Online high-efficiency haemodiafiltration achieves higher serum free light chain removal than high-flux haemodialysis in multiple myeloma patients: preliminary quantitative study

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Abstract

Background. Fast reduction of serum free light chain (FLC) levels correlate with renal recovery in cast nephropathy. Because convection has the capacity to remove proteins of higher molecular weights, we hypothesized that haemodiafiltration (HDF) would be superior to haemodialysis (HD) for FLC clearance.

Methods. We retrospectively identified all renal replacement therapy (RRT) sessions performed in multiple myeloma patients with pre- and post-treatment FLC measurements during a 2-year period. Using kinetic modelling, we calculated reduction percentages corrected for net ultrafiltration, effective clearances, net mass removal and Kt/V for both kappa (κ) and lambda (λ) serum FLC.

Results. We analysed 27 (10 HD and 17 HDF) RRT sessions realized in a total of six subjects. HDF resulted in higher FLC removal rates when compared to HD. Moreover, high-efficiency (i.e. substitution volume > 15 L/ses- sion) HDF demonstrated median efficient FLC clearances roughly twice superior to high-flux HD for both κ (59.0 versus 33.8 mL/min, respectively; P < 0.01) and λ (40.5 versus 19.7 mL/min, respectively; P = 0.02) FLC. In post-dilution HDF treatments, corrected FLC reduction percentages positively correlated with substitution volumes. Total plasma proteins increased during RRT in the HDF group.

Conclusions. This preliminary quantitative study demonstrates the superiority of high-efficiency HDF over high-flux HD for serum FLC removal in multiple myeloma patients on RRT. No negative impact on total plasma proteins was noted.

Keywords: haemodiafiltration; haemodialysis; kidney failure; multiple myeloma; serum free light chains

Introduction

Renal impairment is a frequent complication of multiple myeloma, being present in ~20% to almost half of newly diagnosed cases depending on the definition used [1–5]. On the more severe part of the spectrum, acute kidney injury (AKI) requiring renal replacement therapy (RRT) can be present in up to 10% of patients at diagnosis [3, 6]. In the latter, ~90% of kidney biopsies will show a diagnosis of cast nephropathy [7] in which serum free light chains (FLC) are directly implicated by coprecipitating with Tamm-Horsfall protein in the distal tubule [8–13].

While kidney involvement independently portends a worse prognosis in most studies [1–3, 6], patients who recover renal function have been reported to fare better than those who do not [2, 3, 7, 14]. Recent data looking at renal involvement in multiple myeloma has clearly shown a positive linear relationship between the extent of serum FLC decreases at Day 12 and the proportion of patients recovering independent renal function [15]. While effective chemotherapy represents the cornerstone of the light chain-reducing armamentarium (by decreasing monoclonal protein production) [16], even novel drug regimens are insufficient by themselves to achieve high-kidney recovery rates in dialysis-dependent multiple myeloma patients (only ~20% in a multiple bortezomib series [17–20]).

From this perspective, different methods of removing monoclonal proteins have been evaluated for their capacity to achieve faster reductions in plasma loads and better renal outcomes. Plasma exchange has been the first such therapy evaluated but the largest study to date evaluating its effectiveness in AKI patients has been negative on a composite end point [21]. Moreover, mathematical modelling has shown its inability to decrease plasma light chain burdens in the absence of an almost complete tumour kill [16]. More recently, haemodialysis studies using two filters with a high-molecular weight cutoff (HCO 1100 filters; Gambro...
Dialysis atoren GmbH, Hechlingen, Germany) in series have shown both in vitro and in vivo efficacy for FLC removal [16] and encouraging results in a small prospective trial [7]. However, high cost, elevated protein leakage requiring albumin perfusions after treatments and calcium and magnesium wasting are drawbacks of its utilization.

High-efficiency (i.e. substitution volume > 15 L/session) haemodiafiltration (HDF), an RRT that is widely available and likely cheaper than dialysis with HCO filters, is known to remove molecules of higher molecular weights than haemodialysis (HD) [22–24]. Kappa (κ) and lambda (λ) FLC being of apparent molecular weights between that of β2-microglobulin (β2M) and albumin (22.5 kDa and dimeric 7.45 kDa) [25], we hypothesized that HDF would be more efficient than HD to reduce their levels. We report hereafter the data collected at our institution looking at the removal of serum FLC with HD and online HDF in patients with multiple myeloma.

Materials and methods

Patient population and characteristics

We retrospectively identified all patients with kidney failure and multiple myeloma, according to the International Myeloma Working Group (IMWG) criteria [26], treated with RRT at our institution from January 2008 through December 2009. RRT sessions with both pre- and post-treatment FLC assays were identified with the help of hospital’s medical results database (Mediweb v6.1.3; Agfa Healthcare, Mortsel, Belgium). Patients with at least one such treatment were included in the study.

For every patient included, a revision of the hospital medical file was undertaken to record the patients’ demographic and anthropometric characteristics. Multiple myeloma (type, stage, date of diagnosis, organ involvement and chemotherapy) and renal failure characteristics (type, kidney biopsy, contributing factors, estimated glomerular filtration rate at RRT start and presence of chronic kidney disease) were registered for every patient.

RRT characteristics

Treatment parameters were recovered for every RRT session with the help of the institution’s dialysis database (FileMaker Pro 7.0v3; FileMaker, Santa Clara, CA). Whenever treatment data were not available electronically (treatment in the ambulatory or intensive care units), the patients’ medical files were recovered from the hospital archives and paper dialysis flow sheets were used. For every treatment included in the study, we recorded the dialysed used, treatment modality (high- or low-flux HD; pre-, post- or mixed-dilution HDF), mean blood and dialysate flow rates, substitution volume (HDF), session length, weights before and after treatment, and ionic Kt/V whenever the information was available. Concomitant pre- and post-treatment total plasma proteins were also recorded using the medical results database.

Sample collection and FLC assays

The blood samples for serum FLC were collected by the attending nurse immediately before treatment start (pre-treatment concentration) and after dialysis from the arterial blood line using the slow-flow method (post-treatment concentration). Serum κ and λ FLC concentrations were measured by nephelometry on a Siemens BN1 analyser using the FREELITE immunoassay (The Binding Site, Birmingham, UK). Normal serum reference ranges and sensitivity for this test have been described previously [27].

Calculations

FLC reduction ratios were calculated using the usual equation:

\[
\text{Reduction ratio} = \frac{C_{\text{pre}} - C_{\text{post}}}{C_{\text{pre}}},
\]

where \(C_{\text{pre}}\) and \(C_{\text{post}}\) are serum FLC concentrations pre- and post-treatment, respectively. Reduction percentages were calculated by multiplying the reduction ratio by 100%.

Because immunoglobulin FLC are somewhat small proteins, they distribute evenly in extracellular water [28]. This is similar to β2M kinetic, the proteins being of comparable molecular weights. We therefore utilized a single-compartment kinetic model already described for β2M [29] to correct post-dialysis FLC measurements for net ultrafiltration:

\[
C_{\text{post-corr}} = C_{\text{post}}/(1 + ΔBW/ECV),
\]

where \(C_{\text{post-corr}}\) denotes the concentration of FLC after RRT corrected for net ultrafiltration; ΔBW is the difference between pre-treatment and post-treatment body weights; and ECV is the extracellular volume of body fluids after RRT. This last parameter was calculated as equal to one-third of the total body water established by Watson’s anthropometric formula [30].

Using the same kinetic model, we were also able to estimate serum FLC effective clearance with the following calculation, as described previously [31, 32]:

\[
K_d = (ΔBW/T) \times \left[1 - \log\left(C_{\text{post}}/C_{\text{pre}}\right)/\log\left(ΔBW/ECV\right)\right],
\]

where \(K_d\) is the effective clearance and \(T\) is the treatment time. In the event that no net ultrafiltration had taken place during the treatment session (i.e. ΔBW = 0), clearance was estimated by dividing the FLC mass removed by the product of FLC time-averaged concentration (TACFLC) and treatment time:

\[
K_d = (C_{\text{pre}} - C_{\text{post}}) \times ECV/\left(T\times \text{TACFLC}\right).
\]

We then calculated the mass of removed serum FLC by multiplying effective clearance by session length and TACFLC. Finally, multiplying effective FLC clearance by the treatment time and dividing by the post-treatment extracellular fluid volume enabled us to calculate the Kt/V for serum FLC.

Statistical analysis

Statistical significance of between-group differences was analysed using two-tailed Student’s t-test, Type 2 (homoscedastic) or 3 (heteroscedastic) according to F-test difference of variance results. When comparing pre- and post-treatment results for the same RRT session, Type 1 analysis for paired samples was used. Correlation analyses were undertaken using Pearson’s product-moment coefficient and associated P-test using online statistics software [33]. P level <0.05 was considered significant.

Results

During the period under study, we identified 37 RRT sessions with pre- and post-treatment FLC assays in six multiple myeloma patients. Patient characteristics are given in Table 1. Crucial treatment parameters could not be recovered in 10 sessions that were consequently excluded from analysis.

Of the remaining 27 sessions, 10 (37.0%) were HD treatments and the others, HDF (high efficiency in 11). Treatment parameters are shown in Table 2. In the HD group, dialysate data could be retrieved for eight sessions. Of these, six were high-flux treatments: four were provided with HF80s (Fresenius Medical Care, Bad Homburg, Germany) filters and two, with protein-adsorptive BK-F (Toray Industries Inc, Tokyo, Japan) membranes. Two low-flux HD sessions were done using F8 (Fresenius Medical Care) filters. On the other hand, all HDF treatments were completed with HF80s haemofilters except for two: one treatment each with an FX1000 (Fresenius Medical Care) and an Elissio 210H (Nipro Medical Corporation, Osaka, Japan) filter were recorded. HDF substitution volume was injected after the filter (post-dilution) in every session except for
HDF increases FLC removal over HD

Table 1. Characteristics of multiple myeloma patients included in the studya

<table>
<thead>
<tr>
<th>No.</th>
<th>Gender/age</th>
<th>Myeloma type (peak serum FLC level)/Durie-Salmon stage</th>
<th>Chemotherapy regimen (haematological responseb)</th>
<th>Renal biopsy/renal diagnosis</th>
<th>Concomitant factors</th>
<th>eGFRc at initiation of RRT</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F/60</td>
<td>Relapsing IgG λ MM (4 440 mg/L)/III B</td>
<td>Lena, Dex, Mel, Dex (progressive disease)</td>
<td>No/ARF</td>
<td>HyperCa+</td>
<td>6</td>
</tr>
<tr>
<td>2</td>
<td>F/58</td>
<td>New onset λ LC MM (987 mg/L)/III B</td>
<td>Bort, Dex (very good partial response)</td>
<td>No/ARF</td>
<td>NSAIDs</td>
<td>6</td>
</tr>
<tr>
<td>3</td>
<td>M/59</td>
<td>New onset λ LC MM (444 mg/L)/II B</td>
<td>Bort, Dex (very good partial response)</td>
<td>Yes/CKD, crescentic GN</td>
<td>None</td>
<td>Prevalent on RRT</td>
</tr>
<tr>
<td>4</td>
<td>M/40</td>
<td>New onset κ LC MM (31 400 mg/L)/III B</td>
<td>Bort, Dex (very good partial response)</td>
<td>Yes/ARF, cast nephropathy</td>
<td>None</td>
<td>5</td>
</tr>
<tr>
<td>5</td>
<td>M/54</td>
<td>Relapsing κ LC MM (2 560 mg/L)/II B</td>
<td>Bort, Dex, Lena, Mel, Dex, Bort, Dex, Doxo</td>
<td>Yes/CKD, LCDD</td>
<td>HyperCa+</td>
<td>Prevalent on RRT</td>
</tr>
<tr>
<td>6</td>
<td>M/64</td>
<td>λ LC MM in very good partial response (132 mg/L)/III B</td>
<td>post Mel, HSCT (stable disease)</td>
<td>No/CKD</td>
<td>HyperCa+</td>
<td>Prevalent on RRT</td>
</tr>
</tbody>
</table>

aGFR, estimated glomerular filtration rate; IgG, immunoglobulin G; MM, multiple myeloma; LC, light chain; Lena, lenalidomide; Dex, dexamethasone; Mel, melphalan; Bort, bortezomib; Doxo, pegylated liposomal doxorubicin; HSCT, haematopoietic stem cell transplantation; ARF, acute renal failure; CKD, chronic kidney disease; GN, glomerulonephritis; LCDD, light chain deposition disease; HyperCa+, hypercalcaemia; NSAIDs, non-steroidal anti-inflammatory drugs; F, female; M, male.
bDefined according to the International Myeloma Working Group (IMWG) uniform response criteria for multiple myeloma [34].
cCalculated using four variable MDRD equation (in mL/min/1.73 m²).

Table 2. RRT treatment parametersab

<table>
<thead>
<tr>
<th>Modality</th>
<th>No.</th>
<th>Median blood flow rate (mL/min)</th>
<th>Median (IQR) dialsate flow rate (mL/min)</th>
<th>Median (IQR) substitution volume (L)</th>
<th>Median session length (min)</th>
<th>Median (IQR) net UF volume (L)</th>
<th>Median (IQR) ionic Kt/V</th>
</tr>
</thead>
<tbody>
<tr>
<td>HD</td>
<td>10</td>
<td>400</td>
<td>600 (500–700)</td>
<td>N/A</td>
<td>240</td>
<td>2.7 (2.1–3.1)</td>
<td>1.38 (1.23–1.60)</td>
</tr>
<tr>
<td>HDF</td>
<td>17</td>
<td>400</td>
<td>500 (500–650)</td>
<td>24.0 (18.3–25.6)</td>
<td>240</td>
<td>1.7 (1.1–2.6)</td>
<td>1.40 (1.38–1.47)</td>
</tr>
</tbody>
</table>

aUF, ultrafiltration.
bNo statistically significant between-group differences.

one session of each of pre-dilution, mixed-dilution and unknown dilution missing data.

Median reductions in raw serum FLC levels were significantly higher in the HDF versus HD group when considering both κ (57.5 versus 24.1%, respectively; P < 0.01) and λ (37.7 versus 14.1%, respectively; P = 0.02) FLC. High-efficiency HDF performed better than high-flux HD for both FLC types (59.9 versus 26.1%, respectively; P < 0.01) and 41.8 versus 14.1%, respectively; P < 0.02) FLC. This difference was even more manifest when comparing high-efficiency HDF to high-flux HD for both κ (65.0 versus 38.7%, respectively; P < 0.01) and λ (47.7 versus 25.4%, respectively; P = 0.02) FLC (Figure 1). There was a statistically significant linear correlation between κ (r = 0.61; P = 0.04) as well as λ (r = 0.58; P < 0.05) corrected FLC reduction percentages and substitution volumes in the post-dilution HDF group (Figure 2a), while dialsate and blood flow rates did not correlate (data not shown) and an inverse linear correlation was found with treatment time (r = −0.69; P = 0.01 for κ and r = −0.56; P = 0.06 for λ). When looking at the association between treatment parameters, a negative linear correlation was found between
Significance (clearances show a trend in the same direction without reaching statistical significance).

Table 3. Summary of κ and λ FLC removal values by RRT modality a,b

<table>
<thead>
<tr>
<th>RRT modality (n)</th>
<th>Corrected reduction (%)c</th>
<th>Effective clearances (mL/min)</th>
<th>Kt/V</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>κ</td>
<td>λ</td>
<td>κ</td>
</tr>
<tr>
<td>HD (10)</td>
<td>36.6 (30.7–45.4)</td>
<td>25.4 (16.2–35.7)</td>
<td>0.65 (0.06–0.48)</td>
</tr>
<tr>
<td>HDF (17)</td>
<td>59.9 (54.4–67.5)</td>
<td>47.7 (36.3–55.7)</td>
<td>0.31 (0.20–0.48)</td>
</tr>
<tr>
<td>P</td>
<td>&lt;0.01</td>
<td>0.04</td>
<td></td>
</tr>
<tr>
<td>hf HD (6)</td>
<td>38.7 (33.4–45.4)</td>
<td>25.4 (24.8–30.4)</td>
<td></td>
</tr>
<tr>
<td>h-e HDF (11)</td>
<td>65.0 (56.7–71.1)</td>
<td>47.7 (36.3–55.7)</td>
<td></td>
</tr>
<tr>
<td>P</td>
<td>&lt;0.01</td>
<td>0.02</td>
<td></td>
</tr>
</tbody>
</table>

Note: Results are expressed as median (IQR).

 treatment length and substitution volume (r = −0.71; P < 0.01). Finally, κ FLC reduction ratios were higher than their λ counterparts, both in HD (P = 0.02) and HDF (P < 0.01) treatments.

Median efficient treatment clearances estimated with equation 3 or equation 4, whichever was appropriate, were higher in the HDF than in HD groups for both κ (59.0 versus 29.0 mL/min, respectively; P < 0.01) and λ (32.0 versus 19.7 mL/min, respectively; P = 0.04) FLC (Figure 3). Similar results were found when comparing high-efficiency HDF to high-flux HD for κ (59.0 versus 33.8 mL/min, respectively; P < 0.01) and λ (40.5 versus 19.7 mL/min, respectively; P = 0.02) FLC. Effective clearance values were linearly correlated with substitution volumes in the post-dilution HDF group but statistical analysis did not reach significance (r = 0.55; P = 0.07 for κ and r = 0.53; P = 0.07 for λ) (Figure 2b). Higher median-effective clearances were achieved with high-flux than with low-flux HD treatments for κ (33.8 versus 6.4 mL/min, respectively; P = 0.01) while the difference was not statistically different for λ (19.7 versus 3.4 mL/min, respectively; P = 0.69) FLC. However, no difference was noted between high-flux membranes with and without adsorbent capacities (data not shown). Once again, removal was significantly higher for κ than for λ FLC in both HDF (P = 0.01) and HD (P = 0.01) treatment groups.

When analysing the median-estimated net mass removed per treatment session, we compared patients with κ and λ multiple myeloma separately. We noted a trend in higher FLC mass removal in κ multiple myeloma patients with HDF than with HD treatments (16.6 versus 4.5 g/session, respectively; P = 0.10). The trend was weaker when comparing patients with λ producing myelomas (HD 0.8 g/session versus HD 0.6 g/session; P = 0.65). Finally, median-estimated Kt/V for κ serum FLC was higher in the HDF versus HD group (0.97 versus 0.50, respectively; P < 0.01) while the difference did not reach statistical significance when analysing λ serum FLC (HDF 0.57 versus HD 0.31; P = 0.06) (Figure 4). On the other hand, high-efficiency HDF was statistically superior to high-flux HD for both FLC types (1.11 versus 0.54, respectively; P < 0.01 for κ and 0.68 versus 0.31, respectively; P = 0.02 for λ).

Fig. 2. Serum FLC reduction percentage corrected for fluid removal (a) and clearance (b) as a function of substitution volume in post-dilution HDF. Corrected reduction percentages show a linear correlation, both for κ (r = 0.61; P = 0.04) and λ (r = 0.58; P < 0.05) FLC, while clearances show a trend in the same direction without reaching statistical significance (κ, r = 0.55; P = 0.07 and λ, r = 0.53; P = 0.07).

Fig. 3. Box-plot representation of estimated kappa (KL) and lambda (LL) serum FLC effective clearance levels, for HD and HDF treatment groups. Estimated FLC clearances were higher in the HDF than in HD groups for both κ (59.0 versus 29.0 mL/min, respectively; P < 0.01) and λ (32.0 versus 19.7 mL/min, respectively; P = 0.04) FLC.
Concomitant pre- and post-treatment total plasma proteins were available in 10 HDF and 4 HD sessions. Plasma proteins increased with RRT treatments in the HDF group [median + 2.5 g/L, interquartile range (IQR) 0.3–7.5 g/L; P = 0.04] and showed a trend in the same direction for the HD group (median + 1.5 g/L, IQR 0.3–4.3 g/L; P = 0.36).

Discussion

Higher reduction ratios and clearance values for both κ and λ serum FLC in the HDF versus HD group is in agreement with previous studies showing an increased removal of middle- and high-molecular-weight proteins with convective therapies [22–24]. The statistically significant linear correlation between corrected serum FLC reductions and the treatment convection volumes in the post-dilution HDF group clearly underlines the importance of convection in increasing FLC removal. Moreover, when looking at Figure 2, one can appreciate that high substitution volumes (e.g. >25 L/session) are needed in order to fully maximize the clearance potential of post-dilution HDF. This could also explain to a large extent why Hutchison et al. [35], using substitution rates of 55 and 56 mL/min (representing just over 13 L of substitution volume per 4 h session), found that post-dilution HDF using a HCO filter increased FLC clearances over simple HD but not to the extent achieved with HD using two HCO filters in series. Taken together, these facts substantiate the predominant role of convective dose in the removal of FLC and middle molecular weight molecules.

The lower reduction ratios and effective clearances of λ when compared to κ FLC, both in HD and HDF groups, can be mainly explained by the twice higher molecular weight of the dimeric λ chains. On this account, the main haemofilter used for both HD and HDF treatments in our study was the Fresenius HF80s, which has a molecular cutoff of ~35 kDa (between that of κ and λ FLC apparent molecular weights). This size limitation could have therefore lowered the sieving coefficient of λ light chains in comparison to κ. Other theoretical explanations could reside in different adsorption properties of the filters and charge and polymerization differences between the two light chain types [36].

The analysis of FLC mass removal per treatment session showed a trend in higher removal in the HDF versus HD group but was relatively low in both groups for λ FLC. This can be explained, in part, by the quite low pre-treatment monoclonal FLC levels in our patients with λ light chain secreting myelomas (median 153 mg/L) compared with their κ counterparts (median 679 mg/L). This is also in accordance with previous work demonstrating that the amount of FLC in dialysate fluid is strongly correlated with pre-dialysis serum FLC concentrations [16].

One surprising data that needs further discussion is the strong inverse correlation that we found between treatment session length and corrected FLC reduction percentages. This could be explained by the retrospective design of our study and the inevitable biases that one such study is fraught with. In fact, treatment session length could have been increased in response to treatment interruptions in patients prone to hypotension or other treatment complications or with poor access blood flow (acute catheters) in order to achieve prescribed dialysis dose. To substantiate this affirmation, we noticed a statistically significant inverse correlation between treatment length and substitution volume delivered. It seems therefore probable that the association of lower FLC removal with increased treatment time was not causal but mediated by decreased substitution volumes.

Finally, our results need to be compared with previous work looking at FLC removal with dialysis. Median FLC reduction rates in the high-efficiency HDF group (κ 59.2% and λ 41.8%) appear lower than that previously described with HCO dialysis in patients who received uninterrupted (κ 69% and λ 71%) or interrupted (κ 65% and λ 72%) chemotherapy [7]. However, HCO treatment regimen consisted of treatment session lengths of 8 h (twice as long as the median treatment time in our study) for the first 2 weeks and then 6 h thereafter. Albeit protein blunting of the filters is of concern with longer treatment sessions [35], this difference in session durations could have nonetheless resulted in higher FLC mass removal and therefore, greater reduction percentages in their work. Moreover, when comparing instantaneous FLC clearances, our results seem higher with high-efficiency HDF than with two HCO filters in series for κ (median 59.0 mL/min versus mean 25.6 and 25.5 mL/min) but similar for λ (median 40.5 mL/min versus mean 42.9 and 33.0 mL/min) serum FLC [16]. This could represent a real increase in average FLC removal with high-efficiency HDF but important differences between the two studies preclude such a conclusion. First of all, in the previous work by Hutchison et al., the clearance rates were calculated using FLC dialysate content while our results rely on pre- and post-treatment serum measurements solely. Therefore, some theoretical dialysis membrane adsorption of serum FLC would have been included in our calculations but not in those on HCO filters. Secondly, our clearance calculations are based on kinetic modeling that could have overestimated (delayed equilibration of serum FLC between interstitial and vascular compartments, omission of endogenous and renal clearances) or underestimated (myeloma FLC production during RRT sessions not taken.
into account) treatment clearances. Therefore, further studies are needed before firm conclusions regarding high-efficiency HDF clearances of serum FLC can be drawn.

Other limitations of our study reside in its retrospective nature, small number of patients, lack of intrapatient comparisons between modalities and absence of information on clinical outcomes. Regarding this last point, it would be of outmost interest to see if the increase in FLC clearances with HDF translates into faster and more sustained serum FLC reductions and, ultimately, increased renal recovery rates in cast nephropathy patients. However, our study design precludes us from answering these questions at the moment, we believe it brings sufficient preliminary data to help design prospective clinical studies that could do so in the future.

In the end, this preliminary retrospective work clearly shows the superiority of HDF over HD, and more specifically of high-efficiency HDF over high-flux HD, in removing serum FLC in a population of multiple myeloma patients. This advantage is strongly positively correlated with substitution volume in post-dilution mode, therefore substantiating the crucial role of convective dose in this improved FLC removal. However, more work is needed in order to compare high-efficiency HDF serum FLC clearances with that achieved by other therapies described in the literature (plasma exchange, HCO dialysis). Should high-efficiency HDF provide similar removal rates to the latter, clinical studies would be justified owing to a likely lower cost and absence of albumin leakage with high-efficiency HDF.

Acknowledgements. The authors are indebted to Annie Rodriguez who provided help on this work and Aline Chulon (The Binding Site) who provided help on this work and Aline Chulon (The Binding Site) who supplied the FLC assays at no charge. A.G.V. has benefited from a fellowship grant from the Fondation du Centre Hospitalier de l'Université de Montréal (CHUM).

Conflict of interest statement. None declared.

References

Comparison of Molecular Adsorbents Recirculating System (MARS) dialysis with combined plasma exchange and haemodialysis in children with acute liver failure

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Abstract

Background. Molecular Adsorbents Recirculating System (MARS) is an extracorporeal liver support system eliminating albumin-bound and water-soluble substances. While it is increasingly applied in patients with acute liver failure (ALF), no comparison with standard dialysis methods has yet been performed.

Methods. This is an analysis of ten children (0.1–18 years) with ALF, who underwent a total of 22 MARS sessions. Standard adult MARS sets were used in seven (23.5–72 kg) and MARS Mini in three children (2.8–13 kg). In eight children, MARS was alternated with combined plasma exchange (PE) and haemodialysis (HD) treatments. Mean treatment duration was 7.2 (6–10) h for MARS and 5.7 (4.5–6.6) h for PE/HD.

Results. Standard MARS treatment only slightly decreased serum bilirubin (16.3 ± 6.5–13.8 ± 5.9 mg/dl) and ammonia (113 ± 62–99 ± 68 μmol/L) and international normalized ratio (INR) tended to increase (1.5 ± 0.3 and 2 ± 1.1). Mini-MARS did not reduce serum bilirubin (19.7 ± 3–20.5 ± 3.2 mg/dl), ammonia slightly decreased (70 ± 24–56 ± 9 μmol/L) and INR increased (2.5 ± 0.7–2.9 ± 1.1, all P = n.s.). In contrast, PE/HD reduced serum bilirubin (23 ± 8.4–14.7 ± 7 mg/dl), ammonia (120 ± 60–70 ± 40 μmol/L) and INR (2.4 ± 0.8–1.4 ± 0.1, all P < 0.05). Intraindividual comparison showed a slight increase in bilirubin by 2 ± 22% with MARS and a reduction by 37 ± 11% with PE/HD (P < 0.001 versus MARS) and a decrease in ammonia of 18 ± 27 and 39 ± 23% (P < 0.05). INR increased during MARS by 26 ± 41% and decreased with PE/HD by 37 ± 20% (P < 0.01). All treatment sessions were well tolerated. Five children died, including the three children treated with Mini-MARS.

Conclusion. Our experience suggests superior efficacy of combined PE/HD as compared to intermittent MARS therapy for treating ALF.

Keywords: children; haemodialysis; liver failure; molecular adsorbents recirculating system; plasma exchange

Introduction

Acute liver failure (ALF) is a rare but life-threatening disorder. In children, it is most commonly observed as acute-on-chronic disease, secondary to metabolic disorders or is caused by infection [1]. In adults, paracetamol intoxication predominates [2]. Whereas liver function recovers in more than one-third of patients on supportive management [2, 3], liver transplantation is required in cases of persistent ALF. Likewise, the majority of patients with acute-on-chronic liver failure and with progressive chronic hepatic disease require liver transplantation. Limited organ availability often results in considerable bridging time to transplantation, causing an increasing need for effective liver support therapies.