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Hemodiafiltration (HDF) versus expanded hemodialysis (HDx)

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Abstract

Medium cutoff (MCO) membranes have resulted in a novel dialyzer class designed to improve membrane permeability and have been postulated as an alternative to online hemodiafiltration since MCO membranes may achieve similar solute clearances. These membranes have been incorporated into clinical practice, and the term expanded HD (HDx) has been proposed to differentiate from high-flux hemodialysis. Efficacy, safety, and quality of life comparison of HDF versus HDx have been reviewed in this article.

1 | INTRODUCTION

Advances in the physicochemical composition of dialyzers, specifically the cutoff and the internal architecture of the pores, have resulted in a novel class called medium cutoff (MCO) membranes, designed to improve membrane permeability and get closer to the behavior of the glomerular filtration barrier.[1–3] Although MCO membranes maintain high solute clearance of less than 10 kDa molecules, they achieve good removal capacities for middle and large-middle molecules (in the range of 10–50 kDa) in hemodialysis (HD) treatments while maintaining an acceptable marginal albumin loss compared with high cutoff membranes.[4] For these reasons, MCO membranes have recently been incorporated into clinical practice, and the term *expanded HD* (HDx) has been proposed to define a treatment that conveniently combines diffusion and convection inside a hollow fiber dialyzer equipped with an MCO membrane.[5] HDx has been postulated as an alternative to online hemodiafiltration (OL-HDF) since MCO membranes may achieve similar solute clearances.[5–9]

Post-dilution online hemodiafiltration (post-HDF) has progressively evolved and can be considered a safe, fully consolidated treatment with multiple clinical advantages.[10] The ESHOL study reported longer survival in patients receiving post-HDF,[11] and post hoc analysis of three randomized clinical trials with mortality as the primary endpoint showed an association between convective volume and survival.[11–13] In this regard, obtaining a replacement volume greater than 21 L per session has been recommended to achieve this survival benefit.[14]

For its part, pre-dilution HDF (pre-HDF), more commonly used in Japan because of its use of low blood flow rates (Qb), has also been associated with longer survival compared with HD.[15] The Japanese Society for Dialysis Therapy reported that the pre-dilution mode was adopted in 90.8% of patients undergoing online HDF, with a mean volume of substitution fluid per session of 40.6 L, while the remaining 9.2% of the patients received post-HDF with a mean substitution fluid volume of 9.2 L.[16]

2 | EFFICACY COMPARISON OF HDF VERSUS HDX

Several papers have reported data on the reduction ratio of low, middle, and large molecular weight uremic toxins as dialysis efficacy surrogates. All of these studies report that the clearance of middle and large weight molecules is superior with HDx compared to high-flux HD.[17–22] However, this higher reduction ratio has not been clearly related to a reduction in long-term serum levels.[23] Moreover, HDx also seems to maintain this superiority over HD in short-daily HD performed at home.[24]

Nevertheless, there is a disparity in results when comparing the reduction ratios obtained with HDx with those of HDF. Some studies report better reduction ratios with MCO membranes than with HDF,[7,25] while others report noninferiority of HDx versus post-HDF,[9,26–29] and others still report slightly lower removal.[8,22] This disparity indicates that different factors involved in the dialysis treatment may impact the efficacy of each or both techniques.

Two of these potential confounding factors, the membrane surface area and Qb, which are determinant in both HD and HDF, have been studied in HDx. There is evidence that an incremental surface area of the MCO membrane from 1.7 to 2.0 m^2 does not translate into greater removal of small and large molecules, while an increase in Qb from 300 to 450 ml/min does enhance clearance of small molecules but not that of middle and large molecular weight molecules in a comparable short treatment time. None of these dialysis treatment modifications significantly impacts albumin loss.[30]

Another potential element is the dialysis technique, which has been explored in two articles assessing the differences between removal and the properties of HDx compared with those of HD, pre-HDF, and post-HDF, with low Qb showing that HDx is superior to HD and pre-HDF and close—but inferior—to post-HDF.[31,32]

When post-HDF is prescribed, the dialyzer membrane should also be chosen with caution, because the performance of the different dialyzers varies, even when other dialysis parameters remain unchanged.[9,22,33,34] Studies comparing HDF with polyamide[25,26,35] and first-generation helixone[28] filters versus HDx obtained slightly inferior results compared with last-generation polysulfone filters.[8,9,22]

The influence of the amount of convective volume in HDF seems to be decisive in achieving or enhancing the performance of HDx. One study reported that HDF had greater efficacy than HDx when the ultrafiltration flow and convective volume exceeded certain values.[36] In this regard, HDF was superior to HDx with convective volumes of 19.2 and 17.6 L, with Qb of 350 and 400 ml/min, respectively; these figures are far lower than the recommended 23 L proven to achieve survival benefits.[36]

3 | SAFETY COMPARISON OF HDF VERSUS HDX

The safety of MCO dialyzers is ensured by restricting pore sizes to limit albumin losses below 5 g per session.[4,37] In this regard, most published studies report that MCO membranes lead to a higher albumin loss than HD and show inconsistent results compared to HDF,[7–9,17,22,28,38,39] although in all cases the loss could be considered clinically tolerable in certain conditions that remain to be clearly defined. However, it is crucial to mention that these membranes should only be used in HD mode, as a case report has described how MCO membrane used for HDF led to increased albumin losses with a progressive reduction in serum levels.[40]

Some studies show that serum albumin levels either remain stable or show only a temporary drop.[19,21,26,28,41,42] This innocuous albumin loss may be due to activation of albumin synthesis in the liver and may be desirable to facilitate protein-bound toxin clearance.[5,23]

On the other hand, there is a need to elucidate the potential negative effects of the higher permeability of MCO membranes with an increase in the clearance of other substances such as medications, vitamins, trace elements, amino acids, peptides, and hormone binding proteins, especially in frail dialysis patients, who are predisposed to malnutrition.[38] In this regard, it is already known that permeability to bacterial products such as endotoxins or pyrogens is not increased in HDx[43,44]; indeed, HDx shows a lower infection rate than HD.[39] Furthermore, in an in vitro study, the retention of erythropoietin, heparin, insulin, vancomycin, and several coagulation factors is comparable between HD, HDF, and HDx.[45]

There are scarce data exploring if MCO membranes confer cardiovascular benefits compared with other dialysis modalities. On the contrary, HDF has been associated with improved cardiovascular survival compared with HD.[46,47] The CARTOON trial addressed the non-inferiority of HDx to HDF in terms of cardiovascular outcomes and reported that coronary artery calcium scores seemed to be worsening with HDx compared to HDF.[48]

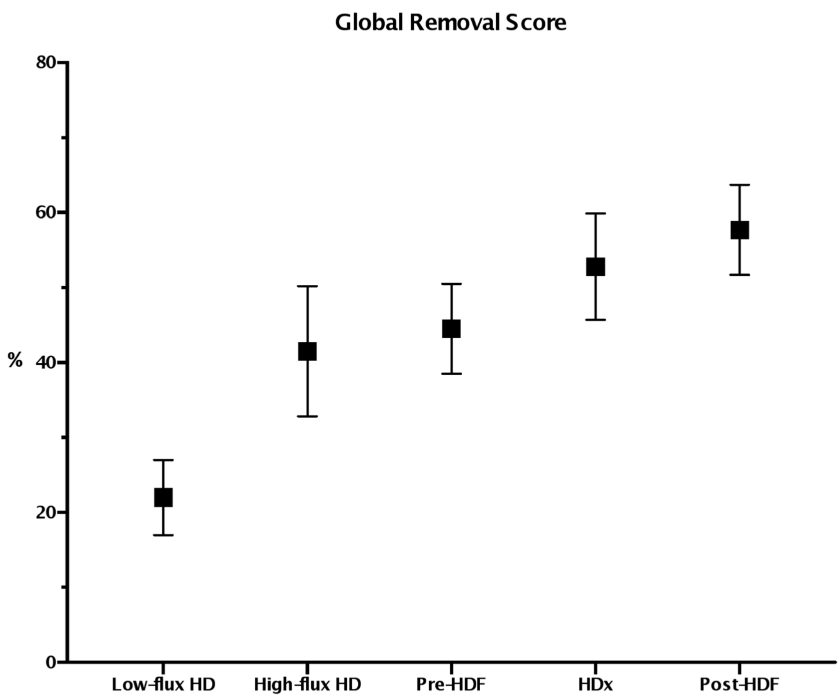

FIGURE 1 Estimated global removal score values in low-flux HD, high-flux HD, pre-dilution HDF, expanded hemodialysis, and post-dilution HDF modalities. $Global\ removal\ score = \frac{Urea_{RR} + \beta_2\ microglobulin_{RR} + Myoglobin_{RR} + Prolactin_{RR} + \alpha_1\ microglobulin_{RR} + \alpha_1\ acid\ glycoprotein_{RR} - Albumin_{RR}}{6}$

4 | QUALITY OF LIFE HDF VERSUS HDX

Some studies have focused on patients' quality of life under HDx treatment, but in comparison with HD. To date, there is no head-to-head study having compared quality of life or patient-reported outcomes in HDx versus HDF.

5 | CONCLUSIONS

Although long-term randomized clinical trials with hard outcome data are still lacking, the results of short-term and observational studies appear to be promising as they show that HDx with MCO membranes has a remarkable efficacy close to that seen with HDF and with no safety concern, confirming benefits of internal convective clearances.

The current positioning of HDx compared with the rest of dialysis modalities, expressed in a simple and practical way as the global removal score,[9] is represented in Figure 1, which shows that HDx represents the closest alternative to post-HDF and is clearly superior to HD and pre-HDF.

CONFLICT OF INTERESTS

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