Inflammatory Activity and Oxidative Stress in Hemodialysis and Peritoneal Dialysis

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Abstract

Background. Some authors suggest that the inflammatory status is a factor, influencing the oxidative stress in dialysis patients. Evaluating the level of oxidative stress by two lipid peroxidation markers and its dependence on the chronic inflammation in patients treated by the two main methods of blood purification, this study intends to compare the inflammatory activity and the plasma levels of lipid peroxidation in hemodialysis (HD) and in peritoneal dialysis (CAPD) and to ascertain the possible relationship between the oxidative stress and chronic inflammation in dialysis patients.
Methods. Plasma concentration of the lipid peroxidation products malondialdehyde (MDA); oxidized LDL cholesterol (o-LDL) and the inflammatory marker C-reactive protein (CRP) were measured in, 35 HD patients (pre HD session); 15 CAPD patients and 15 normal controls (NC).
Results. Both groups of patients (HD and CAPD) had higher levels of MDA and o-LDL than NC ($p < 0.001$). Patients on CAPD, had similar levels to HD patients before HD session, but the CRP concentration was higher in HD than in CAPD patients ($p < 0.05$). No correlation was observed between CRP and MDA or o-LDL levels.
Conclusions. Although HD and CAPD patients show an equal levels of oxidative stress, CRP levels are higher in HD patients and this is indicative of a higher degree of inflammatory activity in HD patients, perhaps due to the stimulation of the chronic inflammation process by the dialyzer membrane, dialysate buffer, or bacterial fragments in the dialysate.

Key words: inflammatory status, oxidative stress, lipid peroxidation, hemodialysis, malondialdehyde, oxidized LDL cholesterol, peritoneal dialysis, hemodialysis, C-reactive protein.

Introduction

There are large amounts of polyunsaturated fatty acids associated with membrane proteins in all biological membranes. Peroxidation of these fatty acids can disrupt the structure and function of membranes (1,2). Malondialdehyde (MDA) and oxidized LDL cholesterol are end-products of the polyunsaturated fatty acids and related esters breakdown and their measurement provides one of the reliable indexes of lipid peroxidation and oxidative stress in general (2-4). MDA and oxidized LDL cholesterol are found increased in plasma and erythrocytes of dialysis patients, suggesting a presence of enlarged oxidative lipid destruction in this population (3,4). On the other hand, uremia is defined by a number of authors as a chronic inflammatory status (5-9) and it is quite interesting for the investigators to know weather and how this status influences the oxidative stress. The two main blood purification methods of uremia – hemodialysis and peritoneal dialysis which possess their own characteristics, impact the chronic inflammation and acute-phase reaction (10,11). However, some variations upon their influence on the level of the oxidative reactions in the respectively treated patients might exist. The study compared an inflammation-activity marker and two lipid peroxidation markers in plasma between the groups of patients on hemo- and peritoneal dialysis therapy and to get our own opinion concerning the given problem and to ascertain the possible relationship between the oxidative stress and chronic inflammation in dialysis patients.

Patients and methods

The study included 35 HD patients (1st group) (19 M and 16 F) mean age 48 ± 27 years and mean duration of dialysis 26 ± 23 months; 15 CAPD patients (2nd group) (10 M and 5 F) mean age 44 ± 22 years and mean duration of dialysis 21 ± 19 months and 15 healthy controls (3rd group) (8 M and 7 F) mean age 52 ± 25 years.
The primiry kidney diseases of the patients in the first group were as follows: pyelonephritis - 11; glomerulonephritis – 9; polycistic kidney disease – 6; and other renal diseases – in 9 patients. In the second group – pyelonephritis - 7; glomerulo-nephritis – 4; polycistic kidney disease – 2; and other renal diseases – in 2 patients.
All patients in the first group underwent bicarbonate hemodialysis procedures and cellulose-acetate dialyzers were used in all cases.
CRP levels were measured in all investigated subjects by a non-sensitive assay (Syncron LX 20; Beckham Coulter, CA); Malondialdehyde (MDA) was measured, using Aust's spectrophotometric assay (Sigma, U.K.); o-LDL was measured by ELISA. Urea, creatinine, hemoglobin, albumin and total protein were measured by auto-analyser Hitachi 704.
The blood was collected in the morning time for CAPD (2nd group) and controls (3rd group) and pre-HD session time for HD patients (1st group).
None of the patients showed an evidence of systemic infection (fever or leukocytosis). Patients with congestive

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heart failure, active form of hepatitis in the last 6 months and autoimmune disease or receiving immunosuppressive drugs were not included in the study. None of the patients in the second group (CAPD pts.) suffered from peritonitis during the last 6 months prior to the study.
Statistical analysis was performed routinely: values are given as Mean ± SD; analysis of variances was applied to assess differences between the groups.

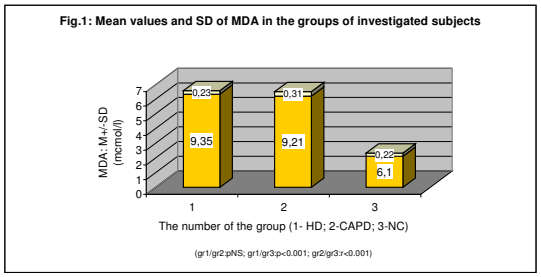
Results

The values of the investigated parameters of the three compared groups are shown in the next table:

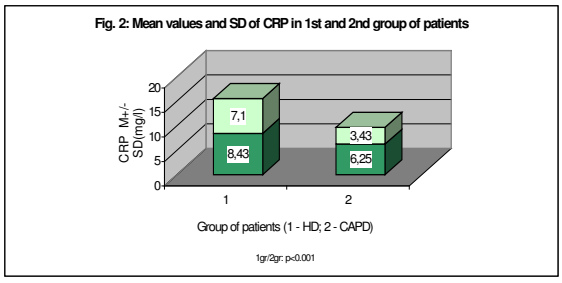
Table 1. Mean values of the investigated parameters with standard deviation

Parameter	1st group (HD pts)	2nd group (CAPD pts)	p (1st /2nd gr)	3rd group (N controls)	p (1st /3rd gr)	p (2nd /3rd gr)
CRP(mg/l)	8.43±7.1	6.25±3.43	0.001	1.32±0.71	0.001	0.001
MDA(µmol/l)	9.35± 0.23	9.21±0.31	NS	6.12±0.22	0.001	0.001
o-LDL(mU/ml)	348±220	365±242	NS	96±45	0.001	0.001
Urea(mmol/l)	24±9.5	26±6.3	NS	6.2±1.3	0.001	0.001
Creatitine(µmol/l)	850±140	910±130	NS	91±24	0.001	0.001
T-protein(g/l)	68±7.2	62±5.9	0.01	66±2.6	0.001	0.001
Alb (g/l)	34±1.6	33±1.3	NS	37±1.4	0.001	0.001
Hb (g/l)	110±8.5	115±9.8	NS	125±4.8	0.001	0.001

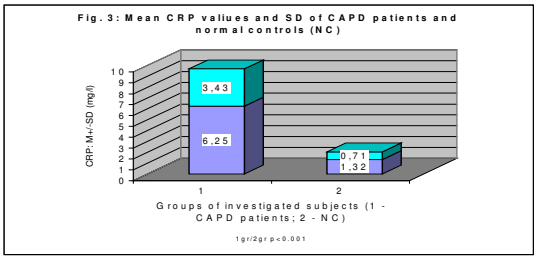
Oxidative stress i.e. lipid peroxidation was present in both patient's groups, as MDA and o-LDL were significantly higher in 1st and in 2nd group than the levels of the same parameters in the controls (3rd group) ($p<0.001$). Evidently no sizable differences were registered between 1st and 2nd group;(dialysis treated patients) ($p>0.05$); (Fig.1):



Values of CRP were found significantly lower in the CAPD patients (2nd group) than in HD patients (1st group) ($p< 0.001$) (Fig 2):



But in the same time CRP levels of CAPD patients (2nd group) were significantly higher than the controls (3rd group) ($p<0.001$)(Fig. 3):



No correlation was found between CRP and MDA or between CRP and o-LDL in any of the groups. There was no correlation as well between CRP, MDA and o-LDL from one side and urea, creatinine, hemoglobin, albumin and total protein from the other.

Discussion

Free radicals are highly reactive molecules generated by biochemical 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 and renal diseases (1,3,7). They are eliminated from the body by their interaction with antioxidant enzymes such as glutathione peroxidase, superoxide dismutase and catalase, etc. Increased production of free radicals may cause lipid peroxidation and damage in macromolecules and cellular structure of the organism, endothelium and erythrocytes, i.e. - so called "oxidative stress reaction" (3,4). A number of investigations have shown that oxidative stress is present in CRF and especially in dialysis patients (1,4,7). However the data about the extent of oxidative stress in patients on the two main dialysis methods of treatment – hemodialysis and peritoneal dialysis are still controversial (1,7).
The prevalence of chronic inflammation, as reflected by increased levels of proinflammatory cytokines or acute-phase proteins, such as C-reactive protein (CRP), is high in dialysis patients as well (11-13). The origin of inflammation in patients with chronic renal disease remains unclear. It has been suggested that some dialysis-related alteration in the immune and host-defense system may be relevant, as they seem to correlate to the high production of pro-inflammatory cytokines and proteins (14,15) Moreover, the type of dialysis membrane in hemodialysis procedure has been suggested to play a role, as well as time on dialysis, as it correlated negatively with cytokine release (16). In addition, the HD procedure itself may be involved.
Our results suggest, that induction of the inflammatory activity is lower during CAPD compared to HD, since most probably stimulation by the dialyzer membrane, dialysate buffer, or bacterial fragments in the dialysate is avoided in CAPD. Several mechanisms that have been proposed to induce cytokine production during HD may be involved in

activation of the oxidative stress in our HD patients: the generation of complement fractions as a result of plasma protein-membrane contact, the backfiltration of contaminated dialysate to the blood compartment, and the direct contact of blood cells with the dialysis membrane (10,16). A certain number of studies observed an inflammatory response of the HD procedure, but it still remains to be clarified, which factors of this procedure may be involved in the so called "chronic inflammatory status" (10,15,17). This observation might possibly indicate a lower risk of long-term complications in patients on CAPD, as suggested by our own results. However CAPD patients and HD patients are in uraemic status, which is an inflammatory state "per se". This is the reason why HD and CAPD patients included in this study had CRP levels significantly higher compared to the controls.

Conclusion

The elevation of lipid peroxidation markers and lack of differences in the levels between HD and CAPD groups in our investigation suggest that the oxidative stress is influenced by uremia, but not markedly influenced by the non-equally presented chronic inflammatory agents in HD and CAPD patients. As a conclusion we could say, that probably the treatment with antioxidant drugs is equally required in both HD and CAPD population.

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