Significance of monodialdehyde in rheumatoid arthritis patients

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Abstract

Background: Rheumatoid arthritis is an auto immune disorder involving multi systems and its cause is unknown. From the available studies it is believed that, increased oxidative stress and decreased anti-oxidant status is the hallmark of this disease. Malondialdehyde is one such important lipid peroxidation indicator. This study was done to evaluate the significance of serum Malondialdehyde in rheumatoid patients.

Materials and Methods: Our study was made in a tertiary institute between January 2015 to June 2017 for a period of 2 and half years. A total of 100 patients were included in the study. 50 of them were rheumatoid arthritis patients and another 50 were normal control subjects. Serum levels of Malondialdehyde were assessed using the thiobarbituric acid assay method with UV-VIS Spectrophotometer.

Results: The serum monodialdehyde levels in rheumatoid people were 3.300 ± 0.450 nmoles/ml and it was 2.600 ± 0.490 in normal subjects group. On calculating 'p' value for both the groups, it was < 0.01. Hence it was significant statistically between both groups. There was 23.14% increase of monodialdehyde levels in rheumatoid patients when compared to normal healthy population group.

Conclusion: Pathogenesis of rheumatoid arthritis is a result of formation of increased free radicals formation during the disease process. Detection of Malondialdehyde in the serum of rheumatoid arthritis patients and its values is a simple tool which helps in diagnosing and to know the disease activity status.

Keywords: Malondialdehyde, Oxidative stress, Auto immune disease.

Introduction

Rheumatoid arthritis is an auto immune disease involving multiple systems. It is characterized by the gradual destruction of cartilage and articular surfaces of the bones.(1) Clinically rheumatoid arthritis is characterized by pain and swelling of multiple joints, morning stiffness and deformities of the joints.(2) The pathogenesis of articular cartilage and synovial destruction is still under evaluation stage.(3) Various theories have been explained in the literature. Activated phagocytes and other leukocytes migrate to the synovium and articular cartilage area and initiate phagocytosis. During phagocytosis, these cells produce oxygen free radicals. These free radicals are highly toxic in nature. They produce cause damage to the cells of multiple systems. Cell membrane and its components such as proteins and lipids are damaged by these free nascent radicals.(4) Monodialdehyde is a byproduct of increased conversion of cell membrane polyunsaturated fatty acids. Monodialdehyde is one of many such byproducts and it causes cell membrane and DNA damage resulting in cell death. MDA is the important marker of Lipid peroxidation.(5) Oxidative stress status are the hallmark of disease activity and also serve as a diagnostic tool for the assessment of rheumatoid patients. Estimation of the serum levels of Malondialdehyde in rheumatoid patients and comparing them with normal individuals serves as an important tool in diagnosing the oxidative stress in rheumatoid patients.

Materials and Methods

This study was performed in a tertiary institute between January 2015 to June 2017 for a period of 2 and half years. A total of 100 patients were included in the study. All the patients were the ones who visited the orthopaedic outpatient department of the institute. Out of the 100 patients, 50 patients were normal healthy subjects and were put under Group I. 30 of this group patients were males and 20 were female patients with age ranging from 30 to 60 years(with a mean age of 39 years). Group II patients comprised 50 patients who were diagnosed to have rheumatoid arthrits. They were diagnosed by using criteria described by American Rheumatology association,(6) X ray, Rheumatoid factor, Anti CCP and ANA tests. In group II, 26 patients were males and 24 were females, with age ranging from 38 to 74 years (mean age 55 years). Patients were selected in such a way that their socioeconomic, hygienic and nutritional status matched in both the groups, so that they should not have any influence over the levels of Malondialdehyde.

Chronic alcoholics, chronic renal failure patients, hypertensive, diabetic and infective patients were not included in the study.

Blood was taken in fasting conditions; around 5 ml of blood was collected in a test tube. Once the blood clotted at room temperature, centrifugation done at around 3000 revolutions per minute for 20 minutes. Samples which showed haemolysis were discarded.

UV-VIS Spectrophotometer was used to measure optical density.

Malondialdehyde concentrations in the serum were assessed by using the thiobarbituric acid assay method.[7] Basic principle of this assay method is that monodialdehyde and thiobarbituric combine to form a red coloured complex, which can be detected by UV-VIS Spectrophotometer at 535nm.

Results and Analysis

A total of 100 patients were included in the study, who were categorized in to group I and group II. In control group were 50 normal healthy subjects who volunteered for the study. In that, there were 30 males and 20 females. The second group comprised of rheumatoid arthritis patients. A total of 50 patients were there in this group, 26 males and 24 females (Table 1).

Table 1: Age and gender distribution

Subjects	Age range	Males	Females	Total subjects
Group I- Healthy control	30-60 years	30	20	50
Rheumatoid arthritis patients	38-74 years	26	24	50

The values with statistical significance (p value) and percentage increase or decrease of MDA levels in normal healthy group and Rheumatoid arthritis group were tabulated and compared (Table 2). The serum levels of monodialdehyde in group II of rheumatoid patients were 3.300 ± 0.450 nmoles/ml and it was 2.600 ± 0.490 in normal subjects group. On calculating 'p' value for both the groups, it was < 0.01. Hence it was significant statistically between both groups. There was 23.14% increase of monodialdehyde levels in rheumatoid patients when compared to normal healthy population group.

Table 2: Mean +/- SD values, "p" value and percentage variation in MDA levels (nano mols/ml) in two groups

Values	Group I- Control	Group II-RA
Mean +/- SD	2.600 ± 0.490	3.300 ± 0.450 nmoles/ml
'p' value	<0.01	Significant
Percentage variation	23.14%	significant

Discussion

Rheumatoid arthritis is a disorder of autoimmune origin involving multiple systems. The characteristic of pathogenicity of this disease is the production of multiple free oxygen radicals which in turn cause significant damage to cell membrane and its proteins and lipids resulting in cell death. Monodialdehyde is also one of the significant free oxygen radicals which cause cell membrane destruction.

In our study, MDA levels were significantly higher in RA patients as compared to normal healthy individuals ('p' value<0.01). Monodialdehyde is a byproduct of lipid peroxidation. MDA reacts with lysine residues to form immunogenic molecules which flare up the inflammatory process and thus causing cell damage by oxidative injury.

Monodialdehyde is a marker of amount of lipid peroxidation happening in the cells. In the present study there was a significant raise in the serum levels of monodialdehyde in patients with rheumatoid arthritis which shows a higher level of oxidative stress injury in the pathogenesis of rheumatoid arthrits. Alver et al,[8] in their study found increased MDA levels in RA serum and erythrocyte. Results of our study were comparable to other studies[9-12] which also showed raised levels of serum monodialdehyde in patients with rheumatoid arthritis.

Existing studies in the literature which are made on levels of serum monodialdehyde in patients with rheumatoid arthritis have demonstrated higher levels of serum monodialdehyde in these patients. These studies have also shown that monodialdehyde has a significant contribution towards progression of the disease in rheumatoid patients. One study has also shown that formation of monodialdehyde and acetaldehyde complex is highly elevated in patients with rheumatoid disease and form many antibody complexes which significantly destroy the synovium and joint cartilage, resulting in rapid progression of the disease process.[13]

Conclusion

Increased levels of Oxidative stress patients with rheumatoid arthritis is a result of formation of increased free radicals secondary to increased rates of peroxidation of lipids and polyunsaturated fatty acids. Assaying Malondialdehyde levels in the serum of patients with rheumatoid arthritis is a simple tool which helps in diagnosing and to know the disease activity status. It's a cost effective diagnostic tool which can be performed on outpatient basis. However, further studies are necessary to the status of other anti-oxidant markers and their therapeutic effects.

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