Oxidative stress with homocysteine, lipoprotein (a) with lipid profile in amyloid nephropathy

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ABSTRACT

Secondary amyloidosis is a well known cause of nephrotic syndrome. Therefore, this study was carried out to investigate oxidant and antioxidant status in amyloid nephropathy patients. The blood samples were analyzed for quantitation of malondialdehyde as index of lipid peroxide, vitamin C, total antioxidant capacity, homocysteine lipoprotein (a) and lipid profile. Significantly increased levels of serum total cholesterol, triglycerides, low density lipoprotein, lipid peroxide, lipoprotein (a), homocysteine (p<0.001) and decreased levels of serum total antioxidant capacity, high density lipoprotein, total protein, albumin, plasma vitamin C (p<0.001) were noticed in the patients with amyloid nephropathy as compared to control subjects.

INTRODUCTION

Nephrotic syndrome and its’s complication is defined as the glomerular disease with massive proteinuria and hypoalbuminemia, hyperlipidemia and other complications are numerous.[1]The nephrotic syndrome occurs in association with a diverse array of primary and secondary glomerular disorders.[2]Nephrotic syndrome complications are numerous and may represent the first sign of the syndrome, among these complications leads to thromboembolism, infections, negative nitrogen balance and renal failure.[3]Renal amyloidosis is an uncommon cause of nephrotic syndrome, the clinical conditions in Chinese people remain obscure.[4]Renal amyloidosis is not a frequent diagnosis of nephrotic syndrome in Taiwan, but it should be suspected in every patient over 50 years old with a recent onset of proteinuria.[4] Renal amyloidosis is diagnose only by renal biopsy. Primary renal amyloidosis is a disease of poor prognosis.[4]Secondary systemic amyloidosis with NS in association with chronic inflammation disorders, chronic infections and CHD with abnormalities in Lipoproteins metabolism.[5]

The objective of this study was to investigate possible associations between oxidative stress and the severity of amyloid nephropathy in nephrotic syndrome patients with the estimation of the serum HCY, Lp (a), TAC, MDA, plasma ascorbic acid (vit C), interrelationship of all biochemical parameters and correlate with severity of AN.
EXPERIMENTAL

The present study was conducted at the Department of Biochemistry S.S. Medical College Rewa (M.P.) with collaboration of Department of Biochemistry N.S.C.B. Medical College Jabalpur (M.P.).

The study group:- The present study was case control study conducted on 2 groups.

Group I: Comprised with control (135).

Group II: Comprised with adult AN patients (56).

Age of the patients group II ranged from 30 to 80 years, patients were from same geographical area and none was taking a special diet, untreated AN patients newly diagnosed by biopsies evidences of nephritis. Group I was judged to be free of any illness by clinical examination, AN patients were not with any other active complication medical condition or with systemic diseases. Fasting venous blood were drawn from all.

Total antioxidant capacity (TAC) in serum was estimated by using spectrophotometric method described by D-Koracevic et al.[6] MDA one of the aldehydic by product of lipid peroxidation in serum was estimated by its thiobarbituric acid reactivity, spectrophotometric method described by Hunter et al.[7] Plasma ascorbic acid (Vit C) was measured by colorimetric method described by Roe and Kuether et al.[8] Lp (a) was estimated by ‘Turbidimetric method’ a commercially available kit from “human diagnostic kit”. HCY was estimated by a commercially available kit from a “Keragen diagnostic kit method”.

The study protocol was approved by the ethics committee of the DAVV University of M.G.M. Medical College. The mean and standard deviation were determined for each variable in all groups. All the results were expressed as mean +/-SD. Student “t” test was used to assess statistical significance of the results between group I and group II.

RESULTS AND DISCUSSION

All results of group II were compared with group I. The level of all biochemical parameters were significantly changed between groups I and II. Descriptive statics of diagnostic parameters in group I & group II presented in TABLE 1 & TABLE 2. There was a statistically significant decreased level of the serum HDLC, total protein, albumin, TAC, plasma Vit C level and increased serum Tchol, TGs, LDLC, MDA, HCY & Lp (a), level in group II when compared to group I.

TABLE 1: Comparison of routine diagnosed parameters-lipid profile, serum proteins in group I & group II

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group I</th>
<th>Group II</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>135</td>
<td>56</td>
</tr>
<tr>
<td>TGs (mg/dL)</td>
<td>112.09±10.16</td>
<td>197.44±8.5*</td>
</tr>
<tr>
<td>Tchol (mg/dL)</td>
<td>173.71±15.44</td>
<td>333.0±16.3*</td>
</tr>
<tr>
<td>VLDLC (mg/dL)</td>
<td>22.40±1.98</td>
<td>39.20±4.2*</td>
</tr>
<tr>
<td>HDLC (mg/dL)</td>
<td>49.15±7.4</td>
<td>32.39±5.8*</td>
</tr>
<tr>
<td>LDLC (mg/dL)</td>
<td>103.68±8.24</td>
<td>259.37±14.02*</td>
</tr>
<tr>
<td>TP (g/dL)</td>
<td>6.90±1.6</td>
<td>4.52±0.30*</td>
</tr>
<tr>
<td>Alb (g/dL)</td>
<td>4.34±0.37</td>
<td>2.60±0.55*</td>
</tr>
</tbody>
</table>

*group I compare to group II, * p<0.001; Highly Significant

TABLE 2: Comparison of diagnosed biochemical parameters between control (group I) and patients (group II) with AN

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group I</th>
<th>Group II</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>135</td>
<td>56</td>
</tr>
<tr>
<td>Lp(a) (mg/dL)</td>
<td>18.15±9.7</td>
<td>34.49±7.8*</td>
</tr>
<tr>
<td>HCY (umol/L)</td>
<td>10.75±3.1</td>
<td>21.16±4.3*</td>
</tr>
<tr>
<td>TAC(mmol/L)</td>
<td>2.37±0.87</td>
<td>1.40±0.63*</td>
</tr>
<tr>
<td>MDA(nmol/mL)</td>
<td>1.56±0.96</td>
<td>5.0±0.32*</td>
</tr>
<tr>
<td>Vit C(mg/dL)</td>
<td>1.48±0.65</td>
<td>0.65±0.36*</td>
</tr>
</tbody>
</table>

*p value *group I compare to group II * p<0.001

All results expressed in mean and standard deviation (SD).

TABLE 3- Description about correlation coefficient and significance with diagnosed parameters in the study group II. There were positive correlation between Lp (a) & MDA, HCY was positively correlated to the serum MDA & Lp (a) where HCY supported to oxidative stress in study group II. HCY was negatively correlated to the serum TAC, TP & Alb it was related to the decreased defense system of antioxidant protection of the body, which is related increased oxidative stress in study group II & proteinuria and albuminuria was not related to the HHCY in study group II. Total antioxidant capacity was negative correlated to serum Lp (a), supported for decreased antioxidant defense and oxidant/antioxidant imbalance in the study group II. Total protein was negative correlated to MDA, where decreased concentration of total protein supported to increased lipid peroxidation in the patients group II.

(n=No. of subjects and patients) *Highly Significant
In the present study AN patients had more severe oxidative stress than normal persons where oxidative stress plays an important intermediary role in the pathogenesis of amyloidal complications.

The amyloidogenic protein transthyretin (prealbumin) undergoes homocysteinylation at its single cysteine residue (Cys10) both in vivo & vitro in HHCY burden. This in turn may contribute to the pathological consequences of amyloid disease. Injury appears to be involved in either the amyloid formation process or in post fibrillar modification in several types of amyloidosis. The role of oxidative stress in pathogenesis of secondary amyloidosis, propose radical scavenger treatment for such amyloidosis.

Laboratory data showed severe hyperlipidemia with lipoprotein and nephrotic syndrome in primary systemic amyloidosis. In renal amyloidosis, proteinuria is most important symptoms. Losartan seemed to prevent an increase in proteinuria without altering the creatinine clearance level in patients with amyloidosis type AA during a 12-month period.

Lp (a) concentration was not correlated with serum cholesterol, triglyceride, serum creatinine, daily urinary protein loss, or selectivity index in NS, Lp (a) concentrations correlated negatively with the daily protein loss in urine. The most surprising results were the marked Lp (a) concentrations in serum of the patients with primary amyloidosis and nephrosis syndrome. A regulatory role of the kidney in the metabolism of Lp (a) and different effects on the serum Lp(a) concentration, depending on the type of damage to renal tissue. Apolipoprotein A-I amyloid differs sharply from other systemic amyloidoses that are mainly characterized by glomerular and vascular deposits. The tubulointerstitial nephritis as a result of hereditary apolipoprotein A-I amyloidosis is a rare disease and a challenging diagnosis to recognize. The presence of urine lipids and their fractions in chronic glomerulonephritis (CGN) and renal amyloidosis with nephrotic syndrome (NS), nephrotic lipiduria was largely characterized by an increase of the concentration of total lipid (TL) and of the relative content of phospholipid (PL), with the changes of the later parameter being mostly characteristic of CGN patients. NS was associated with a high excretion of lipids with urine which is likely to reflect their elevated filtration under nephrotic hyperlipidemia. However; our results are only preliminary and need to be confirmed by larger studies.

**ABBREVIATIONS AND FOOTNOTES**

Malondialdehyde - (MDA); Total antioxidant capacity - (TAC); vitamin C - (vit C); Lupus nephritis - (LN); Homocysteine - (HCY), Lipoprotein (a) - LP (a); Cardiovascular diseases - CVD.

**CONCLUSION**

In the present study conclude that oxidative stress is enhanced in AN patients due to hyperhomocysteinemia and hyperlipoproteinemia and hypoprotenemia which may contribute to the development of AN related complication with more frequency such as cardiovascular diseases and end stage renal diseases, acute and chronic infection and many other complications. Patients with AN had imbalance oxidant/antioxidant status and increased subsequent oxidative stress is due to low intake of antioxidants in diet, HHCY, hyperlipoproteinemia & hypoprotenemia. We can only hypothesize that in patients at the acute phase of the disease, decreased total antioxidant capacity may lead to abnormal lipid peroxidation, resulting in a high rate of glomerular injury. On the other hand prolonged lipid oxidation may lead to diminished antioxidant activity. Long term follow up in a large number of patients would be necessary to confirm these results. Antioxidant supplements for oxidative stress can achieve excellent long term results in the treatment of...
amyloid nephropathy.

ACKNOWLEDGEMENT

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REFERENCES