ORIGINAL RESEARCH PAPER

Genetics

Volume - 7 | Issue - 3 | March - 2017 | ISSN - 2249-555X | IF : 4.894 | IC Value : 79.96

Significantly Enhanced MDA levels in Rheumatoid arthritis and Osteoarthritis cases as a measure of oxidative damage

KEYWORDS: Malondialdehyde, Rheumatoid arthritis, Osteoarthritis

Dr. Arshia Fatima

Department of Genetics, Osmania University 500007.

Dr. Mohd Ishaq

Department of Genetics, Osmania University 500007, Salar-E-Millat Research Centre for cellular and Molecular Medicine, PEH, DCMS, Hyderabad India.

ABSTRACT The main objective of the study was to investigate the ongoing free radical induce damage in Rheumatoid arthritis and Osteoarthritis patients by measuring the Malondialdehyde (MDA) level with a view to gain insight into the pathogenesis of these disorders. A total of 131 RA patients and 47 OA patients were studied along with 95 healthy controls were included in the study. The Mean MDA level in RA and OA patients were 509.20 ± 16.31 nmol/dl and 514.18 ± 25.23 nmol/dl respectively. These levels were significantly higher than that in the control group i.e 205.78±9.87 nmol/dl. The significance of increased lipid peroxidation as assessed by MDA level in these two clinical conditions has been discussed.

CONCLUSION: The MDA levels were significantly increased in both RA and OA patients indicating the ongoing free radical production. The increased MDA levels suggest possible evidence of free radical production and damage to cellular membranes, proteins and DNA. This may be an important mechanism in the pathogenesis of these arthritic disorders.

INTRODUCTION

Arthritis" involves joint inflammation characterized by swelling, stiffness redness of overlying skin, pain and decreased range of motion of the joints. The different forms of arthritis are Rheumatoid arthritis and Osteoarthritis [1]

RA is an autoimmune disorder where there is inflammatory damage to the lining of the joint, called the "synovium," resulting in pain and swelling and loss of function in the joints mostly in hands and feet [2]. Contrary to this Osteoarthritis can cause joint pain and stiffness affecting mostly the spine and the weight-bearing joints (the knees and hips) [3].

RA is the most common inflammatory arthropathy worldwide and affects 0.75% of Indian population [4]. It is a disease of an age-related incidence. It is present in all ethnic populations and at all ages, and its prevalence increases with age[5]. The disease follows a chronic course and the outcome may be unsatisfactory despite treatment. This is because, the etiology of RA is not properly known and the pathogenesis remains to be fully elucidated [6, 7].

Oxygen derived free radicals have been implicated in the causation of RA [8,9]. This oxidative stress may contribute to the cyclic self-perpetuating nature of rheumatoid inflammation. It is important that, the predominant reaction in RA is enormous cellular proliferation rather than cellular destruction [10].

The biochemical studies shows that RA patients showed a marked increase in ROS formation, lipid peroxidation, protein oxidation leading to enhance level of MDA compare to normal [11]. The age at onset of RA influences prognoses and helpful in treatment of the disease. Thus MDA is one of the prognostic marker in the disease progression[12].

Increased serum MDA levels in RA suggest the role of free radicals in the pathogenesis of this inflammatory arthropathy and support the need for further studies assessing the therapeutic role of free radical scavengers in RA [13]. Overproduction of free radicals by inflammatory processes in RA causes oxidative injury and damage to antioxidant defense system in RA patients. The elevated lipid peroxidation in plasma in the present study, indicated by elevated MDA levels can be related to a compensatory defense system in RA. Thus, MDA levels in RA could be used as biochemical marker of disease activity and monitor treatment response.

Osteoarthritis (OA) is other clinical condition that cause pain and physical disability in patients. Although OA is considered as a global disease affecting all joint tissues cartilage degradation is the end point [14]. The degradation of cartilage results from the combination of mechanical stress and biochemical factors, mainly metalloproteinases and ROS. The activity of ROS is balanced by enzymatic and non-enzymatic antioxidants,that act by inhibiting oxidative enzymes, scavenging free radicals or chelating ion metals [15, 16].

There are report of a strong association between osteoarthritis and advancing age. The time between symptom onset and physician diagnosis is a period when people with osteoarthritis can make lifestyle changes to reduce pain, improve function and delay disability[17]. There is over expression of proinflammatory agents such as nitric oxide, interleukin 1 (IL-1), and tumor necrosis factor (TNF) α in chondrocytes and joint stromal cells on cellular levels at the time of the onset of disease[18].

In the present study we estimate the MDA level in both RA and OA patients and compare with normal controls with respect to gender and age at onset .

MATERIAL AND METHODS:

`A total of 131 RA patients and 47 OA patients were taken from local Rheumatology centre of Hyderabad under supervision of Rheumatologist. The 97 controls samples were randomly collected from general population. MDA is used as an index for determining the lipid peroxidation of cell membrane as it is stable product of lipid peroxidation. It was estimated as per the procedure described by Nadiger etal 1987 method [19]. The basic principle of the test is the reaction of MDA with thio-barbituric acid (TBA) to form pink colour compound. The optical density of this compound is taken to estimate the serum MDA level.

RESULT AND DISCUSSION

The mean MDA level in the sera of RA and OA patients were 509.20±16.31* nmol/dl 514.18±25.23* compared to 205.78±9.87* nmol/dl in normal control samples. Thus statistically significant difference was noted in the mean MDA level of RA and OA patients compare to those in controls (Table-1). These results support the role of oxidative stress induced damage in these two clinical conditions. Our results are concordant with those of previous studies [20,21]. This indicate free radical induce tissue damage in these arthritic conditions.

Volume - 7 | Issue - 3 | March - 2017 | ISSN - 2249-555X | IF : 4.894 | IC Value : 79.96

The mean MDA levels in RA patients and control samples with respect to gender is depicted in Table 2. It was comparable in both male and female cases of rheumatoid arthritis. The mean MDA level in RA female patients was 511.58 ± 18.65 nmol/dl and in male counterparts it was 500.45 ± 33.98 nmol/dl.

However in OA the mean MDA level was considerably higher in male 641.02 ± 68.52 nmol/dl compare to their female counterpart 488.16 ± 25.42 nmol/dl. It is likely that the increasing level shows positive correlation with long duration of disease.

The mean MDA levels do not show specific pattern of variation with advancing age at onset in RA patients. However in OA patients there is an increase in mean MDA levels with increasing age at onset from 41-50 years range (Table-3). The elevated levels of inflammatory marker is associated with the development of erosions in RA patients which is related with age at onset[22].

Since male patient to develop RA require greater genetic susceptibility it may be likely that a defective scavenging system may lead to oxidative tissue damage. The possible defect may exist in the form of a single nucleotide polymorphism in SOD or catalase coding genes which may reduce gene activity [23,24]. The elevated free radical generation in inflamed joints have been implicated in RA. Serum MDA levels may appear to be a sensitive marker of inflammation in chronic auto immune disorder and helpful in understanding the inflammation at cellular level.

Table 1 : Mean MDA Levels in RA and OA cases

Category	Total	Mean S±.E
RA	131	509.20±16.31*
OA	47	514.18±25.23*
Control	95	205.78±9.87*

*p< 0.05

Table 2: Mean MDA Levels in RA and OA cases with respect to sex

Category	Total	Number	Male Mean ±.S.E	Number	Female Mean ±S.E
RA	131	28	500.45±33.98	103	511.58±18.65
OA	47	8	641.02±68.52	39	488.16±25.42
Control	95	47	215.49±16.00	50	198.67±11.32

Table 3: Mean MDA Levels in RA and OA patients with respect to age ononset

Class Interval	Number	RA Mean ± .S.E	Number	OA Mean ± S.E
10-20	9	562.67±88.60	---	---
21-30	15	489.77±48.39	2	512.82±128.20
31-40	28	473.90±38.49	7	494.50±43.59
41-50	34	542.99±31.47	16	524.83±57.40
51-60	34	516.60±28.12	16	484.77±28.04
61-70	7	430.40±49.87	6	587.61±88.22
71-80	4	496.79±92.06	---	---
	131	509.20±16.31	47	514.18±25.23

REFERENCES

1. Pirotta M. Arthritis disease - the use of complementary therapies. Aust Fam Physician. 2010; Sep;39(9):638-40. Review.
2. Deborah P.M. Epidemiology of rheumatoid arthritis: determinants of onset, persistence and outcome. Clin. Rheum. 2002;16:707–722.
3. Guilak F, Fermor B, Keefe FJ, Kraus VB, Olson SA, Pisetsky DS, et al. The role of biomechanics and inflammation in cartilage injury and repair. Clin Orthop. 2004; 423:17e26
4. Malaviya AN, Kapoor SK, Singh RR, Kumar A, Pande I. Prevalence of rheumatoid arthritis in the adult Indian population. Rheumatol Int. 1993; 13(4):131-4
5. Rasch EK, Hirsch R, Paulose-Ram R, Hochberg MC. Prevalence of rheumatoid arthritis in persons 60 years of age and older in the United States: effect of different methods of case classification. Arthritis Rheum. 2003; 48: 917-926. 10.1002/art.10897.
6. Henrotin Y, Kurz B, Aigner T. Oxygen and reactive oxygen species in cartilage degradation: friends or foes? Osteoarthritis Cartilage. 2005 ;13: 643-654.
7. Mirshafiey A, Mohsenzadegan M. The role of reactive oxygen species in immunopathogenesis of rheumatoid arthritis. Iran J Allergy Asthma Immunol. 2008; 7: 195-202.
8. Jaswal S, Mehta HC, Sood AK, Kaur J. Antioxidant status in rheumatoid arthritis and role of antioxidant therapy. Clin Chim Acta . 2003; 338: 123-129.
9. Mahajan A, Tandon VR. Antioxidants and rheumatoid arthritis. J Indian Rheumatol Assoc . 2004; 12: 139–142.
10. Nurcombe HL, Bucknall RC, Edwards SW. Neutrophils isolated from the synovial fluid of patients with rheumatoid arthritis: priming and activation in vivo. Ann Rheum Dis. 1991; Mar; 50(3):147-53.
11. Mateen S, Moin S, Khan AQ, Zafar A, Fatima N. Increased Reactive Oxygen Species Formation and Oxidative Stress in Rheumatoid Arthritis. 2016; PLoS One 11: e0152925.
12. García-González A, Gaxiola-Robles R, Zenteno-Savín T Oxidative stress in patients with rheumatoid arthritis. Rev Invest Clin. 2015; 67: 46-53.
13. Chaturvedi V, Handa R, Rao DN, Wari JP; "Estimation and significance of serum and synovial fluid MDA levels in RA". Ind J med Res. 1999; 109:170 -174.
14. Ishiguro N, Kojima T, Poole AR. Mechanism of cartilage destruction in osteoarthritis. Nagoya J Med Sci 2002; 65:73e84
15. Maneesh M, Jayalekshmi H, Suma T, S. Chatterjee S, Chakrabarti A, Singh T.A. Evidence for oxidative stress in osteoarthritis. Indian J Clin Biochem, 20 (1) (2005), pp. 129–130.
16. Amal Mohamad El Barbary, Manal Aly Abdel Khalik, Alaa Mohamad Elsalawy et al. Assessment of lipid peroxidation and antioxidant status in Rheumatoid arthritis and Osteoarthritis, The Egyptian Rheumatologist, Elsevier. 2011; 33 (4): 179-185.
17. Gignac M, Davis AM, Hawker G, et al. "What do you expect? You're just getting older": A comparison of perceived osteoarthritis-related and aging-related health experiences in middle- and older-age adults. Arthritis Care and Research 2006; 55(6): 905-12.
18. Kaneko S, Satoh T, Chiba J, et al. Interleukin-6 and interleukin-8 levels in serum and synovial fluid of patients with osteoarthritis. Cytokines Cell Mol Ther. 2000; 6:71–9.
19. Nadiger HA, Mathew CA, Sadasivudu B. Serum malanodialdehyde (TBA reactive substance) levels in cigarette smokers.Atherosclerosis. 1987 ; Mar;64(1):71-3.
20. Kalavacherla US, Ishaq M, Rao UR, Sachindranath A, Hepsiba T. Malon di aldehyde as a sensitive marker of inflammation in patients with RA, J Assoc Physicians India. 1994; Oct; 42(10):775-6.
21. Mishra R, Singh A, Chandra V, Negi MP, Tripathy BC, et al. A comparative analysis of serological parameters and oxidative stress in osteoarthritis and rheumatoid arthritis. Rheumatol Int. 2012;
22. Pease CT, Bhakta BB, Devlin J, Emery P: Does the age of onset of rheumatoid arthritis influence phenotype? A prospective study of outcome and prognostic factors. Rheumatology (Oxford). 1999, 38: 228-234.10. 1093/rheumatology/38.3.228.
23. Vijayakumar D. Suresh K, Manoharan S. Lipid peroxidation and antioxidant status in blood of RA patients, Ind J Clin Biochem, 2006; 21 (1): 104-8
24. Afonso V, Champy R, Mitrovic D, Collin P, Lomri A. Reactive oxygen species and superoxide dismutases: role in joint diseases, joint Bone Spine 2007; 74: 324-329