ROLE OF MALONDIALDEHYDE IN THE SERUM OF RHEUMATOID ARTHRITIS AND OSTEOARTHRITIS

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ABSTRACT

Objective: To measure malondialdehyde in order to determine oxidative stress in rheumatoid arthritis and osteoarthritis subjects and comparing them with healthy individuals.

Methodology Malondialdehyde estimation were done by using the UV-VIS spectrophotometer in the department of biochemistry SP medical college, Bikaner. Thiobarbituric acid assay method was used to estimate Malondialdehyde .

Results: A statistically significant elevation of MDA level in serum of rheumatoid arthritis (RA) and osteoarthritis (OA) subjects was seen ($p<0.0001$). The serum MDA level was also significantly increased in the subjects than in the controls. The serum MDA level was also significantly increased in the subjects than in the controls.

Conclusion: Oxidative stress is due to increased free radical production which is the main mechanism in the pathogenesis of of RA and OA.

Key Words: Reactive oxygen species, Oxidative stress, Lipid peroxides, Rheumatoid arthritis, Osteoarthritis, Malondialdehyde

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INTRODUCTION

Arthritis is inflammation of one or more joints. Arthritis literally means "joint inflammation" and describes over 100 conditions affecting joints and their surrounding tissues. Because the term does not describe the cause or type of joint inflammation, it is qualified with an adjective such as rheumatoid, osteo-, or psoriatic[1]. RA is an autoimmune disease with characteristic features of rheumatoid factor in serum[2], morning stiffness, inflammation, peripheral joints swelling, articular tissues destruction and deformed joint[3].

OA is a disease of synovial joints manifested by joint cartilage erosion, underlying bone remodeling, formation of osteophyte and Synovitis[4]. The age related changes in cartilage in OA include alterations in proteoglycan & collagen. Chondrocyte has a key role in the process on cellular basis.

At the sites of inflammation of joint increased free radical activity is associated with activation of neutrophils, phagocytosis by macrophages, which involve respiratory bursts phenomenon and uncoupling of variety of cellular redox systems. These process lead to ultimately increased peroxidation of unsaturated lipids of the membrane. The main mechanism behind the destruction of cell membrane and cell damage is the lipid peroxidation which occurs normally and continuously at low levels in all cells and tissues. These reactions are toxic to cell and membrane. Uncontrolled lipid peroxidation converts polyunsaturated fatty acids present in cell membrane to the primary product of lipid hydro-peroxides and to secondary metabolites such as malondialdehyde, causing cell injury and death via DNA strand breakage and membrane damage[5]. MDA is the important marker of Lipid peroxidation[6].

Arthritis is a chronic disorder without known aetiology. Disease activity by forming reactive oxygen species (ROS) and lipid peroxides play a vital role. In patients suffering from rheumatoid arthritis (RA) and osteoarthritis (OA) oxidative stress status are the hallmarks as observed recently. Measuring malondialdehyde in order to determine oxidative stress in RA and OA subjects and comparing them with healthy individuals was the objectives of the study.

METHODOLOGY

This study was conducted on 150 subjects aged between 40-70 years in the Department of Biochemistry, S.P. Medical college, Bikaner, Rajasthan. They were divided into Three groups.

They were randomly selected irrespective of their caste and creed. A thorough physical examination was carried out on all the patients. Routine hematological &

radiological investigation was also done. 50 cases selected from orthopedics OPD diagnosed by orthopedicians and 50 from Rheumatology OPD diagnosed by rheumatologists. The presence of RA and OA in patients was diagnosed by X- ray, rheumatoid factor, C-reactive protein, & antinuclear antibody test.

Inclusion Criteria: Normal nutritional habits with no supplements during the last three months included in the study. The females group in our study were in post-menopausal period or in pre post-menopausal period.

Exclusion criteria: None were alcoholic or smokers. Hypertension, diabetes, history of trauma to joints and history of anti-inflammatory drugs in the previous three months were excluded from the study.

The socio-economic status of both the groups were almost similar and thus, they had similar hygienic conditions, adequacy of nutrients and quality food intake. Therefore, any factor related to aforesaid conditions was ruled out to have any influence over the metabolism of Malondialdehyde (MDA) and reduced Glutathione (GSH).

5 ml fasting blood using disposable syringe from anticubetal vein was withdrawn and was transferred to clean dry test tube, slowly by the side of the tube after removing needle to avoid hemolysis.

The blood was allowed to clot at room temperature for 30 minutes. The serum was separated by centrifugation at 3000 revolution per minutes (rpm) for 15 minutes in the morning. Sample with signs of hemolysis were discarded. The optical density (OD) is measured by UV-VIS Spectrophotometer.

MDA concentration was estimated as reactive substances by a thiobarbituric acid assay method described by Buege and Aust (1978) [9]. This method quantifies lipid hydro-peroxides by measuring aldehyde break down product of lipid- peroxidation. Basic principle of the method is the reaction of one molecule of malondialdehyde and two molecule of thiobarbituric acid to form a red MDA- TBA complex, which can be measured at 535nm.

RESULTS

The present study was conducted on 150 subjects aged between 40-70 years of both gender. The study group was further divided into three groups. In RA group (n=50) 16 males and 34 females, in OA group (n=50) 19 males and 31 females and in control group 23 males and 27 females enrolled the study. (Table 1)

The serum MDA levels in the RA patients was 3.81±1.0 nmoles/ml and it was 3.27±1.153 nmol/ml in OA. In controls the value was (1.72±0.44 nmol/ml) (P<0.0001). Comparison of mean values of blood parameters in normal control subjects with Rheumatoid arthritis (RA) and Osteoarthritis (OA) is shown in figure 1.

DISCUSSION

RA and OA is characterized by increased markers of oxidative stress. Recent evidence suggests that human articular chondrocyte can actively produce ROS which are released during inflammation of the synovial membrane of synoviocyte. These ROS with oxidative activity play a key role in the chondrocyte catabolic program, being the mediators and effecters of cartilage damage.

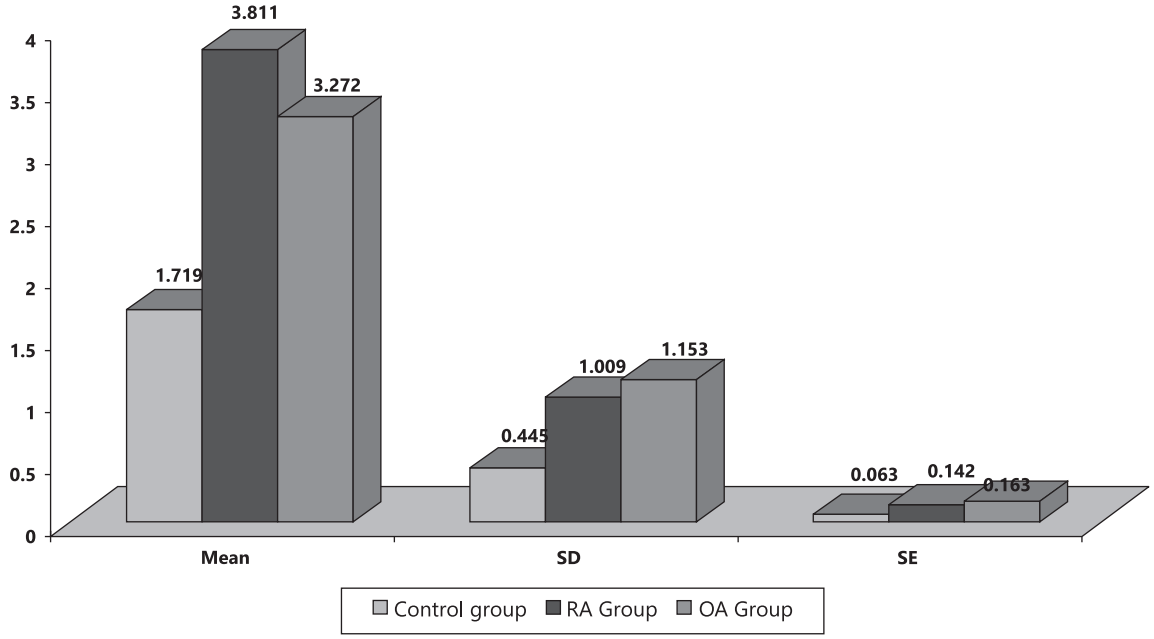
A chain reaction initiates the damaging effect of the process which provides continued supply of free radicals which in turn causes further peroxidation. It also leads to formation of complex mixtures of lipid hydroperoxide aldehydic end products such as MDA.

The present study showed significant increase in lipid Peroxidation product MDA. Since MDA is an index of lipid Peroxidation, its level was estimated in patients with RA as well as OA to estimate the extent of lipid peroxidation. MDA levels were found to be increased in both RA and OA patients than in healthy individuals, in-

Table 1: Age and gender distribution

Subjects	Age (40-70) (n=50)	Males	Females	Total subjects (n) in each group
Rheumatoid arthritis patients (RA)	40-49 = 13	5	8	Total Males= 16
	50-60 = 17	5	12	Total Females =34
	61-70 = 20	6	14	
Osteoarthritis patients (OA)	40-49 = 11	4	7	Total Males= 19
	50-60 = 17	6	11	Total Females =31
	61-70 = 22	9	13	
Healthy control	40-49= 10	4	6	Total Males= 23
	50-60 = 19	9	10	Total Females =27
	61-70 = 21	10	11	

Figure 1: Mean Serum MDA concentration (nmoles/ml) in RA subjects and OA subject with that of controls



dicating an increase in the process of lipid peroxidation in these patients. The results of present study of MDA concentration was similar to results obtained by previous studies [10-14] which suggested that serum MDA level in RA and OA patients increases significantly.

In this study, a significant correlation was observed when serum MDA level of RA and OA patients was compared with healthy controls. This study results were concordant with Gambhir et al[10], Mane et al[11] , Tiku et al[12], Shivani et al[13], Kartas et al [14], Maneesh et al[15], Amal Mohammad et al [16] and Manoj et al[17]. The increase in serum MDA level in RA and OA patients might be due to the excessive oxidative damage due to increased ROS.

CONCLUSION

Oxidative stress is due to increased free radical production which is the main mechanism in the pathogenesis of of RA and OA. Further research is required in this area to know the status of other antioxidant marker & about their beneficial therapeutic effects in these disorders.

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CONTRIBUTORS

SV conceived the idea, planned the study, and drafted the manuscript. SH helped acquisition of data and did statistical analysis. VRK drafted and critically revised the manuscript. All authors contributed significantly to the submitted manuscript.