Abstract: Background: The prognosis of liver transplantation for liver cancer is determined by recurrence in the liver graft. In this study, the effects of immunosuppressors, FK506 and cyclosporine A (CsA) on the migration of liver cancer cells were investigated.

Methods: The effects of FK506 at concentrations of 1-100 ng/mL and CsA at 1-1000 ng/mL on the growth of poorly and well differentiated human hepatocellular carcinoma cell lines, HLE and HuH-7, respectively, were examined. After treatment of these cells with FK506 and CsA, the growth of these cells, their cytotoxicities and invasion assay on the Matrigel basement membrane invasion chamber were evaluated. In addition, the effects of FK506 and CsA on the changes in the production of a soluble intercellular adhesion molecule-1 (sICAM-1) of these cells were measured.

Results: FK506 and CsA at concentrations of 1-10 ng/mL inhibited the growth of both HLE and HuH-7 and those immunosuppressors at concentrations over 100 ng/mL exhibited cytotoxicity on these cells. FK506 at concentration of 1 ng/mL significantly inhibited the invasion of poorly differentiated HLE, but not well differentiated HuH-7, after treatment for 2-5 days in culture (p<0.05), but FK 506 at 10 ng/mL showed less inhibitory efficient. CsA at concentrations of 1-10 ng/mL, however, did not inhibit or transiently inhibited the invasion of both cell lines. The production of ICAM-1 in HLE and HuH-7 was suppressed by FK506 at concentrations of 1-10 ng/mL after treatment for 3-5 days but the effect was not significant in the initial phase at days 1-2 and the last phase at days 5-6.

Conclusions: FK506, but not CsA, at a clinical dose of 1 ng/mL significantly inhibited the invasion of the poorly-differentiated HLE, but not HuH-7 and also inhibited the production of sICAM-1 in HLE. J. Med. Invest. 51: 63-69, February, 2004

Keywords: FK 506, cyclosporine A, liver cancer cell, invasion, ICAM-1
Inhibitory effect of FK506 and CsA on the growth and invasion of human liver cancer cells

Cell lines and culture

Cell-growth analysis

Evaluation of cytotoxicity

Invasion assay

Analysis of the levels of soluble ICAM-1 (sICAM-1) in human cancer cells
Inhibitory effects of FK506 and CsA on the growth of HLE

Inhibitory effects of FK506 and CsA on the growth of HuH-7
Evaluation of the FK506 and CsA cytotoxicity on HLE and HuH-7

Inhibitory effects of FK506 and CsA on the invasion of HLE and HuH-7

Measurement of sICAM-1 levels in the media of HLE and HuH-7
Effects of FK506 and CsA on ICAM-1 production in HLE

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