

Effect of Cyclosporine on the Production of Superoxide Anion

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Oxygen free radicals contribute to the cyclosporine (CsA)-induced and toxicity including nephrotoxicity and hepatotoxicity. To know whether CsA can stimulate directly the production of superoxide anion, we treated CsA to the purified mitochondrial fractions. The mitochondria sample from normal rat's liver was obtained by centrifugation on density gradient made of sucrose. To know the superoxide production depend on the CsA concentration, isolated mitochondria was incubated with each concentration of CsA. After incubation for 240 min at 37 °C, the amount of superoxide radical production was measured according to the method of Auchlar and Voisin. And to know the superoxide production depend on the time, 140 µg of CsA per ml of final reaction mixture was incubated from 60 min to 240 min. Superoxide production was 5.48 ± 1.64 nmole nitroblue tetrazolium reduced/mg protein/min in cremophore treated group, 7.91 ± 1.94 in 8.9 µg of CsA-treated group, 7.79 ± 1.77 in 17.5 µg treated group, 9.60 ± 1.65 ($p < 0.05$) in 35 µg treated group, 9.37 ± 2.01 ($p < 0.05$) in 70 µg treated group, 12.04 ± 2.14 ($p < 0.05$) in 140 µg treated group, 10.96 ± 2.30 ($p < 0.05$) in 280 µg treated group. Superoxide production in control group was 41.82 ± 10.60 after 60 min incubation, 16.46 ± 8.56 after 120 min, and 5.48 ± 1.64 after 240 min. In CsA-treated group, it was 39.30 ± 6.45 after 60 min, 18.50 ± 7.84 after 120 min, and 12.04 ± 2.14 ($p < 0.05$) after 240 min. The production of superoxide anion was increased depend on the incubation time with CsA and on the CsA concentration. According to this result, CsA can stimulate directly the production of superoxide anion which causes damages in transplant patients.