

The use of different dialysis membranes in therapy of patients with multiple myeloma

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Abstract

Free light chains accumulation is the reason of kidney injury in patients with multiple myeloma. The removal of free light chains can improve patients prognosis and survival, and in some cases allows for dialysotherapy discontinuation. Unfortunately, conventional dialysis is not effective enough in terms of free light chains removal. New high cut-off (HCO) techniques remove free light chains more effectively than conventional dialysis. In some cases, this technique may turn out better than hemodiafiltration. However, there are some differences between specific techniques in the removal of kappa and lambda light chains. Lambda light chains are better removed by polymethyl methacrylate membranes with a change of filter during dialysis. Kappa light chains are thoroughly removed by polymethyl methacrylate membranes and HCO (35,000 Da) polysulfone membranes. Unfortunately, it is very difficult to differentiate between the effect of HCO dialysis therapy and concomitant chemotherapy because some of the data is not fully conclusive. Using the proper technique for an individual patient may give optimally effective treatment results.

Key words: treatment, multiple myeloma, dialysis membranes

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Introduction

Conventional hemodialysis is unable to remove effectively the circulating free light chains in patients with multiple myeloma (MM). New high cut-off (HCO) dialysis techniques make it possible to decrease levels/concentrations of free light chains, especially with simultaneous chemotherapy treatment. Hemodiafiltration with ultrafiltrate regeneration on resin using 'super-high-flux' (polyphenylene super-high-flux (S-HF), with a nominal cut-off of 42 kD) membrane also effectively decreases free light chains concentrations. This kind of hemodiafiltration does not have any influence on albumin concentration.¹ Using HCO membranes allows for stopping dialysis in some patients with MM (3 out of 5 in this study).²

Utilizing HCO membranes was associated with a higher rate of hemodialysis independence at 6 months (56.5% HCO hemodialysis vs 35.4% conventional hemodialysis) and 12 months (60.9% HCO hemodialysis vs 37.5% conventional hemodialysis). The frequency of adverse effects was similar in both groups (43% of complications connected with hemodialysis in the HCO group in comparison to 39% in the conventional group), and mortality was similar in both groups.³

Similar results were achieved in terms of dialysis independence after 6 and 9 months of treatment when HCO dialysis membranes with bortezomib were used – 6 out of 10 patients no longer needed dialysis, compared to 2 out of 10 patients undergoing conventional dialysis with bortezomib.⁴

Other authors found that in patients with MM, using HCO membranes results in lower mortality in comparison to conventional membranes. The survival rate after 1 year of treatment was 25% in the group of patients dialyzed using HCO dialyzer compared to 0% when a conventional dialysis was performed. Complete renal response rate, defined as an increase from <50 mL/min to >60 mL/min for at least 2 months, was 10.5% among patients treated with HCO dialyzers compared to 0% among patients treated with conventional dialysis. Partial renal response rate, defined as an increase of estimated glomerular filtration rate (eGFR) from <15 mL/min to 30–59 mL/min, was 15.8% and 5.3% in HCO dialysis- and conventional dialysis-treated patients, respectively, while minor renal response rate, defined as an increase from <15 mL/min to 15–29 mL/min or from 15–29 mL/min to 30–59 mL/min, was 26.3% and 15.8% in HCO dialysis- and conventional dialysis-treated patients, respectively. Increased survival rate of patients and renal response rate correlated with a decrease of free light chains concentration. Total treatment costs were comparable in both groups of patients treated with usage of HCO membranes and conventional dialysis.⁵ While HCO membranes are more expensive than conventional ones, better overall treatment results lead to decreased total treatment costs, offsetting the higher price of HCO membranes.⁶

Polymethylmethacrylate membranes

The use of adsorptive membranes, such as polymethylmethacrylate-based BK-2.1 membrane, was also associated with better outcomes among patients with myeloma and cast nephropathy.⁷

Combining Theralite 2100 SUPRA device (Bellco, Mirandola, Italy), bortezomib and dexamethasone treatment resulted in a decrease of free light chains concentrations ranging from 72.8% to 99.7% in 3 weeks. Response to treatment was achieved in 80% of patients with acute kidney injury in the course of MM.⁸

High cut-off membranes dialysis effectively diminished free light chains concentrations in patients with acute kidney injury. A total of 11.6 six-hour HCO dialysis sessions per patient were performed, with free light chains decreasing by 93.7% in the course of treatment. Single dialysis session decreased free light chains by about 57.7%.⁹

On the other hand, a comparison of dialysis using polymethyl methacrylate membranes (PMMA), one of the most common HCO dialysis membranes, with conventional dialysis for patients simultaneously treated with bortezomib indicate no differences between these modalities after 3 months of treatment. The results of treatment were dependent on the hematologic response for treatment (56% of patients with hematological response and 6.7% of patients without hematologic response were independent from dialysis).¹⁰

Double polymethacrylate membranes

Nonetheless, it was proved that the double polymethylmethacrylate filter (DELETE system) (Toray BK-F; Toray Industries, Inc., Tokyo, Japan) was effective in terms of free light chain removal in chronic dialysis patients with MM.¹¹

Exchange of PMMA filter after 2 h of dialysis increased lambda light chains removal rates compared to classic PMMA, as it mitigated rapid PMMA saturation with free lambda chains, which diminishes their efficacy in removing the lambda chains. This kind of dialysis is called enhanced adsorption dialysis (EAD). The reason of this phenomenon is fast PMMA saturation with free lambda chains. Saturation of PMMA with free light chains decreases free lambda light chains removal efficacy.

This phenomenon was not observed in kappa light chains removal. It is suggested that the EAD method may be important in the treatment of MM patients with high concentrations of lambda light chains.¹² High cut-off PMMA dialysis removes free light chains mainly through adsorption. In the course of hemodiafiltration, more free light chains are removed than in the used dialysis solution. High cut-off PMMA removes kappa light chains more effectively than hemodiafiltration.¹³

Other membranes

More effective clearance of kappa light chains compared to lambda light chains was observed also in 24 h dialysis using a HCO (35,000 Da) polysulfone membrane.¹⁴ Light chains appear not only in MM; they are classified as free medium urea toxins. Comparison of free dialysis membranes: PMMA, polyphenylene HFR17 filter and conventional polysulfone filter F7HPS in terms of kappa and lambda free light chains removal indicates that PMMA and polyphenylene HFR17 filter are more effective than conventional polysulfone filter F7HPS.¹⁵

Efficacy control

It should be taken into account that dialysis membranes with nominally the same parameters may have a different efficacy of clearance.¹⁶ The structure of monoclonal protein is different in every patient and the real efficacy of free light chains should be controlled. Free light chains concentration should be checked every week of dialysis treatment.¹⁵ Actually, published data indicates that better prognosis is correlated with the extent of free light chain reduction in serum.⁵

Controversies

Contrary to the data indicating the superiority of HCO hemodialysis over conventional dialyzers, there are 2 multicenter randomized controlled trials in which this superiority was not confirmed. In MYRE study (98 participants and 48 hospitals in France), no statistically significant difference was shown in the hemodialysis independence rate between patients treated with HCO compared to conventional hemodialysis for 3 months (41.3% and 33%, respectively, $p = 0.42$), although a significantly higher clearance of light chains in HCO dialyzers group was noticed.³ Significant difference in hemodialysis independence appeared 6 and 12 months of treatment (56.5% vs 35.4% and 60.9% vs 37.5%, respectively) but, as the authors of MYRE study concluded, these results should be considered exploratory. In EuLITE study (90 patients and 16 hospitals in UK and Germany), hemodialysis independence was observed in 56% of patients treated with HCO dialyzers and in 51% patients in the standard hemodialysis group ($p = 0.81$). More infections were observed as adverse events in HCO hemodialysis group, including lung infections (26 vs 13 infections, 14 vs 3 lung infections).¹⁷


Summary


The efficacy of HCO dialysis membranes in terms of diminishing free light chains resulted in guidelines of the International Myeloma Working Group Recommendations

for the Diagnosis and Management of Myeloma-Related Renal Impairment: The use of HCO dialyzers in combination with anti-myeloma therapy should be considered (grade B).¹⁸ The use of HCO dialyzers in combination with anti-myeloma therapy seems to be a good option for treating patients with MM. However, future studies should precise the indications for this therapy.

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