (Table 1) and levels of uric acid were significantly higher with RA (P < 0.001) than control group (Table 1). Most of the patients (96.70%) in our study were RF +ve and 60% of the RA patients were found hypertensive that indicates that hypertension is highly prevalent in the rheumatoid arthritis patients (Table 2). The same line of observations was noticed by Panoular and Metsios, who has highlighted the importance of hypertension as a cardiovascular risk factor in patients with RA. They observed 70% of the female with RA had hypertension and only 22% patients have BP within the normal range.

CONCLUSION:
Involvement of oxygen free radicals (OFR) in the pathophysiology of inflammation in a number of organs and tissues has been reported in literature. Evidence of OFR generation in patients with RA has been observed by measuring one of the final products of lipid peroxidation i.e. malondialdehyde, which was found to be increased significantly in patients compared to control. Total Thiol, TAA and Vitamin E was significantly decreased in RA patients than that found in controls while MDA and uric acid was significantly increased in RA than that of the healthy control group. The findings of this study conclude that excessive production of ROS disturbs the redox status, including antioxidant and can exacerbate inflammation and affecting tissue damage in RA.

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Conflict of Interest: None

References:


