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Research Article

RESPONSE OF FERRITIN TO OXIDATIVE STRESS IN RHEUMATOID ARTHRITIS

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ABSTRACT

Objective: Rheumatoid arthritis (RA) has been categorized as a disease of connective tissue and an autoimmune disease but was not, until recently recognized as a disease due to oxidative stress. Ferritin, an iron binding protein is involved in intracellular storage of iron pool, which play a central role in the maintenance of delicate intracellular iron balance. The ability of cells to induce rapid ferritin synthesis prevents the effect of free radical damages to cellular components. The objective of the current study is to evaluate the serum ferritin level and its response to oxidative stress in rheumatoid arthritis.

Methods: The study group included 50 patients with RA and 50 age and sex matched healthy controls. The serum ferritin, albumin, hsCRP, Malondialdehyde (MDA) and Vitamin C levels were estimated.

Result: Serum ferritin, hsCRP, and MDA levels were found to be significantly increased in RA patients, whereas Vitamin C level was significantly decreased in RA patients when compared to controls.

Conclusion: The study conclude that rise in serum ferritin, an acute phase reactant is due to inflammatory response to the rising oxidative stress in RA.

Keywords: Rheumatoid arthritis, Ferritin, Malondialdehyde (MDA)

INDRODUCTION

Ferritin a key protein of iron metabolism is capable of dual function in iron detoxification and iron storage present in serum and biological fluids [1]. It is a multimeric protein consists of 24subunits of types H and L which surrounds a cavity in which iron can be stored in a readily available non toxic form [2]. The synthesis of ferritin is regulated by cytokines at various levels of protein synthesis, during cellular differentiation, proliferation and inflammation. The expression of ferritin is also regulated by hormones, growth factors, second messengers and hypoxia [3]. Both oxidant and antioxidants response inducers regulate ferritin gene transcription [4]. During certain conditions the disregulation of ferritin cause this intracellular iron storage protein to act as pro-oxidant [5]. Therefore the present study aims to determine the ferritin level in RA and its response to oxidative stress.

MATERIALS AND METHODS

The study was conducted at SRM Medical College Hospital and Research Centre, kattankulathur. The study consisted of two groups; Group I include 50 patients with Rheumatoid arthritis was compared with Group II which include 50 age and sex matched healthy controls. The diagnosis of RA was based on 1988 revised American Rheumatoid Association (ARA) criteria. Venous blood drawn from the subjects following 12-14 hours fasting. Serum ferritin estimated by ferritin EIA, Bio research Inc, hsCRP by immunoturbidometry method, MDA by TBARS method [6], Vitamin C by 2,4-dinitrophenylhydrazine method using Spectrophotometrically [7]. The study was approved by the institutional ethical committee. An informed consent was taken from all the participants. Statistical analysis was performed using SPSS software version 17. Student's t-test was used for comparison of qualitative data and the p value <0.05 is considered statistically significant. Data were expressed as mean±SD.

RESULTS

Table 1 shows the comparison of ferritin and other parameters of oxidative stress and antioxidant levels between RA patients and control. The serum ferritin, hsCRP and plasma MDA levels were significantly increased in RA patients when compared to control. Whereas the level of Vitamin C was found to be significantly decreased ($p<0.05$) in RA patients than controls.

Table 2 shows the correlation between serum ferritin and oxidative and antioxidant parameters. Serum ferritin showed significant positive correlation with hsCRP and plasma MDA ($r = 0.84$ and $r = 0.82$ respectively) and significant negative correlation with vitamin C ($r = -0.46$) among the RA patients.

Table 1: Levels of serum Ferritin and parameter of oxidative –antioxidant system seen in rheumatoid arthiritis and healthy controls.

Parameters	RA (Group I) (n=50) Mean±SD	Control (Group II) (n=50) Mean±SD	p-value
Ferritin (ng/dl)	213±0.30	146±0.22	<0.001**
MDA (nmol/ml)	16.7±1.36	6.2±0.9	<0.001**
Vitamin C (mg/dl)	4.6±0.9	8.8±2.1	<0.05*
hs-CRP (ng/L)	6.64±3.2	0.74±0.3	<0.001**

Data are expressed as Mean±SD. p value <0.05 is considered as significant. (* p<0.05; ** p<0.01)

Table 2: Correlation of serum ferritin between oxidative and antioxidant parameters.

Parameter	MDA	vitamin C	hsCRP
Ferritin	r = 0.82 (P=0.01*)	r = -0.46 (P=0.02*)	r = 0.84 (P=0.001**)

Correlation is significant at p value <0.05; (* p<0.05, ** p<0.01)

DISCUSSION

RA is a chronic progressive autoimmune disorder characterized by symmetric erosive synovities and also shows multisystem involvement. Reactive oxygen species are clearly involved in the pathogenesis of the disease [8].

Ferritin a ubiquitous and specialized protein is involved in the intracellular storage of iron in serum and other biological fluids and its secretion processes are still unclear and the ability of cells to induce rapid ferritin synthesis prevents the effects of free radical damages to cellular components. Free iron has the capacity to participate in oxygen free radical formation via fenton chemistry [9]. Ferritin plays a central role in the maintenance of this delicate intracellular iron balance [10]. However only recently critical evaluation of the role of ferritin in protection from oxidative stress has began. Several studies have indeed suggested that ferritin protects against oxidative stress.

Inflammation and oxidative stress plays a important role in ferritin expression. During the acute phase response the pro-inflamatory cytokines such IL-1B and TNF-α increase the synthesis of H and L subunits of ferritin through an increased translation of performed ferritin mRNA [11].

IL-B induces ferritin gene expression by translational control of its mRNA, but this inflammatory induction of ferritin is different from Iron-dependant ferritin gene expression in that its requires the background presence of some cellular iron. In the molecular level it is not clear why ferritin synthesis is increased under inflammatory conditions. Hypothetically higher amount of ferritin may trap more body iron and protects against worsening of the infection [12]. In the present study evaluation of ferritin level with subsequent increase in plasma MDA level and decrease in vitamin C level indicates the association between serum ferritin and oxidant status. And furthermost significant correlation between serum ferritin and hsCRP level adds to its association with inflammatory reaction. Thus the finding suggests that moderately high serum ferritin is not just a marker of iron store but more an indicator of inflammation as well as other factor like oxidative stress. The study concludes that rise in serum ferritin in RA is solely an inflammatory response to minimize oxidative stress.

Conflict of interest: None

REFERENCE

1. Grisele Zandman, Goddard, Yehuda shoenfeld. Ferritin in autoimmune disease. Autoimmunity Reviews 6, 457-463 2007.
2. Halliwell B, and Gutteridge J.M.C. The free radical in biology and medicine. Biochem.J. 219,1-14, 1984.
3. Oberg BP, McMenamin E, Lucas E etal. Increased prevalence of oxidative stress and inflammation in patients with moderate to severe chronic kidney disease. Kidney Int, 65; 1009-1016; 2004.
4. Redid AS. Bollineni Js, Basker s, Nimmagadda VR, Basker M. Serum ferrritin and oxidative stress in patients undergoing hemodialysis. Nephron; 86:202-203; 2000
5. Leferve G, Beijean-Leymarie M, Beyerle F, Gustor JP, Therond P. Evaluation of lipid peroxidation by measuring theobarbituric acid reactive substances. Ann Biol clin 1998 56(3):305-319.
6. Kucera M, Racek J, Holecek V. Free oxygen radicals and rheumatic disease. Vnitr Lek, 42(5):320-33; 1996.
7. Arnet TC, Edworthy SM, Bloch DA, Mc Shane DJ, Fries JF, Cooper NS etal. The American rheumatism association 1987 revised criteria for classification of rheumatoid arthritis. Arthritis Rheum, 31:315-24; 1988.
8. Kalantar-Zadeh, Rodriguez RA, Humphreys MH. Association between serum ferritin and measures of inflammation, nutrition and iron in hemodialysis patients. Nephrol dial transplant,19:141-149; 2004.
9. Mc cormick DB, Green HL. Vitamins In: Burtis CA, ashwood EK, eds. Tietz textbook of Clinical chemistry W.B.Saunder; Philadelphia,1994:1313-1314.
10. Cimen MY, cimen GB, Kaemaz M, Ozturk Hs, Yosgancioglu R, dark J. Oxidant-antioxiant status of erthyrocytes from patients RA.clin Rheumatol, 19(4)275-77; 2000.
11. Chaturvedi V, Handa r, Rao DM, Wali JP. Estimation and significance of serum and synovial fluid malondialdehyde levels in RA. Ind J Med Res, 109:170-4; 1999
12. Kaneda H. A study on the lipid peroxide and its scavenging enzyme in RA. Nippon seikeigeka Gakki zusshi , 56(5):387-97; 1982.
13. Maithreyi r, Janani AV, Krishna r, Shweta A, rufus ranjit Singh Edwin, Surapareni Krishna Mohan. Erythrocyte Lipid Peroxidation and antioxidants in chronic alcoholics with alcoholic liver disease. Asian J pharma Clin Res, vol 3 (3) 2 ; 181-185; 2010.
14. Swadesh Kishore Shrivastava, Amit Kumar Mishra, Natasha Jain, Shiv Kumar Mishra, Archana Tiwari. An elaborated view of RA cycle, latest with highly specific diagnostic techniques and the effect of free radicals and antioxidant on rheumatoid arthritis. Asian J pharma Clin Res.Vol 5(2)2-6;2012.