DIALYSIS MEMBRANE PORE SIZE DOES NOT DETERMINE LPS RETENTION

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Introduction and Aims

Ultrapure dialysis fluid having low bacterial and lipopolysaccharide (LPS) content is beneficial by reducing the inflammatory load of dialysis. It is often hypothesized that dialysis membranes having larger pores are less effective in retaining LPS in dialysis fluid and that the use of ultrapure fluid therefore gets more important as membrane pore size increases. The purpose of this study was to challenge this hypothesis for membranes that are commonly used in hemodialysis, in particular low-flux, high-flux and high cut-off membranes.

Methods

Test items were mini-dialyzers containing hollow-fiber membranes with a 3-layer structure and made of polyarylethersulfone (PAES) and polyvinylpyrrolidone (PVP) polymer blends that are typically used in filters for hemodialysis. The polymer system and the inner membrane surface of 360 cm² were kept constant and only pore size was varied. Pore sizes as pore radius of the membranes were determined by their dextran sieving characteristics according to Boschetti-de-Fierro et al [International Journal of Artificial Organs, 2013, 36, 455-463]. LPS retention was tested in a closed loop in vitro circuit simulating a hemodialysis treatment setting on bench-top scale. The membranes were exposed to human plasma for 40 minutes and were intensively rinsed afterwards. The circuit was filled with bicarbonate based dialysis fluid and LPS from E.coli O55:B5 was added to the dialysate side. The LPS load corresponded to about 10 times the acceptable dose of standard dialysis fluid. After 20 minutes recirculation without ultrafiltration and 20 minutes recirculation with ultrafiltration from dialysate to blood side and ultrafiltration rate of 16 % of the blood side flow, LPS concentrations were measured on the blood and dialysate side by the chromogenic kinetic limulus amebocyte lysate assay. The logarithmic retention value (LRV) as the decadic logarithm of the dialysate and blood side LPS concentration ratio was taken as measure for endotoxin retention capacity.

Results

Pore radius and LRV values for the different membranes are given in the table as mean values ± standard deviation of 3 independent experiments.

Membrane type	Pore radius [nm]	LRV
Low-flux membrane	3.1 ± 0.2	2.8 ± 0.2
High-flux membrane	4.5 ± 0.2	3.3 ± 0.3
High-flux membrane with extended permeability	6.5 ± 0.2	3.5 ± 0.1
High cut-off membrane	10 ± 2.0	3.3 ± 0.5

Discussion

For the 3-layer PAES/PVP membrane type tested, the pore size did not have a significant impact on the LPS retention capacity. These findings disprove the hypothesis that such membranes with larger pores are less effective in retaining LPS. Consequently, these results indicate that ultrapure dialysis fluid quality does not need to be considered a general condition for using dialysis membranes with larger pores. The results are in agreement with earlier work by Schindler et al [Blood Purification, 2006, 24, 203-211] and the LPS retention properties of the investigated membranes can be explained by the formation of high molecular weight aggregates of LPS molecules in dialysis fluid and a mixed retention mechanism for LPS comprising size exclusion and adsorption.

Summary

- The relation of pore size and retention properties of LPS was investigated
- In vitro simulations of dialysis treatments were performed
- For the 3-layer PAES/PVP membrane type tested, the pore size did not have a significant impact on the LPS retention capacity
- The results indicate that ultrapure dialysis fluid quality does not need to be considered a general condition for using dialysis membranes with larger pores.
- Further experiments can be used to explore the retention mechanism

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