Total Antioxidant Activity And Oxidative Stress In Rheumatoid Arthritis Patients

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ABSTRACT

Background: Rheumatoid arthritis (RA) is a chronic multisystem disease of unknown cause. It is believed that increased formation of oxidative stress and decreased antioxidant status are the hallmarks in these patients as observed in recent years. **Aims & Objective:** To analyze the total antioxidant activity and oxidative stress in rheumatoid arthritis patients. **Method:** Blood glutathione, uric acid, total antioxidant activity (TAA), malondialdehyde (MDA), vitamin C, ESR along with Rheumatoid Factor (RF) were measured in 300 patients affected by rheumatoid arthritis and the results were compared with a group of 200 normal subjects. **Results:** Mean serum level of MDA and uric acid were found to be significantly high ($P < 0.001$). The mean level of glutathione showed significantly decreased p value ($P<0.05$), while the erythrocyte sedimentation rate (ESR) was higher. The level of TAA and vitamin C was found to be significantly lower ($P < 0.01$) than the normal subjects. **Conclusion:** Data suggests that the decreased level of glutathione, vitamin C and TAA and elevated levels of serum MDA and uric acid as a result of homostatic imbalance between antioxidant defence system and enzymatic antioxidants.

Key-words: Glutathione, Malondialdehyde, erythrocyte sedimentation rate, total antioxidant activity, rheumatoid arthritis, rheumatoid arthritic factor, Dithiobis Nitrobenzoic acid.

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INTRODUCTION

The term rheumatoid arthritis was first used by Sir Archibaid Ganod in 1876 to describe a chronic non-suppurative inflammatory arthropathy, distinct from gout and osteoarthritis.[1] It is a chronic multisystem disease, which begins insidiously with fatigue, anorexia, and generalized weakness, but the hallmark of the disease is the symmetrical involvement of peripheral joints leading to pain, tenderness and morning stiffness. The exact cause of rheumatoid arthritis is not known.[2] Reactive oxygen species play a significant role in the pathogenesis of certain chronic diseases such as rheumatoid arthritis. The synovial fluid in the inflamed joint swarms with activated neutrophils, which produce large amounts of superoxide radical (O_2^-), hydrogen peroxide (H_2O_2) and highly reactive hydroxyl radical (OH^-). It has been suggested that the pro-oxidant /antioxidant imbalance in rheumatoid arthritis may be either due to acceleration of some cellular reactions or insufficiency of the antioxidant defense system.[3] Glutathione is a tripeptide with

multifaceted functions. Its main function is the detoxification of oxygen free radicals and reduction of the oxidative stress.[4,5] Vitamin C is the major circulating water soluble antioxidant and plays a pivotal role in protecting plasma lipid peroxidation.[6,7] However, it is rapidly oxidised, when challenged by oxidants released from activated polymorphonuclear cells.[8,9,10] The present study was conducted with the aim to analyze the total antioxidant activity and oxidative stress in rheumatoid arthritis patients.

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 newly diagnosed patients with rheumatoid arthritis attending the OPD of Medicine and Orthopaedics departments were selected for the study with a control group containing 200 healthy age and sex matched individuals. The patients included in this study were taken according to the revised criteria of the American Rheumatism Association (1987) 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),[11] uric acid (Uricase and POD Method; Trinder et al., 1969),[12] Vitamin C, 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 $\pm$SD) with statistical significance ('P' value) of various biochemical parameters in normal subjects (Group 1) and patients affected with rheumatoid arthritis (Group 2) are tabulated and compared in Table 1.

Table 1. Mean±SD of various biochemical parameters in control and RA patients

Biochemical parameters	Normal subjects (Group 1) (n=200)	Rheumatoid arthritis subjects (Group 2) (n=300)
Blood Glutathione (mmol/L)	1.99± 0.57	0.94 ± 0.11 (P<0.05)
Ascorbate (mg/dl)	0.90±0.42	0.67±0.27 (P<0.01)
Malondialdehyde (nmoles/ml)	2.68±0.90	13.69±3.42 (P<0.001)
T.A.A. (μmoles/dl)	892.04±63.33	788.18±111.37 (P<0.01)
Uric acid (mg/dl)	4.12 ± 0.94	7.00 ± 1.98 (P<0.001)

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

	Smoking		Total
	Yes	No164	
Case	135 (55.8%)	(64.0%)93	300 (60.0%)
Control	107 (44.2%)	(36.0%)258	200 (40.0%)
Total	242 (100.0%)	(100.0%)	500 (100.0%)

We observed significantly lower levels of blood glutathione levels (Table 1) in the cases of RA as compared to corresponding levels in normal control. Our findings are in accordance with the observations Sharma et al[3] reported the mean range, but with significant decreased (P < 0.05). Plasma vitamin C plays a pivotal role in protecting plasma lipid from oxidative damage. In our study, the plasma vitamin C level in the patients with RA at the time of presentation were significantly decreased (Table 1) when compared with control group (P<0.01). These results are in accordance with the results of other studies i.e Sharma et al[3] reported level of ascorbate were found to significantly lower (P < 0.01) in group 2 patients than control. Similarly Singh et al[13] have observed the low level of non-enzymatic vitamin C in their study value of vitamin C in control subject was 12.28±3.09 μmol/L while the level of ascorbate in RA 10.22±2.63 μmol/L. MDA is a product of lipid peroxidation and a reliable marker of oxidative stress. In our study level plasma MDA in the patient of RA was highly significant (P<0.001) in comparison to normal control. Total antioxidant activity is the primary defense against oxidative stress in extracellular fluids results from a number of low molecular weight antioxidant molecules. In our study the total antioxidant activity was significantly lower (P < 0.01) in patients with RA than in healthy controls. Uric acid is the end product of purine metabolism, which is a major protective antioxidant against some free radicals and it has the potential for chelating iron and copper reducing them and thus inhibiting lipid peroxidation.[1] In our study levels of uric acid were significantly higher with RA (P < 0.001) than the control group and 60% of RA patients were smokers (Table 2), which is well supported by the observations of Mikuls et al[6] and Hutchinson.[7] In the present study, 80% of the RA patients were found anemic, which shows that anemia is high prevalent in the RA patients and almost same findings were found by Smyrnova.[4]

CONCLUSION

Our study concludes that there is an increased oxidative stress and decrease oxidative defense in patients with RA as evidenced by increased blood levels of MDA, uric acid and a decrease in the plasma activity of the enzymatic antioxidant like vitamin C, TAA, glutathione. There is an inverse association between serum antioxidant levels and inflammation in these cases. Therefore, because of the roles of these nutrients as antioxidant and probability of their deficiency, it seems that there is increased lipid peroxidation in these patients and thus supports the need for further studies evaluating the role of antioxidant as free radical scavengers in arthritis and rheumatoid arthritis patients.

Funding: Nil.

Conflict: None

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