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Research Article

To study the oxidative stress in haemodialysis. Role of inflammation

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ABSTRACT

Oxidative stress and inflammation has been demonstrated in haemodialysis patients. Chronic renal failure is associated with hypertension, increased glycation of proteins, insulin resistance, proteinuria, ca rdiovascular diseases, anaemia, and hypothyroidism. In the present study we study the oxidative stress and haemodialysis, the role of inflammation. The present study was done at Fathima Institute of medical Sciences, Kadapa, India. 30 patients were who are under haemodialysis and 19 are normal healthy subjects were taken in this study. The present study shows that increase in oxidative stress markers and decreased antioxidant defence in HD patients, and inflammation plays a significant role in that. The fac tors age, iron over load, diabetes were not important factors in these patients. Our results suggest that the prevention and the treatment of inflammatory disease is of high priority in patients who are on HD.

Keywords: Inflammation; Lipid profile; Oxidative stress; TBARS; Ubiquinol.

INTRODUCTION

Haemodialysis was one of the most common procedures performed in U.S. hospitals in 2011 occurring in 909,000 stays. This was an increase of 67 percent from 1997.when there were 473,000 stays. It was the fifth most common procedure for patients aged 46–64 years. (Barany P, Divino JC, et al., 1997)

ROS are free radical in nature. Free radical are highly reactive and are capable of damaging almost all type of biomolecules like proteins, lipids, carbohydrates, nucleic acid. ROS are very unstable, short lived and highly reactive molecules. They react with lightning speed with adjacent molecules causing extensive cellular damage. ROS are highly reactive and are capable of damaging every part of the cell and every biomolecule in the living system. (HaverkateF, et al., 1997)

Most of the products of lipid peroxidation are unstable e.g. carbonyls, esters, alkanes, alkenes, 2-alkenal, 2,4-alkadienal and MDA. Of these malondialdehyde is the most extensively studied and is used as a biochemical markers for the assessment of lipid peroxidation. MDA and other aldehydes react with thiobarbituric acid and produce red coloured products namely Thiobarbituric acid reactive substances (TBARS) which can be measured calorimetrically.

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The mitigate the harmful effect of free radicals the aerobic cells have developed antioxidant defence mechanisms. Antioxidants may be considered as the scavengers of free radicals. The antioxidant enzymes are glutathione peroxide, Superoxide Dismutase, antioxidant vitamin are Vit E, Vit C, antioxidant minerals are copper, Zinc, and selenium. The status of antioxidant defence mechanism in renal disease with diabetes is very contradictory as both increases and decreases. (Bergstrom J., 1995; Yeun JY.,2000; Zimmermann J.,1999)

Oxidative stress factors such as inflammation, age, diabetes mellitus, and iron over load are not elevated in HD patients. This study aims to evaluate serum lipid peroxidation markers, malondialdehyde (an oxidant), lipoproteins and antioxidants in haemodialysis patients with the role of inflammation.(Abuja PM, Albertini R.,2001;Abul-Ezz SR.,1991).

Materials and Methods

The Present study was done in the department of Biochemistry, Fathima Institute of Medical Sciences Kadapa. In this study total number of patients divided into 2 groups.

1. 30 haemodialysis patients.
2. 30 control group subjects.

The data were collected in a prescribed proforma and they were completed. Individual having history of chronic renal failure and taking treatment with oral drugs or taking haemodialysis treatment were considered as patients. The controls were healthy individuals, without history of renal disease, diabetic, hypertensive, non- smokers and non-alcoholics.

The analysis of plasma lipid profile by routine method. Plasma albumin were determined immune nephelometric method. Plasma CRP levels were determined by assay method. serum ferritin levels were measured by immune assay method. Plasma TBARS were measured by using the method of fluorometry. Plasma levels of AOPP and vitamin -C were measured by spectrophotometry.α-tocopherol and Ubiquinol were determined by HPLC procedure. Superoxide dismutase were determined by using spectrometry.

Statistical analysis.

All values of patients and controls were showed in mean ± standard deviation (SD) form. Independent samples 't' test was used to test the significance of difference in means between study group and controls. For men and women, a student t-test or ANOVA test was used to compare between control and Renal failure participants respectively. A P-value less than 0.05 were considered statistically significant. Statistical analysis was done by using Microsoft Excel and SPSS for windows version 11.5 (SPSS, Inc., Chicago).

RESULTS and DISCUSSION

Haemodialysis Operationally involves connecting the patient to a haemodialyzer into which their blood flows. After filtration to remove to the wastes and extra fluids the cleansed blood is returned to the patients.it is a complicated and inconvenient therapy requiring a coordinated effort from a healthcare team.

Ongoing oxidative stress present in the patients on MHD may play a pathophysiological role in the development of cardiovascular disease. Indicators of oxidative stress have often been evaluated in ESRD patients. Of these malondialdehyde (MDA), a low molecular weight end product of lipid hydro peroxide decomposition, lipid hydro peroxides which represents the hydro peroxide fraction of the plasma lipids, oxidized LDL.

The causes of inflammation in haemodialysis patients are multifactorial. C-reactive protein (CRP) is a acute phase protein.it is produced in the liver and is present in the circulation in minute concentration. Estimation of CRP levels in plasma is important for the evolution of acute phase response. CRP levels in plasma rise after myocardial infarction trauma and neoplastic proliferation. The increased levels of high sensitive CRP in the circulation are useful for predicting the risk of coronary heart disease.

TBARS and AOPP the Lipid peroxidation markers are significantly increased in Haemodialysis patients.no change of plasma α-tocopherals levels in Haemodialysis patients and controls. Decreased Lipid profile values were seen in HD patients and increased in controls. Ubiquinol levels of plasma were decreased in HD patients when compared with controls and also ascorbate levels were decreased in HD.

In this study increased levels in oxidative stress markers and decreased levels of antioxidant defence in HD patients were seen. Increased lipid and protein oxidative markers were seen in HD patients when compared to controls subjects. TBARS and AOPP the Lipid peroxidation markers are significantly increased in Haemodialysis patients.no change of plasma α-tocopherals levels in Haemodialysis patients and controls. Lipid profile values are decreased in haemodialysis when compared with controls. Ubiquinol levels of plasma were decreased in haemodialysis compared with controls, and also ascorbate levels were decreased in haemodialysis. The plasma CRP levels and TBARS levels were increased and correlated positively and negatively with α-tocopherol and plasma albumin levels. Increased plasma ferritin levels were seen in HD patients when compared with controls. These findings show that haemodialysis patients are exposed to both oxidative stress and inflammation.

Chronic kidney diseases associated with systemic inflammatory process which is most prominent in end-stage renal disease (ESRD).The regulation of inflammation is a complex process resulting from the balance of pro inflammatory and anti- inflammatory stimuli deriving from several sources. (Bandyopadhyay GK., 2005; Barazzoni R., 2006; Cheng TO., 2006) Circulating poly morphonuclocytes (PMNs)and monocytes are well - recognized players in this process, and recentstudiesfurthershowedtheinvolvementofadditionaltissuesandorgansincluding adipose tissue and potentially skeletal muscle and the vasculature.(Chowdhury TA.,1998)

Our study was correlated Evidence of systemic inflammation such as elevated C-reactive protein (CRP) levels correlates with higher coronaryriskinthegeneralpopulation(Daneshetal.,1998),andisassociatedwithimpaired kidney function(Gargetal.,2001).Elevated CRP is associated with endothelial injury and impaired vasodilation, both of which may lead to glomerular damage and progressive loss of kidney function (Ariciand Walls, 2001).

A biological antioxidant may be defined as a substance that significantly delay or inhibits oxidation of a substrate. Antioxidants may be considered as the scavengers of free radicals. The production of free radicals and their neutralization by antioxidants is a normal bodily process. There are different type of antioxidants are present. Antioxidants in relation to lipid peroxidation they are two types preventive antioxidants and chain breaking antioxidants. Antioxidants according to their action and nature enzymatic (superoxide dismutase, catalase etc) and Non enzymatic antioxidants (ascorbic acid, selenium, albumin, uric acid, Bilirubin, etc). (E Prabhakar Reddy, T.Mohana Lakshmi, et al., 2012)

Ferritin is continuously synthesized and degraded. The transfer of iron from ferritin to plasma apo transferrin

Table 1: Shows the values of oxidative stress markers in HD patients and controls

Parameters	Controls (19N)	HD patients(30N)
AOPP	43±19	149±44
TBARS	2.17±0.21	2.83±0.39
SOD	1.39±0.21	1.02±O.24
α-tocopherol	30.2±4.9	27.5±8.6
Ubiquinol	1.29±0.24	1.09±0.31
Ascorbate	76±28	29±23

The plasma CRP levels were correlated positively with TBARS levels and negatively with α-tocopherol levels and plasma albumin levels. Increased plasma ferritin levels were seen in HD patients when compared with controls.

Table 2: Shows the values in HD patients and controls

Parameter	Controls	Patients
Ferritin	240±160	415±203
Carbonyls	0.49±0.38	0.50±0.12

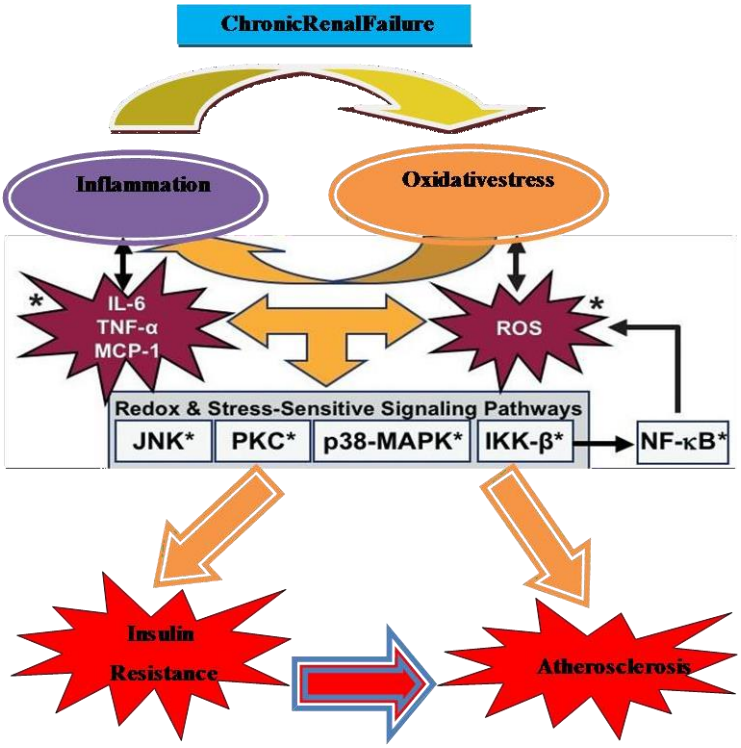

Figure 1: The "oxidative-inflammatory cascade" in chronic renal failure. Potential are as for therapeutic intervention (designatedby*) maymodulate the mediators of the oxidation- inflammation cascade to improve insulin sensitivity and endothelial dysfunction in chronic renal failure

involves reduction of Fe+3 to Fe+2, causing the releases of iron from ferritin. To facilitate its binding to apotransferrin, Fe+2 is oxidized rapidly. The reduction of Fe+3 to Fe+2 is catalyzed by ferritin reductase which requires two co-enzymes NAD and FAD where as oxidation is catalyzed by ceruloplasmin. Some recent studies have indicated a significant association between increased serum ferritin and malnutrition as well as resistance to recombinant human erythropoietin. So Serum ferritin is frequently used as a marker of iron stores in uremic patients several studies have shown that a low serum ferritin concentration is a reliable indicator of iron deficiency among ESRD patients. (E Prabhakar Reddy, T.Mohana Lakshmi, et al., 2013)

CONCLUSION

HD is mainly responsible for free radical production as well as non-enzymatic antioxidant losses. This suggests that HD, far from improving oxidative stress, worsens the same. Diverse mechanisms might account for increased oxidative stress, including antioxidant deficiency, neutrophil activation during dialysis, and chronic inflammation.

HD patients with inflammation have a poor prognosis and these biochemical inflammatory and oxidative markers help us to identify the patients. In most cases the cause of inflammation can be determined through clinical investigation and some of them may be eliminated or normal. By seeing these values the prevention

and the treatment of inflammatory disease is of high priority in patients who are all on MHD.

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