Comparison between High-flux Hemodialysis and Online Hemodiafiltration as a Renal Replacement Therapy in End Stage Renal Disease Patients as Regards Nutritional Parameters

Thesis

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وأنزل الله عليك
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Haitham Mohammed Abdel Hakeem

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List of abbreviations

BUN : Blood urea nitrogen
Ca : Calcium
CRP : C-reactive protein
EPO : Erythropoietin
HDL : high density lipoprotein
HFHD : High-flux hemodialysis
LDL : Low density lipoprotein
LFHD : Low flux hemodialysis
max : Maximum
MIA : Malnutrition, inflammation, atherosclerosis
min : Minimum
n : Number
OLHDF : Online hemodiafiltration
PCR : Protein catabolic rate
PO4 : Phosphorus
Post-creat : Post dialytic creatinine
Post-urea : Post dialytic urea
Pre -creat : Pre dialytic creatinine
Pre-urea : Pre dialytic urea
PTH : Parathyroid hormone
SD : Standard deviation
TGD : Triglycerides
Wt : Weight
TMP **: Trans membrane pressure**

MIA :Malnutrition,Inflammation and atherosclerosis

LBM :Lean Body mass

CRI : chronic renal impairment

DOPPS : Dialysis Outcomes and Practice Pattern Study

AGEs :advanced glycosylation endproducts

DRA :Dialysis Related amyloidosis

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Introduction

Haemodialysis (HD) is predominantly a diffusive process designed to clear small solutes ***(Lowrie et al., 1981).*** Studies have shown that additional HD treatment to increase urea clearance does not appear to improve dialysis patient survival ***(Ekonyan et al., 2002).***

This led to the hypothesis that larger solutes may be important in determining medium- to longer-term dialysis patient survival ***(Davenport et al., 2010).***

To increase the spectrum of solutes cleared during HD, dialysers with greater pore size have been developed, and over the past 30 years, the proportion of patients dialyzing with high-flux membranes has increased compared to low-flux dialysers ***(Vernon et al., 1992).*** Also the clearance of middle sized solutes can be increased further by dialyser membranes designed to increase internal filtration ***(Kerr et al., 1992).***

Hemodialysis treatment modalities are commonly classified according to membrane 'flux' (from Latin fluxus, a flowing, and variant of fluere, to flow). The term, together with the prefixes 'low' or 'high' is an indication of the size range of substances a particular membrane or dialyzer is able to remove, i.e. of its relative permeability ***(Bowry et al., 2011).***

As such, low- or high- flux membranes or therapies are highly general terms and do not allude to any specified or defined size ranges of uremic toxins – which themselves are also arbitrarily and variously classified according to solutes being small, middle or large ***(Bowry et al., 2011).***

Such is the generality of the terms 'low flux' and 'high flux' that it is often overlooked that developments in membrane technology, together with product positioning strategies of industry, has led to a change in the meaning and perception of the terms over recent years ***(Bowry et al., 2011).***

Membranes once considered as high flux only a decade or two ago are now categorized as low flux with the consequence that considerable confusion arises during interpretation of published data ***(Bowry et al., 2011).***

In the HEMO Study, for instance, where the effects of flux and dialysis dose on patient's survival were examined, dialyzers allocated to the high- flux group can, according to European perspectives, essentially be adjudged as low flux ***(Bowry et al., 2011).***

Patients requiring hemodialysis have the option of the following treatment modalities: LF- HD, HF- HD, HDF (hemodiafiltration) or HF (hemofiltration). Each modality differs in terms of the extent to which it relies on diffusion and convection, the two predominant solute transport mechanisms in dialysis ***(Ledebo et al., 2002).***

Adsorption (affinity of molecules for membrane material), is theoretically the third mechanism of removal occurring more by chance than by specific design and cannot precisely be catered for in any of the four treatment options ***(Ofsthun et al., 1995).***

Diffusive transport, driven by differences in concentrations in the blood and dialysate compartments, has the limitation that the rate of diffusion in free solution decreases with increasing molecular weight Thus, the relative contribution of diffusion to overall transport decreases the larger the solute. Diffusion also decreases with increasing membrane wall thickness ***(Ofsthun et al., 1995).***

Convection, which is the predominant mechanism of solute removal across the glomerular membrane, is a consequence of ultrafiltration of fluid across the dialysis membrane wall having a specified structure ***(Ledebo et al., 2002).***

Ultrafiltration, in turn, is affected by a number of factors such as transmembrane pressure gradient and properties of blood (flow, hematocrit and blood viscosity, plasma proteins, etc.) ***(Ronco et al., 2002).***

Both diffusion and convection are determined by the morphological characteristics of the dialysis membrane, i.e. the dimensions (pore size) and structure (degree of porosity) of the membrane wall ***(Ronco et al., 2002).***

Convection is the extent to which solutes (depending on their sieving at the separating region of the membrane) are 'dragged' along by the removed fluid (depending on hydraulic permeability of the support region of the membrane) ***(Ledebo et al., 2002).***

For the four treatment modalities in question, diffusive solute transport decreases in this order: LF- HD ~ HF- HD ~ HDF ~ HF. Solute transport in LF- HD is predominantly based on diffusive principles, having in reality a minor convective component depending on pore dimensions ***(Ofsthun et al., 1995).***

Conversely, convective transport decreases in this order: HF ~ HDF ~ HF- HD ~ LF- HD, with HF (without fluid in the dialysis compartment) being purely convective, having the highest High- flux membranes are thus used for all modalities except for LF- HD ***(Ronco et al., 2002).***

The Significance of Large Exchange Volumes In convective therapies like HF and HDF, convective transport is maximized by extensive ultrafiltration beyond the volume needed to achieve dry weight ***(Ledebo et al., 1998).***

To benefit fully from the convective component for blood purification, large fluid volumes need to be utilized ***(Ronco et al., 2007).*** By operating at peak UFR relative to the blood flow rates achievable for individual patients, high convective clearances for the larger uremic toxins can be achieved ***(Ledebo et al., 1998).***

With the availability of large quantities of highly pure dialysis and substitution fluids, prepared 'on- line', UF volumes well beyond 15 liters are commonly realized ***(Canaud et al., 2006).***

Increased convection and removal of large quantities of fluid have been associated with several clinical advantages pertaining to decreased uremic toxin load, anemia correction, reduction of calcium- phosphate product, improved hemodynamic stability and vascular stability and to lower inflammation, an underlying condition of most diseased states ***(Canaud et al., 2006).***

The degree of convective transport is thus decisive from an overall clinical point of view; by removing (and replacing) larger volumes of fluid from the patient during on- line HDF (the most efficient treatment modality removing small and large solutes), more efficient blood cleansing is achieved ***(OK et al., 2011).***

Consistent with mechanistic considerations, the results of three independent studies involving large numbers of patients have indicated that a survival advantage is evident with high-volume on- line HDF The volume of substitution, a surrogate of the convective dialysis dose, may thus be considered as a critical factor that may impact patient mortality rates ***(OK et al., 2011).***