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Tamoxifen ameliorates peritoneal membrane damage by blocking mesothelial to mesenchymal transition in peritoneal dialysis

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Mesothelial-to-mesenchymal transition (MMT) is an auto-regulated physiological process of tissue repair that in uncontrolled conditions such as peritoneal dialysis (PD) can lead to peritoneal fibrosis. The maximum expression of peritoneal fibrosis induced by PD fluids and other peritoneal processes is the encapsulating peritoneal sclerosis (EPS) for which no specific treatment exists. Tamoxifen a synthetic estrogen has successfully been used to treat retroperitoneal fibrosis and EPS associated with PD. Hence, we used *in vitro* and animal model approaches to evaluate the efficacy of Tamoxifen to inhibit the MMT as a trigger of peritoneal fibrosis. *In vitro* studies were carried out using omentum-derived mesothelial cells (MCs) and effluent-derived MCs. Tamoxifen blocked the MMT induced by transforming growth factor (TGF)- β 1, as it preserved the expression of E-cadherin and reduced the expression of mesenchymal-associated molecules such as Snail, fibronectin, collagen-I, α -smooth muscle actin, and matrix metalloproteinase-2. Tamoxifen-treatment preserved the fibrinolytic capacity of MCs treated with TGF- β 1 and decreased their migration capacity. Tamoxifen did not reverse the MMT of non-epithelial MCs from effluents, but it reduced the expression of some mesenchymal molecules. In mice PD model, Tamoxifen significantly reduced peritoneal thickness, angiogenesis, invasion of the compact zone by mesenchymal MCs and improved peritoneal function. Tamoxifen also decreased the accumulation advanced glycation end-products and reduced the effluent levels of VEGF and leptin. These results demonstrate that Tamoxifen is a therapeutic option to treat peritoneal fibrosis, and that its protective effect is mediated via modulation of MMT process.

Biography

Abelardo Aguilera is a Medical Doctor Specialist in Nephrology and family practice. He has completed his PhD at Universidad Autonoma de Madrid in 2007. He has published more than 100 papers in reputed journals and has been serving as an Editorial Board Member of five to six international medical journals. Currently, he is the Coordinator of Renal and Cardiovascular diseases study group at Hospital Universitario De La Princesa in Madrid. He has conducted five doctoral theses and has received more than 15 national and international research awards.

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