

JOURNAL OF CLINICAL AND DIAGNOSTIC RESEARCH

How to cite this article:

MOUJERLOO M. Variations Of Lipid Peroxidation And Superoxide Dismutase Activity Due To Haemodialysis In Gorgan. Journal of Clinical and Diagnostic Research [serial online] 2010 Aug [cited: 2010 Aug 20]; 4:2763-2767.

Available from

http://www.jcdr.net/back_issues.asp?issn=0973-709x&year=2010 &month= Aug &volume=4&issue=3&page=27632767 &id=1120

ORIGINAL ARTICLE

Variations Of Lipid Peroxidation And Superoxide Dismutase Activity Due To Haemodialysis In Gorgan

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ABSTRACT

Background: Free radicals are formed in all living organisms during normal cell metabolism. Patients with chronic renal failure who are regularly dialyzed are candidates for free radical damage. The aim of this study was to evaluate the variations of lipid peroxidation and erythrocyte superoxide dismutase due to haemodialysis in Gorgan.

Method: The sampling procedure was the purposive sampling of 22 patients (age 43.54 ± 9.21 years of old) with chronic renal failure (CRF) disease who were haemodialysed at the 5th Azar hospital of the Gorgan dialysis center (from September 2007 to February 2008) and 22 age and sex matched healthy controls (43.77 ± 9.33 years of old) were recruited for this study. This study was a clinical trial.

Results: Plasma lipid peroxidation levels showed significant differences between the predialysis and the control group ($P < 0.001$). They were found to be increased in the post-dialysis group when compared with the predialysis and the control groups ($P < 0.001$). Erythrocyte superoxide dismutase levels were found to be decreased in the post-dialysis group when compared with the predialysis and the control groups ($P < 0.001$). There was also significant difference between its levels in the control and the predialysis groups ($P < 0.001$). Erythrocyte superoxide dismutase levels were lower in the dialysis group than in the control group ($P < 0.001$).

Conclusions: The significant differences of the erythrocyte superoxide dismutase levels between the pre- and post-dialysis groups may be related to the loss of this antioxidant through membranes during the dialysis process and the decreased superoxide dismutase levels may also be related to the increase of lipid peroxidation in haemodialysed patients. This situation may play an important role in the development of atherosclerosis in these groups.

Key Words: Haemodialysis- Lipid Peroxidation- Superoxide Dismutase

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Introduction

Free radicals are highly reactive molecules generated by biochemical redox reactions that occur as a part of normal cell metabolism and in the course of free radical mediated diseases such as cancer, diabetes mellitus, cardiovascular diseases and renal diseases [1]. Free radicals are

eliminated from the body by their interaction with antioxidant enzymes such as glutathione peroxidase, superoxide dismutase, catalase, etc. Patients with chronic renal failure, including those receiving regular long-term haemodialysis, have a high incidence of premature

cardiovascular disease. Oxidative stress which occurs when there is excessive free radical production or low antioxidant levels, has recently been implicated as a causative factor in atherogenesis [2]. Free radicals may cause lipid peroxidation and may damage macromolecules and the cellular structure of the organism, the endothelium and erythrocytes. Some studies have shown that haemodialysis is connected with increased free radical production [3]. Cardiovascular disease is one of the major cause of mortality in haemodialysed patients with chronic renal failure. Increased lipid peroxidation and the depletion of antioxidants may contribute to the increased risk of atherosclerosis[4]. This study was designed to determine the variations of lipid peroxidation (the level of lipid peroxidation expressed as malondialdehyde(MDA)) and erythrocyte superoxide dismutase due to haemodialysis in Gorgan.

Material and Methods

The sampling procedure was purposive sampling which carried out on 22 haemodialysis patients with average age 43.54 ± 9.21 years (range 21-55). The mean length of dialysis for each patient was 3.95 ± 0.14 hrs with an average of 2.27 ± 0.45 times a week. Neither of them received antioxidant medicines and foods. The patients were chosen (14 males and 8 females) from among the patients who were referred to the department of haemodialysis at the 5th Azar hospital at the Gorgan University of Medical Sciences (from September 2007 to February 2008) and also, 22 healthy people (14 males and 8 females) for comparing of the patients with them were chosen (mean age 43.77 ± 9.33). Blood samples were obtained from the patients just before and after the process of dialysis and from the control group in heparinized tubes. Plasma was separated as soon as the blood was taken. Urea, creatinine, lipid peroxidation (the level of lipid peroxidation expressed as malondialdehyde(MDA)) and erythrocyte superoxide dismutase(SOD) levels were determined for haemodialysed patients

before and after the dialysis process and for the control group by using the laboratory kit spectrophotometry technique in the laboratory of Biochemistry (faculty of medicine). Plasma malondialdehyde was determined by the Kei Satoh method [5]. Erythrocyte SOD was determined by the Woolliams [6] method. This study was a clinical trial. The findings were analysed by the SPSS-10 software and by the Student's T test analytical method (limited samples). P-values lesser than 0.05 were considered to be statistically significant.

Results

As shown in [Table/Fig 1], the average and the standard deviation of plasma urea and creatinine after the dialysis process were 55.68 ± 7.96 mg/dl and 1.96 ± 0.45 mg/dl respectively, which showed a meaningful reduction in their concentration after the haemodialysis was done ($P < 0.001$).

(Table/Fig 1) The mean and standard deviation of plasma urea, creatinine, malondialdehyde and erythrocyte superoxide dismutase before and after dialysis.

Test	pre-dialysis	post-dialysis	control	P-value
Number of subjects	22	22	22	-
Urea (mg/dl)	123.54 ± 8.51	55.68 ± 7.96	26.37 ± 4.83	<0.001
Creatinine (mg/dl)	15.88 ± 3.07	1.96 ± 0.45	1.08 ± 0.29	<0.001
Malondialdehyde (nmol/ml)	1.27 ± 0.23	2.32 ± 0.38	0.98 ± 0.17	<0.001
Superoxide dismutase (U/g Hb)	1019 ± 20.06	951.4 ± 17.71	1402.68 ± 18.38	<0.001

The average and the standard deviation of plasma malondialdehyde showed significant differences between the pre-dialysis and the control group ($P < 0.001$). Its levels were significantly increased in the post-dialysis group when compared with the pre-dialysis and the control groups ($P < 0.001$, $P < 0.001$). The average and standard deviation of the erythrocyte activity of superoxide

dismutase (SOD) was significantly decreased in the post-dialysis group when compared with the pre-dialysis and the control groups ($P < 0.001$, $P < 0.001$). It also showed significant differences between the pre-dialysis and the control groups ($P < 0.001$).

Discussion

There are varying reports on the changes in the plasma lipid peroxidation and the erythrocyte antioxidant enzyme levels due to haemodialysis. Some of the studies showed an increase, while some others showed a decrease. There are a few reports which describe the differences in the plasma lipid peroxidation and the erythrocyte superoxide dismutase levels between healthy controls and patients on dialysis therapy. Oxidative stress has been described in a number of diseases which are associated with hemodialysis and in those with an increase in the production of lipid peroxidation with respect to healthy subjects [7]. Canestrari et al [8] reported that the levels of plasma malondialdehyde in haemodialysed patients were higher than those in healthy controls. The study of Samouilidou et al [9] on 31 haemodialysis patients and 17 controls showed that plasma malondialdehyde levels of haemodialysis patients were increased in the predialysis group when compared with those in the post-dialysis group. But the levels of plasma malondialdehyde were higher in control groups when compared with the post-dialysis group. Ozden [10], Taylor [11], Toborek [12], Loughrey [2], Balashova [13] and Ferretti [14] et al reported that the levels of plasma malondialdehyde in haemodialysis patients were increased when compared with the control groups. In our study, we determined the levels of plasma malondialdehyde in haemodialysis patients before and after the dialysis process. Our results showed a significant increase of plasma malondialdehyde levels in the post-dialysis group when compared with those of the pre-dialysis group ($P < 0.001$). There was significant difference between the levels in the dialysis group

(pre-, post-) and in the control group ($P < 0.001$, $P < 0.001$). Our results are in agreement with the groups mentioned, in that the plasma levels of malondialdehyde in haemodialysis patients is significantly different from that of controls. Oxidative damage can be caused by the imbalance between the production of free radicals and by the countering effect of the various antioxidant enzymes. Some studies showed that the activities of antioxidant enzymes change in haemodialysis patients due to the dialysis process. There are varying reports on the erythrocyte activities of the enzyme superoxide dismutase. Durak [15], Baanefont-Rouselut [16], Mimic-oka [17] and Weinstein et al [18] reported no change in the levels of the erythrocyte superoxide dismutase enzymes due to haemodialysis. The study of Balashova et al [13] showed decreased activity of the erythrocyte superoxide dismutase enzyme in haemodialysis patients

Salamunic et al [19] reported that the mean catalytic concentrations of superoxide dismutase were increased in patients before haemodialysis when compared with the control values. The mean catalytic concentrations of superoxide dismutase returned to the control range. Kose et al [20] reported an increased erythrocyte superoxide dismutase activity in the post-dialysis group when compared with the pre-dialysis group. But there was a decrease of this enzyme in the post-dialysis group when compared with the control group.

In our study, we found the significant reduction of erythrocyte superoxide dismutase levels in the post-dialysis group when compared with those of the predialysis group ($P < 0.001$). Its levels were also found to be significantly reduced in the pre-dialysis group when compared with those of the control group ($P < 0.001$). The results of our study show the significant difference of antioxidant enzymes between the pre and post-dialysis groups, which is thought to be related to the loss of antioxidant enzymes through the membranes and the decreased

antioxidant enzymes may be related to the increase of lipid peroxidation in haemodialysed patients. This situation may play a role in the development of atherosclerosis in haemodialysed groups. The diagnosis of myocardial ischaemia is difficult in haemodialysis patients since they are not able to perform adequate exercise tests due to limited exercise tolerance. It is particularly useful for detecting acute myocardial infarction in chronic renal failure haemodialysis patients which can prevent sudden cardiovascular abnormality and sudden silent myocardial infarction in these patients [21]. This study provides evidence that increased lipid peroxidation in haemodialysed patients is related to the dialysis process treatment rather than to the disease itself. For this reason, new approaches in dialysis membranes and haemodialysis techniques, the use of different exogenous supplementations of antioxidants and the removal of reactive oxygen species are important in the improvement of the life qualities of the haemodialysis patients..

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