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BRIEF COMMUNICATION

URIC ACID A BETTER SCAVENGER OF FREE RADICALS THAN VITAMIN C IN RHEUMATOID ARTHRITIS

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ABSTRACT

Uric acid an endogenous aqueous antioxidant in normal humans is present in much higher concentrations than vitamin C and has been known to cover 2/3rd of the free radical scavenging capacity in plasma. In the present study average uric acid levels of patients of rheumatoid arthritis were found to be close to the normal individuals. A unique feature was observed after classifying the patients on the basis of the duration of suffering, the patients having longer duration of disease had least uric acid levels as compared to those suffering from relatively lesser period, similar trend was observed in the ascorbic acid estimations. The decline in uric acid values with progression of the disease was much more than what was observed in case of ascorbic acid suggesting the significant role of uric acid in scavenging of free radicals. Too much lowering of Uric Acid should be checked and vitamin C should be supplemented in diet for maintaining the balance between pro oxidant and antioxidant forces to check pro oxidant insult in rheumatoid arthritis.

KEY WORDS

Inflammation, Adenosine Deaminase, Uric acid, Rheumatoid Arthritis.

INTRODUCTION

Rheumatoid Arthritis is a chronic progressive disorder of unknown aetiology as many diseased conditions resemble it because of the multisystem involvement. The prevalence of rheumatoid arthritis is approximately 0.8% -1% and disease is more common in females than males and most patients fall in the range of 30-60 years of age. The prevalence increases with age and the sex difference diminishes in the older age group. Mostly patients present with symmetric erosive sinovitis. Some patients of rheumatoid arthritis show normal pattern of blood tests and X-Rays for months together after the onset of joint pain. It is extremely important to determine whether the case is benign or aggressive to treat the problem appropriately.

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Various blood tests like Erythrocyte Sedimentation Rate, C-Reactive Protein and rheumatoid factor that are used to diagnose the disease show that the patient of Rheumatoid Arthritis may be sero-positive or sero-negative and sufficient data is available to show that 70% of patients of Rheumatoid Arthritis are sero-positive while 30% are sero-negative (1).

Lots of confusion is prevailing in the literature to explain exactly the factors responsible for the causation and progression of the disease. The present study was aimed at finding out the initial events leading to multisystem involvement in causation and progression of the disease only in sero-positive patients, to have a better understanding of the actual process.

MATERIALS AND METHODS

All the patients with rheumatoid arthritis were suffering from active disease at the time of investigation, they were complaining of morning stiffness and pain and they had synovial swellings and increased sedimentation rate. All the patients were of classical rheumatoid arthritis according to American Rheumatism Association criteria.

Table I: Comparison of Erythrocyte sedimentation rate and C-reactive protein in normal individuals and patients and in relation to the duration of the disease

S.No.	Group	Rheumatoid Factor	ESR mm 1st hr Mean±SD Males	ESR mm 1st hr Mean±SD Females	C-reactive Proteins Mean±SD
1.	Normal Individuals	-ve	4.8±0.82	8.5±1.2	13.9±3.58
2.	Patients	+ve	43.8±18.25*	38.2±17.6*	61.5±45.9*
Group I (n=26)	Up to 1 year	+ve	25.50±0.70*	26.0±6.26*	33.62±9.3*
Group II (n=27)	1-5 years	+ve	41.50±13.12*	32.4±20.3*	46.1±32.2*
Group III (n=47)	>5 years	+ve	55.2±20.5*	48.4±17.3*	85.8±51.2*

*p<0.001 When patients were compared with normal individuals, Group I compared with Group II and III, Group II compared with III

The individuals having clinical history of diseases such as Diabetes Mellitus, Cardio Vascular Disease, Inflammatory diseases, Infectious diseases like tuberculosis etc where the free radical damages were commonly found to be increased were excluded.

100 sero-positive patients of rheumatoid arthritis from various wards of Guru Nanak Dev Hospital attached to Government Medical College Amritsar and ESI Hospital Amritsar were included in the course of study. Equal number of age and sex matched normal individuals asymptomatic of the disease who volunteered were included as controls. All the normal individuals and patients were subjected to the following investigations, rheumatoid Factor (2), Erythrocyte Sedimentation Rate (3), C-Reactive Proteins (4), Uric Acid (5), Adenosine Deaminase (6) and Vitamin C (7). Statistical analysis was done using student's 't' test. For analyzing the data these patients were divided into three groups. Group I included patients suffering from rheumatoid arthritis for a period of <1 year, Group II included patients with suffering of disease from 1-5 years and Group III included rheumatoid arthritis patients with >5years of suffering.

RESULTS AND DISCUSSION

All the patients of rheumatoid arthritis included in the present study had positive rheumatoid factor. Erythrocyte Sedimentation Rate was increased and serum C - reactive protein was significantly raised (p<0.001) when compared to that of normal healthy control individuals. With the increase in period of suffering there was a significant increase in ESR (p<0.001) and C-reactive proteins (p<0.001) levels. All these parameters were suggestive of inflammatory response in patients of rheumatoid arthritis (Table I).

These patients had significantly raised (p<0.001)levels of serum adenosine deaminase an enzyme which has been known to be considerably increased in extra cellular and serous fluids during inflammatory reactions of differing pathology (8) suggesting that the active disease involves inflammation. A linear correlation was observed between Erythrocyte Sedimentation Rate, C-reactive protein, adenosine deaminase levels with the progression of the disease suggesting significant role of adenosine deaminase in inflammatory process in these patients.

Uric Acid an endogenous aqueous antioxidant in humans contributes as much as 2/3rd of all free radical scavenging capacity in plasma (9). it is particularly effective in quenching hydroxyl,superoxide, peroxal and peroxynitrite radical and may serve protective physiological role by preventing lipid per oxidation. Urates possess preventive antioxidant property in addition to chain breaking antioxidant activity (10). In the present study average uric acid levels of patients of rheumatoid arthritis were found to be close to the normal individuals but when uric acid levels were analyzed on the basis of the duration of the disease a unique feature was observed. The patients who were having longer duration of the disease had least uric acid levels as compared to those who were suffering from the disease for a relatively lesser period, suggesting the probable utilization of uric acid produced in trapping the free radicals and it's conversion into allantoin. Decrease in uric acid with

Table II: Comparison of Serum Uric Acid, Adenosine Deaminase and Vitamin C in normal individuals and patients and in relation to the duration of the disease

S.No.	Adenosine Deaminase Mean±SD	S.Uric Acid Mean ±SD	Ascorbic Acid Mean ±SD
1	20.7±14.9	5.95±1.7	1.19±0.22
2	58.92±17.94*	5.40±2.24*	0.30±0.11*
Group I (n=26)	33.62±9.3*	7.84±0.89*	0.35±0.11*
Group II (n=27)	37.57±11.94*	6.29±1.72*	0.30±0.10*
Group III (n=47)	85.2±52.6*	3.54±1.42*	0.28±0.09*

*p<0.001 When patients were compared with normal individuals, Group I compared with Group II and III, Group II compared with III

the progression of the disease may be attributed to the compensatory mechanisms of uric acid conferring protection against increased free radical activity.

A closer look into the levels of antioxidant vitamin C revealed that serum vitamin C levels were significantly reduced in rheumatoid arthritis patients ($p<0.001$) when compared to that of normal control subjects. Further the levels of vitamin C were found to fall with the increase in duration of the disease suggesting the consumption of vitamin C for mopping up the free radicals neutralizing the oxidative properties of these free radicals as proposed earlier (11). Uric acid at physiological concentrations reduces the oxoheme oxidant formed by peroxide reaction with Hemoglobin and hence protects lipid per oxidation in erythrocytes and their lysis.

Furthermore antioxidant role of ascorbic acid is as effective as that of uric acid (Table II; $p<0.001$). Since uric acid concentration of plasma in human beings is much more than that of plasma ascorbic acid, the uric acid contributes more to the scavenging action of free radicals than ascorbic acid, these findings are in concordance with previous experimental work of Ames et al in the year 1981 and cover up the lacuna of physiological context as well. It is therefore proposed that the uric acid produced as a result of excessive activity of adenosine deaminase liberated in response to inflammatory process in rheumatoid arthritis plays a significant role in scavenging the free radicals produced. Reduction in the levels of vitamin C (Table II; $p<0.001$) during the progress of active disease again suggests it's role in combating the oxidative stress. The present study supports the powerful antioxidant role of uric acid in scavenging the singlet oxygen and other free radicals. The message to the clinicians is that, they should not target at too much lowering of uric acid values keeping in view the antioxidant effects of uric acid. Vitamin C should be supplemented in diet to raise the levels of vitamin C in the blood so that its antioxidant effects can be potentiated.

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