

Abstract No. : A204

Theme : Basic Research on Biocompatibility, Immunology, Inflammation and Fibrosis

Effects of Tamoxifen on Epithelial-to-Mesenchymal Transition (EMT), Fibrosis and Angiogenesis of Mesothelial Cells

Selgas, R.¹, Aguilera, A.², Bajo, M.A.¹, Loureiro, J.², Del Peso, G.¹, Aroeira, L.S.², Ramirez-Huesca, M.², Perez-Lozano, M.L.², Jimenez-Heffernan, J.A.³, Sanchez-Tomero, J.A.², Fernandez-Perpen, A.², Lopez-Cabrera, M.²; Hospital Universitario La Paz¹, Hospital Universitario La Princesa², Madrid, Hospital General, Guadalajara³, Spain

Peritoneal dialysis (PD)-associated peritoneal sclerosing syndrome (PES) has no specific treatment. Tamoxifen is a synthetic estrogen with anti-fibrotic and anti-metastatic effects interfering with TGF- β and VEGF actions. The present study explores the effect of Tamoxifen on the in vitro and ex vivo EMT of mesothelial cells (MC) and its consequences and the prophylactic effects on patients prone to develop PES. Human peritoneal mesothelial cells (HPMC) were cultured to confluence and stimulated with TGF- β (1 ng/ml) with or without different doses of Tamoxifen. E-cadherin and snail expression was determined by RT-PCR. The synthesis of collagen-I, fibronectin, (ECM components) α SMA, tPA (a powerful fibrinolytic) and CTGF was analyzed by Western Blot. VEGF production was measured in the culture supernatant by ELISA. Proliferation of MC was analyzed by chemo-luminescence and cell cycle by flow-cytometry. The effect of T on wound healing was also study. Tamoxifen inhibited the EMT of MC in a collagen-coated wells. Tamoxifen also inhibited the ECM, tPA production and CTGF expression in HPMC and fibroblast-like MC from PD-effluents. Tamoxifen did not affect cell proliferation and the time of wound heading. We compared survival and incidence of abdominal complications in a group of 14 PD patients diagnosed of type-I membrane failure since 1997 and treated orally with Tamoxifen (20-40 mg/day) for a year, with 14 non treated matched patients. We found a strong PES prophylactic effect among those using Tamoxifen. In conclusion, Tamoxifen prevents peritoneal sclerosing syndromes in prone PD patients. In vitro and ex vivo analysis of mesothelial cells are highly suggestive of a specific inhibitory effect of the drug on EMT and fibrosis abilities of these cells.