ROLE OF ADSORPTION IN THE REMOVAL OF ATHEROSCLEROSIS-ASSOCIATED MEDIATORS BY DIFFERENT DIALYSIS MEMBRANES

Nans Florens1, Benjamin Malard2, Corine Lambert2, and Laurent Juillard1
1Hospices Civils de Lyon, Nephrology, Lyon, France, 2Gambro Industries, MTO Department, Meyzieu, France

Introduction and Aims: Atherosclerosis is an important predictor of mortality in patients with chronic kidney disease and is associated with a wide inflammatory response. A potential benefit derived from removing atherosclerosis-associated mediators is suggested by either oxidative stress limitation and/or preventing plaque disruption. In the present in vitro study we investigated the role of adsorption as a depuration mechanism for 17 molecules using 3 dialysis membranes in a closed loop model.

Methods: We used an in vitro model of hemofiltration using 3 different membrane materials HeprAN, polymethylmethacrylate (PMMA) and polyethersulfone (PES). A human plasma pool (V=1.5L) was pre-incubated with chemokines, cytokines, complements factors in either pathological or supra pathological concentrations and was then filtered in a closed loop model (QB=300ml/min, QUF=60ml/min, V=500ml) simultaneously with the different membranes during 240 min. Respective concentrations of each molecule were measured over time in plasma and ultrafiltrate using enzyme-linked immunosorbent assay to document the removal speed and contribution of adsorption in the global depuration process. At circulation end, each membrane was eluted successively with four different buffers by either ionic (NaCl 1M, glycine pH 2.25) or hydrophobic (glycine pH 11, SDS 2%) desorption mechanism. Electrophoretic patterns were obtained using both Tris-Tricine [1,060 -26,000 Da] and Tris-Glycine [12,300-78,000 Da] gels. The experiment was repeated 3 times with pre-incubation of TNF-α only to document the model variability.

Results: Most of the investigated mediators were effectively removed with the different dialysis membrane. Adsorption mechanism showed a maximal removal speed in the region of 10,000 to 20,000 Da (calculated over the first 10 min of circulation). Especially, negatively charged HeprAN showed overall higher adsorptive clearance than the other membranes, suggesting that the material chemical structure is an important determinant in the depuration mechanism. TNF-α was further significantly removed with HeprAN and PMMA compared to PES (p<0.01) at session end. Qualitative analysis using electrophoresis indicated a preferential selectivity of ionic nature with HeprAN material and of hydrophobic origin with PES. No predominant affinity was observed with PMMA.

Conclusions: Depuration by adsorption was shown to be a potentially important mechanism to target inflammatory molecules associated with atherosclerosis. Future studies are needed to assess the potential therapeutic benefits of adsorptive dialysis membranes towards atherosclerosis progression.