Benefic effects exerted by Phenolic Compounds present in Extra Virgin Olive Oil on the Mesothelial-Mesenchymal Transition induced by Peritoneal Dialysis

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INTRODUCTION and OBJECTIVES

The principal concern limiting the Peritoneal Dialysis (PD) use regards the technique survival due to the loss of peritoneal membrane function. The mesothelial-mesenchymal transition (MMT) processes by which peritoneal mesothelial cells acquire a myofibroblast-like phenotype, leading to peritoneal fibrosis, represents the key factor in PD failure. It is known, that phenolic extracts obtained from extra virgin olive oil (PL-EVOO), energy source of Mediterranean diet, possesses anti-inflammatory and anti-oxidant properties and could counteract the EMT process and angiogenesis in several cellular systems. The aim of the study is to test in vitro whether PL-EVOO administration could prevent and/or reverse the MMT process induced by PD, increasing peritoneal survival.

THE PURPOSE OF THIS STUDY WAS TO TEST IN VITRO IF THE PL-EVOO MITIGATES THE PROCESS OF MMT INDUCED BY THE CHRONIC EXPOSURE WITH DIALYSATE (DL).

METHODS

Immortalized human mesothelial cells (IMC); Peritoneal mesothelial cells (MC) isolated from effluents by centrifugation of dialysis fluid taken from 10 PD patients that were stable and regularly followed-up at our Department. Western blot (WB); real-time-PCR; wound-healing and migration assays.

RESULTS

Firstly, the purity of the MC was determined by the expression of intercellular adhesion molecule-1 (ICAM-1, data not shown). MC have been classified in "Epithelioid-like" and "Fibroblast-like" according to the MC cellular morphology and to the expression levels of epithelial marker, Cytokeratin-18, by flow-cytometry.

Real-time PCR and the WB analysis results showed that in IMC the co-treatment with DL + PLEVOO, mitigated the genic and protein up-regulation of TGF-β1, N-cadherin, Fibronectin, αSMA and Vimentin, as well as of inflammatory markers as COX-2, MCP-1 and TNF-α.

Concomitantly, cell migration assays showed that the co-treatment reduced the migratory capacity of IMC observed upon stimulation with only DL. On the contrary, we observed that in MC Fibroblast-like cells, PLEVOO exposure was not able to significantly mitigate the expression levels of the above reported mesenchymal and proinflammatory markers.

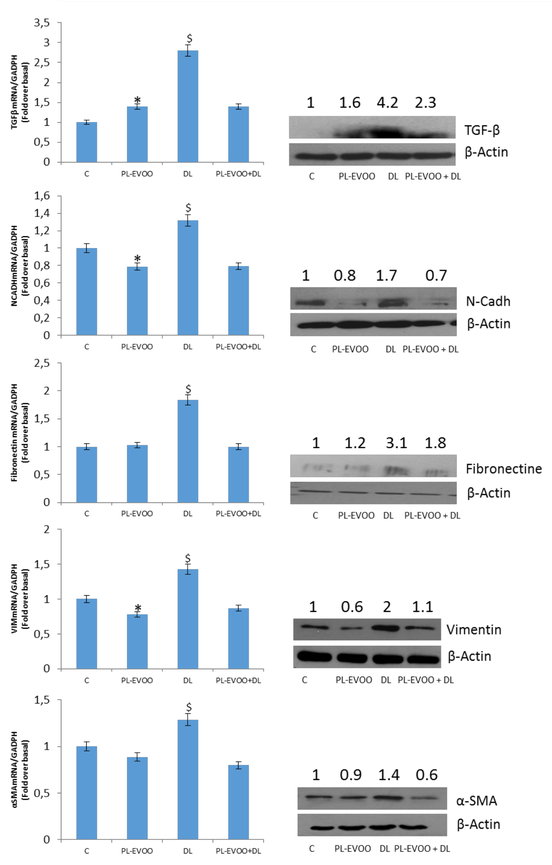

Figure 1. Genic and protein expression of MMT markers in IMC subjected to chronic treatment with DY and/or PL-EVOO (6 days) *p < 0.05 vs untreated cells(C); $p< 0.05 vs treated cells with PL-EVOO+DL.

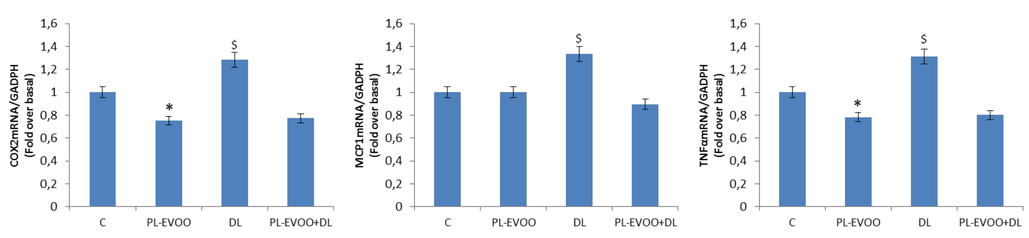

Figure 2. Genic expression of infiammatory markers in IMC subjected to chronic treatment with DY and/or PL-EVOO (6 days). *p < 0.05 vs untreated cells(C); $p< 0.05 vs treated cells with PL-EVOO+DL

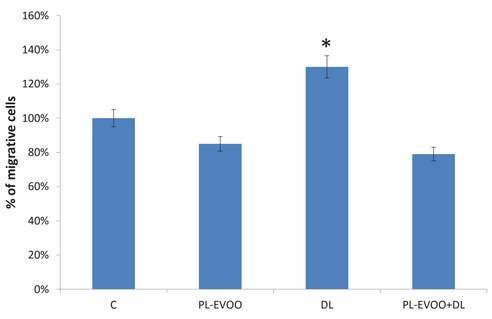

Figure 3. Migration assay in IMC subjected to chronic treatment with DL and/or PL-EVOO (6 days). *p < 0.05 vs treated cells with PL-EVOO+DL

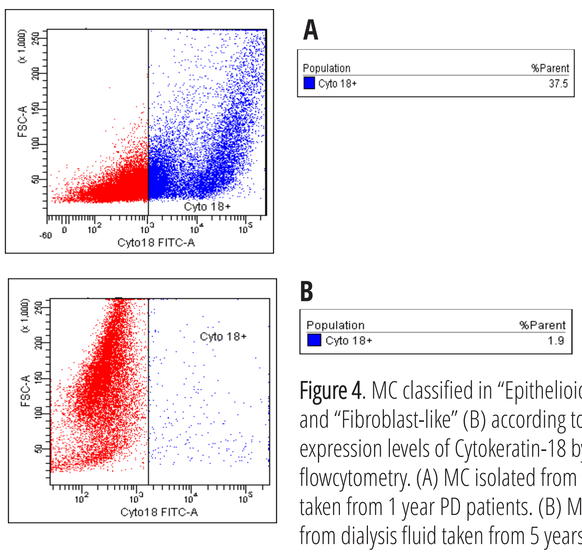

Figure 4. MC classified in "Epithelioid-like" (A) and "Fibroblast-like" (B) according to the expression levels of Cytokeratin-18 by flowcytometry. (A) MC isolated from dialysis fluid taken from 1 year PD patients. (B) MC isolated from dialysis fluid taken from 5 years PD patients.

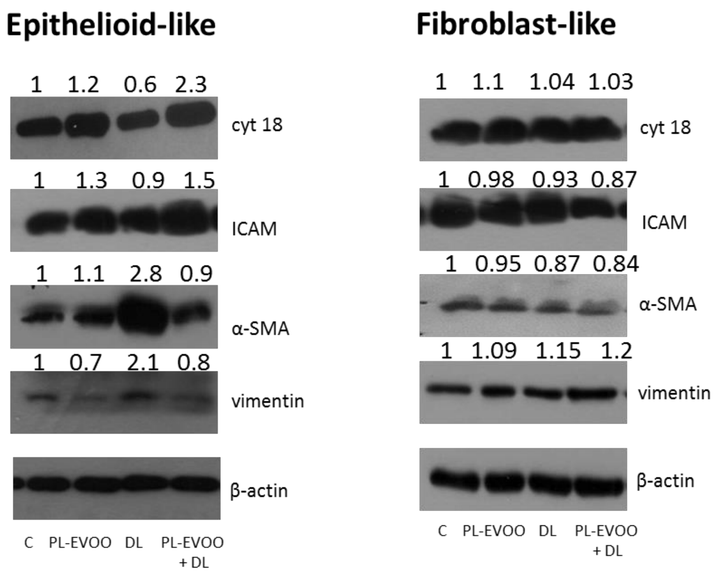

Figure 5. Protein expression of MMT markers in MC subjected to chronic treatment with DY and/or PL-EVOO (6 days).

CONCLUSIONS

OUR DATA DEMONSTRATED THAT PL-EVOO COULD EXERTS A PROTECTIVE EFFECT ON CHRONIC DAMAGE INDUCED BY DL ON MESOTHELIAL CELLS BEFORE THEY HAVE ACQUIRED THE "FIBROBLAST-LIKE" PHENOTYPE.

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