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Purifying Capacity of Polynephron a New Membrane Evolution of Standard Polyetheresulphone

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Abstract

Introduction: *The absorbing capacity of membranes can be considered the third dimension of the depurative action of dialysis: diffusion, convection and adsorption. Some metabolites are almost totally bound to albumin, so, regardless of their molecular weight, removal with low flux or high flux dialysis membranes becomes difficult if not impossible. The aim of our work was to evaluate the purifying efficacy of a new membrane (Polynephron) for the different physico-chemical types of uraemic solutes : small water-soluble compounds , Low Molecular Weight Proteins (LMWP) , Protein Bound Uremic Toxins (PBUT) .*

Materials and Methods: *Four patients (3M / 1 F) of average age 74.8 ± 1.7 y and dialysis 21.8 ± 12.4 months in three-weekly dialysis were evaluated. All patients switched to the Nipro Elisio 21H dialyser filter, for 3 online HDF sessions. In every piece, blood tests were performed at the beginning and end of each dsession to evaluate besides the purification of the main standard parameters, also the removal of medium molecular weight solutes such as myoglobin, beta2 microglobulin and solutes such as indoxyl sulfate (IXS l) and pcresol (PCS l) which represent less than 10% of the free fraction being bound to albumin for more than 90% of their total concentration (IXS and PCS t). The statistical differences, before and after dialysis, were calculated with the Student's t test for paired data.*

Results: *At the end of the 3 HDF sessions there was a significant decrease in both the low molecular weight parameters with a good KT / V and a urea clearance close to 300 ml / min . Serum Albumin and Total proteins increased during HDF but the correction for Hemoconcentration did not show any variation .The concentrations of the parameters at medium PM were reduced by 50-75% , while total PCS was reduced by 27,6%, total IXS by 33,1 % , free PCS and IXS by 53,9 % and 62,2%.*

Conclusion: *In addition to the high diffusional purifying capacity, the membrane shows a partial absorptive capacity demonstrated by the effective removal of metabolites linked to albumin and therefore more difficult to remove. It will be interesting to follow in time the absorptive capacity of this membrane and its clinical implication, especially in comparisons of cardiovascular and atherosclerotic diseases that appear to be related to the concentrations of these metabolites, practically impossible to remove with standard membranes.*

1. INTRODUCTION

The purifying capacity of membranes can be considered three-dimensional in the dialysis process: diffusion, convection and adsorption. Small solutes and middle molecules are easily removed by diffusion and more by convection . On the contrary some metabolites are almost totally bound to albumin,so, independently from their molecular weight , removal with standard dialysis membranes becomes difficult if not even impossible (1). The Polynephron membrane (second generation high – flux polyetheresulphone membrane) functions similarly to a human kidney as regards solute-removal performance : a 3D chemical structure enables a mixture of hydrophilic and hydrophobic domains, while reducing membrane fouling and maximising membrane performance. Advanced pore-spinning technology of this new dialysis membrane creates more homogenous pore sizes to optimisesieving properties. Ripple structure of fibre creates less dialysate channelling, promoting improved diffusive transportation while enhancing small molecule clearances, and reducing the risk of fibre leakage (1,2). The aim of our work was to evaluate the purifying efficacy of this new membrane for the different physico-chemical types of uraemic solutes: small water-soluble

compounds, Low Molecular Weight Proteins (LMWP), Protein Bound Uremic Toxins (PBUT).

2. Materials and Methods

Four patients (3M / 1 F) of average age 74.8 ± 1.7 y and dialysis 21.8 ± 12.4 months in three-weekly dialysis were evaluated. All patients switched to the Nipro Elisio 21H dialyser filter, for 3 online HDF sessions. In every piece, blood tests were performed at the beginning and end of treatments, for the 3 HDF sessions (21 lt infused per session in on – line post- dilution, time per session 4 hours), to evaluate the purification of the main standard serum parameters, also the removal of medium molecular weight solutes such as myoglobin, beta2 microglobulin (immunonefelo-metric methods) and protein bound solutes such as indoxylsulfate (IXS) and pcresol (PCS) which represent less then10% of the free fraction being bound to albumin for more than 90% of their total concentrations (IXS and PCS t). Total and free serum IXS and PCS were analyzed in frozen (-20°C) serum samples (the stability of the two compounds allows this condition). The method involves the denaturation and precipitation of serum total proteins for the separation of the supernatant, on which the total PCS and IXS will be measured (sum of the protein bound fraction and the un bound fraction). The free fraction of these metabolitesis achieved by centrifugal filtration in order to remove the binder's proteins. The dosage is performed by HPLC / MSMS using PCS-D4 as internal standard. The statistical differences, before and after dialysis, were calculated with the Student's test for paired data.

3. Results

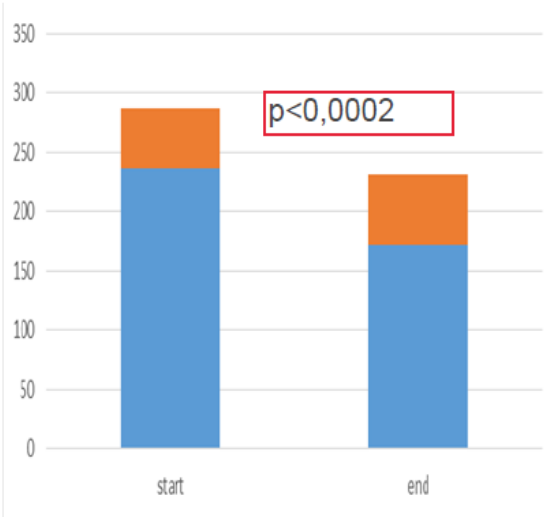
At the end of the 3 on line HDF sessions, there was a significant decrease of serum Creatinine and P ,respectively by 67 % and 63 % (tab 1) with a good KT / V and a high urea clearance (280 ± 17 ml / min) . Serum Albumin and Total proteins increased during HDF but the correction for Hemoconcentration did not show any variation (tab 2). The concentrations of the parameters at medium PM were reduced by 50-75% (Fig 1), while total PCS was reduced by 27,6%, total IXS by 33,1 % , free PCS and IXS by 53,9 % and 62,2 % (Fig 2).

Table1. *Low molecules serum concentrations decrease during HDF (*p<0,0001)*

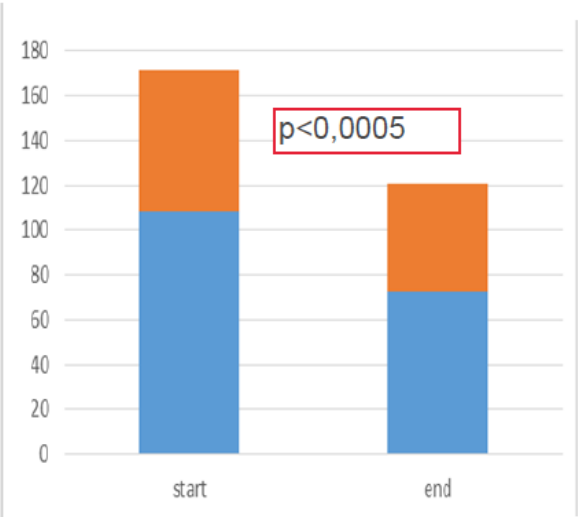
	Creatinine mg/dl	Na mEq/l	K mEq/l	Ca mg/dl	P mg/dl	KT/V	Cl. Urea ml/min
start	9,3±2,7	139±2	5,3±0,7	8,9±0,6	4,6±0,9	1,5±0,1	280±18
end	3,03±1,03 *	141±2	4,1±0,5	9,5±0,8	1,6±0,5 *		

Table2. *SerumHemoglobin, Total Proteins and Albumin behaviour during HDF. Hemo concentration does not modify their values*

	Hb gr/dl	Total Proteins gr/dl	Albumin gr/dl
start	10,4±1,6	6,24±0,3	3,6±0,41
end	12±2,02	7,13±0,74	4,03±0,7



Total P cresol (mg/l)



Total Indoxylsulfate (mg/l)

Free P Cresol(mg/l) Free Indoxylsulfate (mg/l)

Fig1. *Protein Bound UremicToxins behaviour , during HDF performed with Elisio 2,1 H (Standard deviation)*

ß2 microglobulin(mg / dl) Myoglobin (mg/dl)

Fig2. *Middle molecules behaviour (ß2 microglobulin,Myoglobin) , during HDF performed with Elisio 2,1 H (Standard deviation)*

4. Discussion and Conclusions

Despite advances in renal replacement therapy, the adequate removal of uremic toxins over a broad molecular weight range remains one of the unmet needs in hemodialysis. Therefore, membrane innovation is currently directed towards enhanced removal of uremic toxins and increased membrane permeability. Some metabolites are almost totally bound to albumin, so, regardless of their molecular weight, removal with standard low flux or high flux dialysis membranes becomes difficult if not even impossible. At this regard current trend in dialysis membrane engineering is to maximize the permeability for larger molecular weight proteins while retaining albumin. Differently from protein-leaking of old standard dialysis membranes that do not meet these requirements : particularly in convective procedures, such as hemodiafiltration, their albumin leakage is too high (3-8). Studies have evaluated the clearance of protein-bound uremic toxins (PCS and IXS) using different types of dialysis: standard high- flux membranes showed no improvement in clearance of these two toxins , given that the increased permeability of high-flux membranes is isolated primarily to large, non-protein-bound solutes (8-10). The addition of convective transport to conventional dialysis has also been investigated, albeit with conflicting findings: two cross-over studies reported opposing effects of HDF on dialysis clearance, although both studies failed to show a superior benefit on post treatment plasma concentration of the toxins. Thus, it appears that diffusive transport should be combined with convection to obtain an essential tool to improve the removal of protein-bound uraemic solutes (3-10).

POLYNEPHRON™, the membrane which is built into the new Nipro ELISIO® dialyzer, is a

new dialysis membrane, produced by applying an innovative spinning technique. The incentive of its development was to improve the characteristics of an existing dialysis membrane (polyetheresulfone), i.e., realizing a steeper sieving profile for low-molecular weight proteins with-out significant loss of essential larger proteins at best biocompatibility properties, for a more adequate dialysis therapy (1). In addition to the high purifying performance capacity as regards low and middle molecules, the Polynephron membrane showed a significant purification of PBUT , although not completely satisfactory , probably through a partial absorptive capacity or a particular capacity of solute entrappment, which would be demonstrated by the effective removal of metabolites linked to albumin and therefore more difficult to remove (1,2, 5,6) . Even if previous work would explain the removal of protein-related metabolites with the loss, during the dialysis session, of 5/6 g of albumin,our data do not seem to confirm these results because at the end of the dialysis sessions, total protidemia and albumin even if increased, when applied for hemo concentration remained practically unchanged. It will be interesting to follow in time the potential capacities of this "high performance" membrane and its clinical implication, especially in relation to cardiovascular and atherosclerotic diseases that seem to be related to the concentrations of these metabolites, practically impossible to remove with standard membranes.

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