Abstract. Polyunsaturated fatty acids have been reported to be associated with atherosclerotic and inflammatory diseases, as they are the major components of cytoplasmic membranes and the precursor fatty acids for prostaglandins and leukotrienes. Nephrotic syndrome is associated with serum lipid disorders, such as hypercholesterolemia due to the increased production of lipoproteins by the liver. However, there are few reports regarding the fatty acid metabolism in patients with nephrotic syndrome. In the present study, serum lipid concentrations and plasma fatty acid composition were measured in patients with minimal change nephritic syndrome (MCNS) and membranous nephropathy (MN). Seven patients with MCNS (MCNS group), 11 patients with MN (MN group) and 8 healthy subjects (control group) were enrolled in the study. All patients were diagnosed by percutaneous renal biopsy. Fasting blood samples were obtained and the serum lipid profile was measured enzymatically. The fatty acid composition of plasma was analyzed by gas-chromatography after transmethylation. There were no significant differences in serum urea nitrogen and creatinine levels among the three groups. Patients with MN were older than those with MCNS. In the serum lipid profile, hypercholesterolemia was observed both in the MCNS and MN groups. Regarding the plasma fatty acid composition, alpha-linolenic acid levels in the MCNS group were significantly higher than those in the control group (1.06±0.08 wt% vs. 0.77±0.16 wt%, p=0.008) and docosahexaenoic acid levels in the MN group were significantly higher than those in the control group (5.51±1.17 wt% vs. 3.96±1.07wt%, p=0.005). These results suggest that nephrotic syndrome might not only disrupt lipid metabolism but also fatty acid metabolism.

Polysaturated fatty acids (PUFA) have been reported to be associated with atherosclerotic and inflammatory diseases, as they are the major components of cytoplasmic membrane and the precursor fatty acids for prostaglandins and leukotrienes (1-3).

PUFA metabolism have also been reported to be altered by some diseases and drugs. HMG-CoA reductase inhibitors were found by our group to increase plasma arachidonic acid (AA) levels (4) and that cilostazol, an anti-platelet agent, was found to increase plasma docosahexaenoic acid (DHA) levels (5).

Nephrotic syndrome is characterized by serum lipid disorders, such as hypercholesterolemia, due to an increased production of lipoproteins by the liver. However, there are to date few reports regarding the fatty acid metabolism in patients with nephrotic syndrome. In the present study, serum lipid concentrations and plasma fatty acid compositions were measured in patients with nephrotic syndrome and the lipid and fatty acid metabolism was compared between patients with minimal change nephritic syndrome (MCNS) and those with membranous nephropathy (MN).

Patients and Methods

Seven patients with MCNS (MCNS group), 11 patients with MN (MN group) and 8 healthy subjects (control group) were entered in the present study, after providing informed consent. All patients were diagnosed by percutaneous renal biopsy. Fasting blood samples were obtained and serum lipid profiles were measured enzymatically. The fatty acid composition of plasma was analyzed according to previous reports (6). Briefly, total lipids were extracted by the methods of Folch et al. (7). The fatty acids in total lipids were transmethylated with 6% sulfuric acid in anhydrous methanol and analyzed on a C-14 gas-chromatograph (Shimazu, Kyoto, Japan) equipped with an SP-2330 capillary column (Supelco, Bellefonte, PA, USA). The fatty acid composition was calculated as weight% (wt%).

All data were expressed as means±SD and the statistical analysis was performed by Sheffe’s method. A p-value of less than 0.05 was considered statistically significant.
Results

The patients’ background is provided in Table I. The age in the MN group was significantly higher than that in the control and MCNS groups. There were no significant differences in body mass index, blood pressure, blood urea nitrogen, serum creatinine and creatinine clearance among the three groups.

The serum lipid profiles are shown in Table II. Total cholesterol concentrations in the MCNS and MN groups were significantly increased compared to those in the control group. Lipoprotein (a) [Lp(a)] concentrations in the MN group were significantly increased compared to those in control group. Remnant-like particle-cholesterol (RLP-C) concentrations in the MCNS group were significantly increased compared to those in the control group.

The plasma fatty acid compositions are given in Table III. Alpha-linolenic acid (ALA) levels in the MCNS group were significantly higher than those in the control group (1.06±0.08 wt% vs. 0.77±0.16 wt%, p=0.008), and DHA levels in the MN group were significantly higher than those in the control group (5.51±1.17 wt% vs. 3.97±1.07 wt%, p=0.005). There were no significant differences in other fatty acid levels among the three groups.

Discussion

In the present study, the ALA levels in those patients with MCNS and the DHA levels in the patients with MN, were higher than those in the control subjects. The mechanism by which the ALA levels in the MCNS patients were higher than those in the control subjects and why the DHA levels in the MN patients were higher than those in control subjects is not clear, but the following mechanism might clarify the results: a) the conversion from ALA to EPA is reduced in MCNS. The activities of desaturase and elongase might be reduced in MCNS. b) The conversion from EPA to DHA is increased in MN. The activities of desaturase and elongase might be increased in MN. The desaturases are expressed in liver, heart and brain, and are regulated by hormonal and nutritional manipulation (8). Testosterone, whose levels are low in older adults, reduces the activity of desaturase (9). It is possible that the DHA levels in the MN patients were higher than those in control subjects due to the older ages of the former.

In the serum lipid profile analysis, total cholesterol, Lp(a), and RLP-C concentrations in the MCNS and MN groups were higher than those in the control subjects. These results, which are consistent with a previous report (10), might reflect an increased production of lipoproteins by the liver.

In conclusion, the ALA levels in patients with MCNS were higher than those in control subjects and that DHA levels in patients with MN were also higher than those in the controls.
These results suggest that nephrotic syndrome might not only disrupt lipid metabolism, but also fatty acid metabolism.

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References


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