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The Antiproteinuric Effects of Green Tea Polyphenol on Cyclosporine A- Induced Acute Renal Injury in Mice

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It has been reported that there is association between cyclosporine (CsA) nephrotoxicity and proteinuria. Green tea polyphenol, (-)-epigallocatechin 3-O-gallate (EGCG), has potent antioxidants. The aims of this study were to investigate the anti-proteinuric effects of green tea polyphenol on CsA-induced acute renal injury in mice.

The mice (n=20) were divided into 4 groups (n=5/group); group 1 (control group) mice were intraperitoneal (IP) injected 0.9% saline 3 times at 4 day intervals, group 2 (CsA group) mice were IP injected CsA 50 mg/kg 3 times at 4 day intervals, group 3 (iNOS group) mice were received in addition L-NAME 12 mmol/L by subcutaneous injection 3 times at 4 day intervals. Group 4 (polyphenol group) mice were received CsA by IP injection and green tea polyphenol 100 mg/kg by subcutaneous injection 3 times at 4 day intervals. The urine samples were collected to measure urine protein and creatinine. At last day, upon sacrifice of the mice, blood sampling for measurement of blood CsA level, blood urea nitrogen (BUN), creatinine and nephrectomy for morphological study, malondialdehyde and antioxidative enzyme analysis.

The levels of BUN (20.2±5.2 mg/dL vs 18.9±6.4 mg/dL, $p>0.05$), serum creatinine (0.45±0.33 mg/dL vs 0.39±0.29 mg/dL, $p>0.05$) and serum CsA level (5,432±1,089 ng/mL vs 5,765±1,320 ng/mL, $p>0.05$) of CsA group (group 2, only CsA) and polyphenol group (group 4, green tea polyphenol with CsA) were no significantly increased compared to control group (group 1). In the urine protein, there were significantly increased in group 2 (28.6±11.1 g/kg/day vs 9.1±5.5 g/kg/day, $p<0.01$) compared to group 1 and significantly decreased in group 4 (12.1±8.8 g/kg/day, $p<0.01$) compared to group 2 but there were no significant increasement in comparison group 4 with group 1. Renal tissue malondialdehyde level of group 2 was significantly increased compared to group 1 ($p<0.05$) but, there were no significant increasement in comparison group 4 with group 1.

In the histologic examination, there are proximal tubular necrosis and mild interstitial inflammation in the kidney of mice after CsA injection group but no significant pathologic change in green tea polyphenol and L-NAME injected group.

This study provides that proteinuria is early sign of the CsA induced nephrotoxicity and is associated with lipid peroxidation and nitric oxide production. Green tea polyphenol treatment has significantly antiproteinuric effects by antioxidative effect in the kidney from CsA-induced acute renal injury.