Abstract. Background: n-3 Polyunsaturated fatty acids (PUFA) are reported to ameliorate atherosclerotic and inflammatory diseases because they compete with arachidonic acid and reduce its inflammatory metabolites. In the present study, the fatty acid composition of plasma and kidney in rats with anti-Thy1.1 nephritis was investigated. Materials and Methods: A group of male Wister rats weighing about 200 g was injected with anti-Thy1.1 antibody (1.25 mL/kg) through their tail veins (nephritis group). Rats in the control group were injected with saline. Five days after the injection, urinary protein levels were determined. All rats were then sacrificed and fatty acid composition of plasma and kidney were analyzed. Results: Eicosapentaenoic acids (EPA) levels in the kidney phospholipid (PL) fraction in the nephritis group were significantly lower than those in the control group (0.67±0.06 mol% vs. 0.96±0.06 mol%, p<0.05). EPA levels in the plasma PL fraction in the nephritis group were also significantly lower than those in the control group (0.38±0.05 mol% vs. 0.59±0.03 mol%, p<0.05). Urinary protein levels 5 days after the injection were inversely correlated with EPA levels in the kidney PL fraction (r²=0.65, p=0.01). These results suggested that decreased EPA levels in the kidney PL fraction might play an important role in anti-Thy1.1 nephritis.

n-3 Polyunsaturated fatty acids (PUFA) are reported to ameliorate atherosclerotic and inflammatory diseases, because they compete with arachidonic acid and reduce its inflammatory metabolites, namely prostaglandins and leukotrienes (1).

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Anti-Thy1.1 nephritis is characterized by acute complement-mediated mesangiolysis, followed by mesangial hypercellularity and extracellular matrix accumulation (2). This model is now widely used as a model of mesangial proliferative glomerulonephritis.

There were several reports about the beneficial effects of n-3 PUFA on mesangial proliferative glomerulonephritis such as IgA nephropathy (3, 4). However, there are no reports about the metabolism of PUFA in mesangial proliferative glomerulonephritis.

In the present study, the fatty acid composition of plasma and kidney in rats with anti-Thy1.1 nephritis as mesangial proliferative nephritis was investigated.

Materials and Methods

Eight male Wistar rats weighing about 200 g were used in the present study. Three were injected with anti-Thy1.1 antibody (1.25 mL/kg, COSMO BIO Co. Ltd., Tokyo, Japan) through their tail veins (nephritis group). The other 5 rats were injected with saline (control group). Five days after the injection, urinary protein levels were determined. All rats were then sacrificed, and their plasma and kidneys were obtained. Total protein levels, total cholesterol levels and creatinine levels in plasma were analyzed enzymatically. Urinary protein levels were also analyzed enzymatically. The fatty acid composition of plasma and kidney was analyzed as follows: total lipids were extracted by the methods of Folch et al. (5) and were separated into phospholipids (PL) and other fractions by thin-layer chromatography. Fatty acids in the PL fraction were transmethylated with 6% sulfuric acid in anhydrous methanol and analyzed on a C-14A gas-chromatograph (Shimazu, Kyoto, Japan) equipped with an SP-2330 capillary column (Supelco, Bellefonte, PA, USA) (6).

All data were expressed as means±SE. Statistical analysis was performed using an unpaired t-test. A p value <0.05 was considered statistically significant.

Results

The fatty acid composition in the kidney PL fraction is shown in Table I. 18:2n-6, 18:3n-6 and eicosapentaenoic
acid (EPA; 20:5n-3) levels in the nephritis group were significantly lower than those in the control group. The fatty acid composition in the plasma PL fraction is shown in Table II. 18:2n-6 and EPA levels in the nephritis group were significantly lower than those in the control group. Docosahexaenoic acid (DHA; 22:6n-3) levels in the nephritis group were significantly higher than those in the control group. The ratios of EPA to AA and n-6 PUFA to n-3 PUFA in the nephritis group were significantly lower than those in the control group.

Total protein, total cholesterol and creatinine levels in plasma are shown in Table III. Total protein levels in the nephritis group were significantly lower than those in the control group. Total cholesterol levels in the nephritis group were significantly higher than those in the control group. There were no significant differences in plasma creatinine levels between the nephritis and control groups.

Urinary protein levels 5 days after the injection of anti-Thy1.1 antibody in the nephritis group were significantly higher than those in the control group (Table IV). Urinary protein levels 5 days after the injection were inversely correlated with EPA levels in the kidney PL fraction ($r^2=0.65, p=0.01$).

Discussion

In the present study, we found that EPA levels in the kidney and plasma PL fraction in rats with anti-Thy1.1 nephritis were significantly lower than those in the control group. The mechanism for the EPA levels in the kidney and plasma PL fraction in rats with anti-Thy1.1 nephritis being significantly reduced was not clear, but the following mechanism might explain the results: a) EPA in the kidney PL fraction is consumed by the inflammation in anti-Thy1.1 nephritis; b) the conversion of EPA to DHA is increased in anti-Thy1.1 nephritis. The activities of desaturase and elongase might be increased in the nephritis. However, in the kidney PL fraction, DHA levels in Thy1.1 nephritis were not higher than those in the control group. These results were incompatible with our speculation.
Prostaglandin I$_3$ from EPA has inhibitory effects on platelet aggregation and vaso-constriction, and leukotriene B$_3$ from EPA has much less effects on activating leukocytes than leukotriene B$_4$ from arachidonic acids (AA) (7). Consequently, decreased EPA levels in the kidney and plasma PL fractions and decreased EPA/AA in the plasma PL fraction might cause the progression of nephritis. Moreover, urinary protein levels 5 days after the injection were inversely correlated with EPA levels in the kidney PL fraction. These results suggested that decreased EPA might play an important role in Thy1.1 nephritis.

In the present study, the levels of 18:2n-6 and 18:3n-6 in the kidney and plasma PL fractions in Thy1.1 nephritis were lower than those in the control group. The mechanism is not clear, but the desaturases that produce PUFA are expressed in the liver, heart, and brain and are regulated by hormonal and nutritional manipulation (8). We also reported that fatty acid metabolism was altered in patients with nephrotic syndrome (9). Consequently, it is possible that fatty acid metabolism might be altered in Thy1.1 nephritis.

The ratios of n-6 PUFA to n-3 PUFA in Thy1.1 nephritis were significantly lower than those in the control rats in the plasma PL fraction, probably because DHA levels in Thy1.1 nephritis were higher than those in the control group.

**Conclusion**

We showed that EPA levels in the kidney and plasma PL fractions in rats with anti-Thy1.1 nephritis were significantly lower than those in the control rats. These results suggest that decreased EPA levels in the kidney and plasma PL fractions might play an important role in anti-Thy1.1 nephritis.

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**References**


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