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IMBALANCE BETWEEN FREE RADICAL PROPAGATION AND ANTIOXIDANTS STATUS IN CHILDREN WITH NEPHROTIC SYNDROME

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ABSTRACT

Oxygen-free radical have been implicated in a variety of disease processes including nephrotic syndrome. In this study we investigated the free radical activation products and antioxidant status in children with nephrotic syndrome compared with a control group. Serum lipid peroxides (LP) and selenium levels and red blood cell glutathione peroxidase (GSH-PX) and superoxide dismutase (SOD) activities were measured in 35 children (28 males and 7 females) with nephrotic syndrome. Similar number of apparently healthy children with appropriate age and sex were used as a control group. Children with nephrotic syndrome had significantly higher levels of LP (3.37+0.5 nmol/ml) and lower level of serum selenium (150 ±35 ug/L) and red blood cell GSH-PX (32.6+7.8 U/gHb) and SOD (1116 ±151 U/gHb) respectively) when compared with the corresponding levels of the control group (2.53 ±0.6nmol/ml, 230 ±43 ug/L. 51.8 ±13.8 U/gHb & 1422 ± 277 U/g Hb respectively). We concluded that imbalance between generation of oxygen free radicals and antioxidant status may have etiological implications for nephrotic syndrome.

INTRODUCTION

Lipid peroxides (LP) are the product of the chemical damage done by oxygen-free radicals to the lipid components of ceil membrane (Southern & Powis, 1988 and Ohtake et al., 1997). These reactive oxygen intermediates (ROI) have been demonstrated to play a pathobiologic role in a number of inflammatory models of both immune and non-immune glomerular injury (Ardaillou and Baud, 1992). Renal cells, especially glomerular cells, express the capacity to generate ROI in response to several

stimuli. ROI have profound functional effects on mesangial and endothelial cells, as well as, the glomerular basement membrane which contribute to disturbances of glomerular function, for example by altering capillary diameter and surface area (Varani et al., 1991). The extent of injury is dependent on the balance between endogenous ROI production and ROI defense pathways i.e. antioxidants (Andreoli & Me Ateer, 1990). Although antioxidants function to prevent or minimize the injurious effects of oxygen free radicals, excess production of oxidants can overwhelm the protective system and lead to oxidant injury. Glutathione peroxidase (GSH-PX) and superoxide dismutase (SOD) are integral components of the antioxidant system in the body that protect cells against oxidation damage by inactivating ^*02,* Lipid peroxides and phospholipid peroxides (Ursini & Bindoli, 1987). Selenium is an essential component of the enzyme GSH-PX. The aim of this work was to study the free radical propagation and antioxidant status in children with nephrotic syndrome to clarify their role in the disease activity.

SUBJECTS AND METHODS

Thirty five children (28 males and 7 females) with a mean age 8 ± 1.8 years, were diagnosed to have nephrotic syndrome with the following:

1. Full history including history of relapses.
2. Thorough clinical examination including blood pressure measurement, edema, ascites, pleural effusion and other complications as chest infection and peritonitis.
3. Urine analysis for proteinuria and hematuria.
4. Blood sample for serum level of urea (Palton & Crouch, 1977), creatinine, (Henry, 1974), total protein (Henry & Beters, 1968). Albumin (Grant & Kachmer, 1970). and cholesterol (Stein, 1986).
5. Similar number 35 of apparently healthy children with appropriate age & sex were used as a control group. Both cases and controls were investigated for:

- Serum levels of lipid peroxides (LP) (Draper &

Hadley, 1990) and selenium. (Willard et al.,1988). Red blood cell levels of glutathione peroxidase (GSH-PX) (Kraus and Ganther, 1980) and superoxide dismutase (SOD) (Williams etal., 1983).

RESULTS

All cases of nephrotic syndrome in our study had swollen eye lids and/or puffy face, 27 cases had edema of both lower limbs, 10 cases had ascites and 3 of them had pleural effusion, 5 cases were complicated by chest infection and only one case had peritonitis.

Biochemical data of nephrotic syndrome in our subjects were proteinuria ranged form 1.5-5.4 g/24 h, reduced serum total protein (2.6 - 5.9 g/dl) and serum albumin (0.6-3.2 g/dl) and increased serum cholesterol (222-651 mg/dl).

Table (1) shows that children with nephritic syndrome have significantly ($P < 0.001$) higher levels of LP (3.37 ± 0.5 nmol/ml) and lower levels of serum selenium (150 ± 35 ug/L) and red blood cell GSH-PX (32.6 ± 7.8 U/g Hb) and SOD (1116 ±151 U/g Hb) when compared with the corresponding values of the control group (2.53 ± 0.6 nmol/ml, 230 ± 43 u.g/L, 51.8 ± 13.8 U/g Hb& 1422 ±277 U/g Hb respectively).

We have statistically significant positive correlation between proteinuria and LP, but negative significant correlations between proteinuria with selenium, GSH-PX and SOD ($P < 0.001$) (Table 2).

Table (1): Mean ± SD, student (t) test and P values of serum lipid peroxides (LP), selenium, red blood cell glutathione peroxidase (GSH-PX), superoxide dismutase (SOD) in children with nephrotic syndrome compared with controls.

Biochemical 1 parameters	Cases (n=35)	Control (n=35)	t	P
Lipid peroxide (nmol/ml)	3. 37 ±0.5	2.53 ±0.6	6.4	< 0.001
Selenium (fig/L)	I50±35	230 + 43	8.5	< 0.001
GSH-PX (U/g Hb)	32.6 ±7. 8	51.8+ 13.8	7.2	< 0.001
SOD (U/g Hb)	11I6± 151	1422 + 277	5.7	<0.001

Table (2): Correlation coefficient (r) between proteinuria with Lp, Selenium, GSH-PX and SOD in patients with nephrotic syndrome.

Variables / Proteinuria	LP	Selenium	GSH-PX	SOD
r	0.728	-0.507	-0.669	-0.600
P	< 0.001	< 0.001	< 0.001	< 0.001

DISCUSSION

Oxygen radicals are important mediators of host defense and tissue damage (Southern & Powis, 1988 and Futenma et al., 1995). In nephrotic syndrome, glomerular cell express the capacity to generate oxygen radicals that have profound functional effects on mesangial and endothelial cells, as well as the glomerular basement membrane including increased vascular permeability (Varanietal., 1991).

Increased LP concentration in our children with nephrotic syndrome should be used to quantitate indirectly the activation products of oxygen derived free radicals. This result confirms that obtained by Dudar and his Coworkers (1992) and Rajbala et al., (1997) who concluded enhanced activation of lipid peroxidation in nephrotic syndrome. Ohtake etal., (1997) told that the disbalance of the antioxidant system causes corresponding changes in the lipid phase of the cell membrane and increase of its deformability capacity that may be of significance for the development of proteinuria and hematuria in patients with glomerulonephropathy.

This study has demonstrated a significant decrease in red blood cell GSH-PX activity and serum selenium levels in children with nephrotic syndrome. Similar data was that of Baliga et al., (1992) and Ohtake et al., (1997) who found that selenium deficiency could reduce the specific activity of selenium-dependent GSH-PX that have an important role in the pathogenesis of glomerular injury. Selenium administration will increase GSH-PX activity and improve the glomerular

damage & proteinuria (Baliga et al., 1992).

SOD activity was also reduced in our cases with nephrotic syndrome, similar to the findings of Rajbala et al, (1997) who measured SOD levels in 45 pediatric patients with nephrotic syndrome compared with 42 appropriately healthy children as controls.

These findings suggested that nephropathy appeared to be mediated by imbalance of antioxidant enzyme activities (Ohtake et al., 1997).

Proteinuria has been used largely as an indicator of the severity of the glomerular involvement (Alfrey, 1994). We found significant correlations between the severity of proteinuria and increased levels of LP and reduced levels of selenium, GSH-PX & SOD. Antioxidant administration has been proved to reduce proteinuria (Ohtake et al., 1997 and Rajbala et al., 1997). It is felt that children with nephrotic syndrome should regularly take some antioxidants as selenium, vitamin C and vitamin E from the health point of view. We concluded that imbalance between free radical propagation and antioxidant status occurs in children with nephritic syndrome and these data stimulate the necessity of searching treatment directed to reduction of lipid peroxidation activation, normalization of the antioxidant system and stabilization of renal cell membranes.

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