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Original Paper

Serum Free Light Chains Removal by HFR Hemodiafiltration in Patients with Multiple Myeloma and Acute Kidney Injury: a Case Series

Paolo Menè[a] Elisa Giammarioli[a] Claudia Fofi[a] Giusy Antolino[b] Giacinto La Verde[b] Agostino Tafuri[b] Giorgio Punzo[a] Francescaromana Festuccia[a]

[a]Division of Nephrology, Dept. of Clinical and Molecular Medicine, Sant'Andrea University Hospital, "Sapienza" University of Rome, [b]Division of Hematology, Plasma cell Dyscrasias and Multiple Myeloma Unit, Sant'Andrea University Hospital, "Sapienza" University of Rome, Italy

Key Words
Free light chains • Hemodiafiltration • HFR-SUPRA • Multiple myeloma • Acute kidney injury

Abstract
Background/Aims: Multiple myeloma (MM) represents 10% of all haematologic malignancies. Renal involvement occurs in 50% of MM patients; of them, 12-20% have acute kidney injury (AKI), with 10% needing dialysis at presentation. While hemodialysis (HD) has no effect upon circulating and tissue levels of monoclonal proteins, novel apheretic techniques aim at removing the paraproteins responsible for glomerular / tubular deposition disease. High cut-off HD (HCO-HD) combined with chemotherapy affords a sustained reduction of serum free light chains (FLC) levels. One alternative technology is haemodiafiltration with ultrafiltrate regeneration by adsorption on resin (HFR–SUPRA), employing a "super high-flux" membrane (polyphenylene S-HF, with a nominal cut-off of 42 kD). Aim of our pilot study was to analyze the effectiveness of HFR-SUPRA in reducing the burden of FLC, while minimizing albumin loss and hastening recovery of renal function in 6 subjects with MM complicated by AKI. ***Methods:*** Six HD-dependent patients with MM were treated with 5 consecutive sessions of HFR-SUPRA on a Bellco® monitor, while simultaneously initiating chemotherapy. Levels of albumin and FLC were assessed, calculating the rates of reduction. Renal outcome, HD withdrawal and clinical follow-up or death were recorded. ***Results:*** All patients showed a significant reduction of FLC, whereas serum albumin concentration remained unchanged. In three, HD was withdrawn, switching to a chemotherapy alone regimen. The other patients remained HD-dependent and died shortly thereafter for cardiovascular complications. ***Conclusion:*** Our study suggests that HFR-SUPRA provides a rapid and effective reduction in serum FLC in patients with MM and AKI,

Paolo Menè, MD

Chair and Division of Nephrology, Sant'Andrea University Hospital,
Via di Grottarossa 1035-1039, 00189 Rome (Italy)
Tel. +39 (06) 3377-5949, E-Mail paolo.mene@uniroma1.it

while minimizing the loss of albumin. When started early in combination with chemotherapy, blood purification by HFR-SUPRA was followed by the recovery of renal function in half of the patients treated.

Introduction

Multiple Myeloma (MM) is a plasma cell dyscrasia mostly affecting elderly individuals. It represents approximately 10% of all hematologic malignancies and 1% of all malignancies in general [1].

This disease is characterized by a single clone of B cells accounting for >10% of all cells in bone marrow, and producing monoclonal immunoglobulin (Ig) components that become apparent as a separate electrophoretic peak in serum [2].

New chemotherapeutic agents have improved overall patient survival over the past decade [3, 4]. However, renal dysfunction still represents one of the most unfavourable prognostic factors in MM, occurring in 20 to 50 % of all patients at the onset [5, 6, 7]. Up to 40 % of all patients display kidney damage of mild or moderate grade [5], while severe acute kidney injury (AKI) occurs in approximately 9% of cases [6, 8]. Recovery of renal function is a predictor of improved survival [9], although AKI requiring HD is often irreversible [8].

Renal involvment is due to different mechanisms. In general, tubular damage occurs in 80% of cases and glomerular injury in 20%. Severe AKI is often caused by "cast nephropathy", one major component of the so-called "Myeloma Kidney" (MK) complex [10]. This condition is due to obstruction and tubular/interstitial damage upon precipitation of the monoclonal free light chains (FLC) of Ig as intratubular casts [10, 11]. Tubular obstruction is often triggered by dehydration or high-dose diuretic therapy, with subsequent enhanced water reabsorption and intraluminal concentration of paraproteins.When treatment is delayed, this phenomenon can lead to irreversible damage.

A linear relationship has been described between the probability of renal recovery and both the degree and speed of FLC reduction [12]. A reduction of more than 50% of FLC concentration is needed [13] to achieve renal rescue. In view of tubular obstruction and the known direct tubular toxicity of FLC, the goal of any therapy for MK should be to reduce exposure of the kidney to FLC [10, 13].

Rapid inhibition of FLC production from plasma cell clones by chemotherapy might not yield an immediate reduction of serum concentrations, since the clearance of pre-existing FLC is already impaired by renal dysfuction [14, 15]. Therefore, the kidney might be exposed to elevated levels of FLC for several weeks, despite initiation of chemotherapy [16, 17].

The removal of FLC may play a complementary role to chemotherapy in obtaining a faster kidney response [15, 18, 19]. In this scenario, the use of extracorporeal techniques for the treatment of MK provides a direct and rapid support to this purpose, helping to rapidly clear FLC from both intravascular and interstitial compartments [15]. Depuration needs high cut-off membranes allowing filtration of κ and λ FLC, with a molecular weight of approx. 22 kDa and 45 kDa, respectively.

Plasma exchange (PEX) has been used in previous years to remove FLC, although there is no clear evidence about the efficacy of PEX in achieving a sustained reduction of FLC and subsequent clinical benefits. Indeed, to provide a clinical advantage in terms of renal recovery using PEX, an increased number of sessions of greater duration is needed [13, 20-24], amplifying the loss of Ig and clotting factors.

Recently, it has been shown that in patients with hemodialysis (HD)-dependent AKI, extended HD with a high cut-off (45-60 kDa) membrane (HCO-HD), allows a sustained reduction in FLC concentrations with an extent of kidney recovery of about 60% [18, 19, 25]. However, despite the completion of two European randomized controlled trials, whether HCO-HD is beneficial in MK remains unclear [26, 27]. Moreover, high cost, elevated protein

leakage requiring albumin replacement, and calcium/magnesium wasting are the major drawbacks limiting its utilization [28].

On the other hand, a retrospective analysis has shown the depurative superiority of convective over diffusive strategies in MM patients [29]. HFR-SUPRA (hemodiafiltration with regeneration of the ultrafiltrate by adsorption on resin) is a novel modality of replacement therapy, based on separate convection, diffusion and adsorption mechanisms [30, 31]. The procedure consists initially in a convective process (membrane cut-off 42 kDa), followed by the generation of an ultrafiltrate (UF) which then passes through the adsorbent resin cartridge to which toxins and FLC are bound. Subsequently, UF is reinfused in a second dialyzer where the diffusive process takes place. This technique is used in HD patients for its high protein-bound toxin adsorption capacity without removal of albumin [30, 31, 32].

HFR-SUPRA could provide efficient clearance of FLC in view of its molecular size cut-off, which theoretically allows FLC passage, and of the high affinity of the adsorptive cartridge without the disadvantage of albumin loss [33]. Only few reports are presently available on the efficacy of HFR-SUPRA to remove FLC in MM patients with AKI [34, 35].

Thus, the aim of this pilot study was to measure the efficiency of FLC removal by the SUPRA-HFR technology, along with safety outcomes, including the actual extent of albumin loss, if any. Since this was not a clinical trial, no comparison has been done with conventional HD techniques, as far as uremia management or recovery of renal function post-AKI are concerned.

Materials and Methods

Six consecutive patients with newly diagnosed MM complicated by AKI were enrolled from 2011 to 2014. All patients were initially hydrated by i.v. infusions of normal saline alternated with 5% dextrose/water supplemented with $NaHCO_3$ to correct acidosis whenever appropriate (50% of calculated HCO_3^- deficit, on a daily basis). In 4 cases out of 6, daily urine output was approx. 2000 ml/day, without any significant improvement of GFR; one patient had oliguria, non-responsive to i.v. fluids (Table 1). Since their serum creatinine rose to an average of 11.7 ± 8.1 mg/dl with elevated BUN and/or initial volume overload, renal replacement therapy was initiated by five consecutive sessions of HFR-SUPRA on alternate days, along with i.v. dexamethasone and followed within one week by a Bortezomib-based chemotherapy.

Each treatment was performed on a Bellco monitor (Bellco® srl, Mirandola, Italy), with a polyphenilene super high flux filter (S-HF) (surface=0.7 m^2; cut off=42 Kda) for the convective process; a low-permeability polyphenilene filter (LF) (surface=1.7 m^2) was used for the diffusive section and a hydrophobic resin (Suprasorb 80 ml) as an absorptive cartridge.

The 2 initial HD sessions lasted 180 minutes each, the remaining 3 sessions 240 minutes. The basic HD prescription consisted of Q_B of 250 ml/min, Q_D of 500 ml/min, Q_{INF} of 70 ml/min, UF rate variable according to patient's volume status. Anticoagulation was obtained by continuous infusion of heparin sodium.

Serum levels of FLC (κ and λ chains) were assessed before and after each session by nephelometry (Freelite® system, Binding Site Group Ltd, Birmingham,UK). Post-treatment values were corrected for ultrafiltration. Mean FLC reduction for each session, mean FLC clearance, KT/V and mass removal were

Table 1. Clinical and demographic characteristics at the onset of Acute Kidney Injury. Abbreviations: SD, standard deviation; sCreat, serum creatinine; MM, multiple myeloma; FLC, free light chain; mm, micromolecular myeloma; sCa, serum calcium; UO, daily urine output; NSAIDS, nonsteroidal anti-inflammatory drugs; uP, proteinuria; BJ, Bence-Jones proteinuria; DEHYD, dehydratation); CM, contrast media

Patient (initials)	Sex	Age	sCreat (mg/dl)	MM	FLC type	FLC (mg/dl)	sCa (mg/dl)	UO (ml/day)	NSAIDs	uP (g/day)	BJ	DEHYD	sAlb (g/dl)	CM	Monoclonal component (g/dl)	B2micro globulin (mg/dl)	% Plasma cells in bone biopsy	Congo-Red stain
1 (NU)	M	62	11	IgG	κ	7920	9.6	2000	yes	12	+	mild	3.5	yes	-	46.6	90%	neg
2 (SM)	M	70	11	IgG	κ	8920	8.4	2000	yes	2.3	+	no	3.28	no	2.9	19.3	45%	neg
3 (RG)	M	60	6	IgA	κ	9020	8.8	2000	no	0.7	+	no	2.7	no	2.3	20	60%	neg
4 (DT)	F	60	27	IgA	λ	4840	10.0	400	no	0.7	+	no	3.4	no	2.6	28.5	80%	neg
5 (GG)	F	75	11	mm	κ	5300	10.7	600	no	1.5	+	mild	3.9	no	9.9	26.9	80%	neg
6 (ML)	F	45	4	mm	λ	5900	11.0	2000	no	5	+	no	3	no	5.9	17	90%	neg
Mean ± SD		62 ± 10.3	11.7 ± 8.1			5945.0 ± 2262.3												

calculated using equations described by Granger Vallèe [29]. Albumin was evaluated before the first HD and after the whole cycle (5 sessions) of treatment.

Student-t tests for paired or unpaired data were used whenever appropriate for statistical evaluation. A p value < 0.05 was considered significant. The correlation between time and reduction rates of FLC was evaluated by Pearson's coefficient. Data analysis was performed using SPSS-IBM V21.

All patients gave informed consent to treatment, laboratory testing, data collection and publication, following authorization of the Institutional Ethics Committee. Research was conducted in accordance with the ethical standards of the Declaration of Helsinki.

Results

We studied 6 patients (3 males and 3 females, mean age: 62.0 ± 10.3 yrs., range: 46-75) with newly diagnosed MM and HD-dependent AKI as first clinical manifestation (mean creatinine ± SD = 11.6 ± 8.1 mg/dl) (Table 1). The monoclonal component was IgG (2/6 pts), IgA (2/6), and micromolecular (mm) in the remaining 2 pts; λ chains were dominant in 2 patients, whereas κ chains were found in the remaining 4 cases. A renal biopsy (showing a light chain deposition disease / "cast" nephropathy) could be performed only in one patient, due to comorbidities or risk factors (low platelet counts, previous bleeding, renal cysts).

FLC levels before and at the end of each session (corrected for ultrafiltration), and the percentage of reduction for each patient are listed in Table 2. The average FLC removal for a single HFR-SUPRA session was calculated. The 4 patients with κ chain MM (2 IgG, 1 IgA, 1 mm) showed an average reduction of FLC levels in one single session of 37.7±21.3% (p=0.02), 57.0% ± 17.7% (p=0.002), 45.3% ± 10.2% (p=0.001) and 60.6% ± 15.0% (p<0.0001), respectively. The 2 patients with λ MM (1 IgA, 1 mm) had a mean reduction of 71.6% ± 5.0% (p<0.0001) and 48.7% ± 8.7% (p<0.0001), respectively.

The total effect of 5 sessions of HFR-SUPRA on FLC serum levels has been calculated for each patient (Fig. 1). In MM κ patients, we observed a significant drop of serum levels, from 7100 mg/dl ± 1463 mg/dl before the HFR sessions to 1135 ± 530 mg/dl, *p = 0.02*), with a net decrease of FLC of 84.01%. On the other hand, in two λ patients baseline FLC levels after the 5 HFR sessions were reduced by 69.3%, albeit not significantly (1227 mg/dl ± 413 mg/dl vs. baseline 3990 mg/dl ±1202 mg/dl, *p = 0.3*). No statistical significance was found between the average removal of κ chains vs. λ (5964 mg/dl ± 1134 mg/dl vs. 2762 ± 1615, *p=0.1*).

In all patients, despite the rebound observed after each session, the κ and λ FLC levels before starting HFR-SUPRA decreased significantly after five sessions (mean value pre-HFR-SUPRA treatment vs. mean value at end of the 5 sessions 6063 ± 2037 mg/dl vs. 1166 ± 454 mg/dl; *p=0.002*), with a mean decrease of 81% (Fig. 2).

We also assessed the extent of FLC removal as a function of the length of treatment. A lower average removal in 3-hour treatments was apparent vs. 4-hour, although not reaching significance because of the modest difference in length of the sessions (46.4% ± 15.7% vs.

Table 2. Free light chain (FLCs) levels before and after each single session (post-treatment levels are corrected for ultrafiltration). % removal are listed for each patient (Pt). Patients no. 1, 3, and 6 (50%) recovered from HD, while the remaining 50% (patients 2, 4, and 5) remained HD-dependent and died later for cardiovascular complications

Parameter	Pt 1 (κ)		Pt 2 (κ)		Pt 3 (κ)		Pt 5 (κ)		Pt 4 (λ)		Pt 6 (λ)	
	FLC (mg/dl)	% remov.	FLC (mg/dl)	% remov.	FLC (mg/dl)	% remov.	FLC (mg/dl)	% remov.	FLC (mg/dl)	% remov.	FLC (mg/dl)	% remov.
Pre 1st HFR	8700	24.1	6650	47.2	7750	33.0	5300	45.4	4840	68.2	3140	44.1
Post "	6600		3510		5190		2895		1539		1756	
Pre 2nd HFR	8040	19.8	2690	58.4	3200	35.4	5080	46.7	3888	64.5	3180	40.9
Post "	6444		1120		2069		2709		1378		1940	
Pre 3rd HFR	7540	37.1	3080	75.6	9020	54.5	6620	60.1	4750	74.4	4780	63.5
Post "	4743		752		4106		2640		1216		1742	
Pre 4th HFR	7920	34.1	4780	71.33	4430	47.8	4750	74.4	5140	74.4	5210	48.4
Post "	5220		1370		2313		1214		1317		2689	
Pre 5th HFR	6280	73.8	714	32.55	3200	53.8	3960	76.4	3960	76.4	2880	47.2
Post "	1700		482		1479		935		935		1520	
Mean ± SD		37.7±21.3		57.0±17.7		45.3±10.2		60.6±15.0		71.6±5.0		48.8±8.7
p		0.02		0.002		0.001		0.001		<0.0001		<0.0001

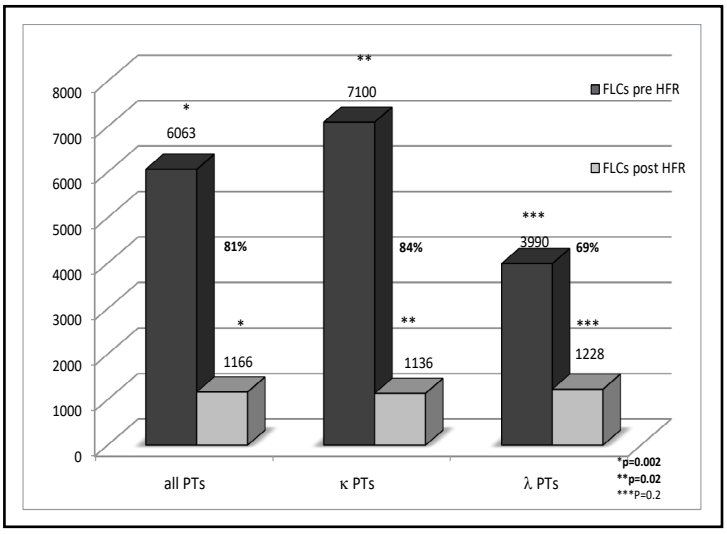

Fig. 1. Comparison between mean FLC levels before and after five HFR-SUPRA treatment sessions for the general cohort (all PTs, values are corrected for ultrafiltration). Patients 1, 2, 3, 5 had monoclonal κ chains, 4 and 6 had λ chains.

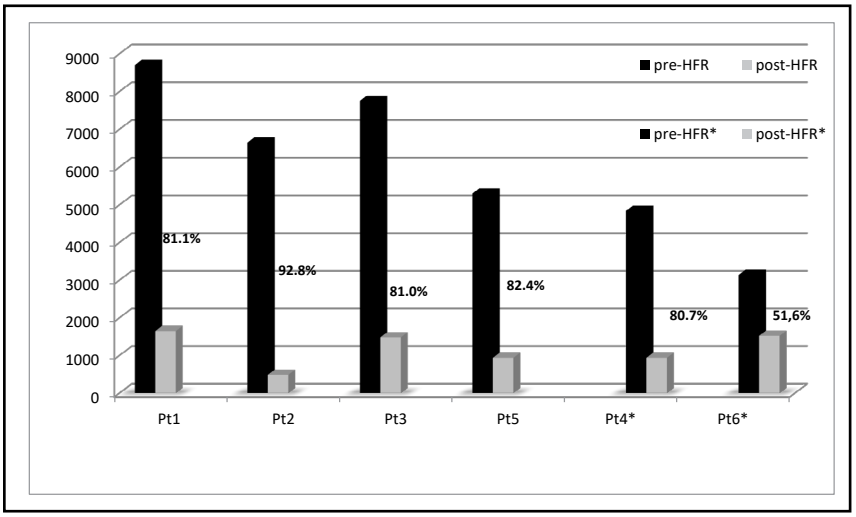

Fig. 2. Mean decrease of FLC levels after five HFR-SUPRA treatment sessions for each patient (Pt, all values corrected for ultrafiltration). Patients 1, 2, 3, 5 had monoclonal κ chains, 4 and 6 had λ chains.

57.0% ± 16.0%, respectively, *p=0.08*). The mean FLC (κ and λ) clearance was 0.37 mg/min.

The average decrease of serum albumin levels at the end of the whole sequence of 5 HFR-SUPRA sessions for each patient was 3.2%, 8.5 %, 3.1%, 5.5 %, 6%, and 7%, respectively. These changes were not significantly different from pre-HFR serum levels. Albumin reinfusion was therefore not necessary.

Three patients (no. 1, 3, and 6 in Table 1) (50%) recovered from HD, while the remaining (50%) were HD-dependent and died later for cardiovascular complications. The third patient of our series, who recovered, died within few months for infectious complications.

A follow-up is available for two of the patients whose kidney function recovered. The first was a 62-y.o. man with IgG κ MM and serum creatinine at Hospital admission of 7.0 mg/dl. He completed 4 cycles of chemotherapy with BTD (Bortezomib-Thalidomide-Dexamethasone) in 3 months, resulting in a partial hematological remission according to the IMWG criteria [2], while renal function was steady at an estimated GFR of 32 ml/min. At that point, autologous transplantation of peripheral blood (PBSC) stem cells was not feasible because of severe infection. After 10 months of follow-up, the BDT scheme was resumed for disease worsening, while renal function was stable, making treatment again possible (eGFR 30 ml/min).

The second patient was a 45-y.o. woman with IgAλ MM and AKI, whose serum creatinine at admission was 4.1 mg/dl. She completed the HFR-SUPRA protocol and chemotherapy

with BDT. Following 2 additional standard HD sessions, kidney function recovered. After 1 month of haematological treatment, the patient achieved a partial remission of the disease and further progressive amelioration of renal function to an eGFR of 30 ml/min. After 6 cycles of chemotherapy, complete recovery of renal function and good response to therapy allowed autologous PBSC transplantation. Eighteen months after the onset of MM and 12 months after the graft the patient had recovered normal kidney function.

Discussion

In the last decade, the introduction of novel therapies has improved the prognosis of patients with MM [3, 4]. However, AKI still represents one of the most relevant conditions associated with poor prognosis [6, 7, 9]. In our own experience and several large series, renal involvment increases mortality from MM to 32-33% despite pharmacologic treatment, with 20 to 37% of patients not recovering fom HD, whereas 46% survive at least 2 months after discontinuation of HD [35, 36]. Only 20-30% of patients become HD-independent as a result of chemotherapy alone, while the association with extracorporeal techniques allows a much greater improvement in kidney function [15, 18]. If AKI is suspected to occur as a consequence of massive paraprotein deposition within the kidney, the therapeutic strategy should therefore immediately aim at the reduction of FLC tissue and circulating levels [9, 13, 17]. Blocking FLC production is the most effective way to reduce their filtered load and thus intratubular aggregation. However, in HD-dependent patients, lowering FLC serum concentrations is a slow process, not only since chemotherapy requires weeks to become effective, but also because of the reduced renal clearance and rapid plasma refilling from extravascular deposits [14, 15].

Among extracorporeal techniques, plasma exchange (PEX) yielded controversial results, seemingly beneficial only when it reduces FLC more than 50 % through frequent, lengthy sessions [13, 20-24]. Moreover, the very high cut-off plasma filters cause a heavy loss of albumin and clotting factors, hampering the prolonged use of this treatment. A meta-analysis of plasmapheresis combined with chemotherapy failed to identify a difference in 6-month HD-dependent survival vs.patients treated with chemotherapy only. On the other hand, PEX/plasmapheresis reduced the percentage of subjects needing regular replacement therapy fom 37.2% to only 15.6% [36]. In patients needing HD, a technique allowing simultaneous clearance of FLC would avoid the need for repeated daily sessions of extracorporeal therapy (separate PEX + HD on alternate days). This would also yield advantages for the duration and possible infections of the temporary vascular access, usually a central vein catether. The introduction of extended high cut-off HD filters (45-60 kDa pore size) combined with chemotherapy enabled renal recovery in about 60-74 % of cases [15, 19] and a stable reduction of FLC at the expense of severe losses of albumin [19]. Two recent European trials failed to show a clear advantage of the use of HCO-HD in cases of MM-related AKI [26, 27, 28], whereas convective strategies showed superiority in removing FLC [29, 30, 31].

HFR-SUPRA is a technology that accomplishes blood purification through three phases that take place separately: a convective depurative process (i) generates an ultrafiltrate by passage through an adsorbent resin cartridge (ii), which has high affinity for FLC and uremic toxins, but not for albumin. This ultrafiltrate is then reinfused in a second dialyzer where the diffusive process and water removal take place (iii) [32, 33, 34, 37, 38].

We have used HFR-SUPRA in individuals with AKI in MM. It should be noted that the study is not a clinical trial aimed at assessing efficacy of a treatment on the outcome of AKI and/or MM, but rather a technical analysis of the performance of this dual-stage HDF technology in removing paraproteins. Only few reports are available in the literature about the efficacy of HFR-SUPRA in removing FLC [38, 39]. In our proof-of-concept study, each session of HFR-SUPRA obtained a mean decrease of FLC between 37.7% ± 21.3% and 60.6%

± 15.0% for κ chains and between 71.6 ± 5.0% and 48.8 ± 8.7% for λ. These data are in keeping with the results obtained by Hutchinson et al. with HCO-HD [15, 19].

It is known that a reduction of FLC by more than 50% is needed to provide clinical benefits [13, 24]. In our experience, 5 sessions of HFR-SUPRA on alternate days allowed a fast and stable reduction of intravascular abnormal FLC of 81% (84% for κ and 69% for λ), despite the serum rebound due to refilling from tissue deposits.

One clear advantage of HFR-SUPRA vs. conventional high cut-off apheretic techniques is to preserve serum albumin levels. This is accomplished by endogenous post-dilution reinfusion and the use of an adsorbent cartridge with low affinity for albumin, which optimizes the depurative potential without the burden of protein depletion [32, 34]. In our study, albumin wasting has not been neither statistically or clinically relevant during the whole treatment. The mean variations of serum levels were negligible for all patients, (-3.1 to 7%), and in no circumstance was albumin replacement required, different from Hutchison's experience [19].

In the literature, higher rates of removal are described for κ chains than for λ [19, 37]. This is explained by the larger molecular weight of λ chains, usually aggregated in polymers. We did not observe a significant difference between the rates of removal of κ vs. λ chains. This could result from the use of an adsorptive cartridge that is less influenced by MW of the ligand. We could hypothesize that the only limiting factors to the clearance of FLC with HFR-SUPRA are the length of HD sessions and saturation of the cartridge. However, Pendón-Ruiz de Mier et al. [39] reported that saturation of the cartridge should not be limiting in a treatment of 240 minutes, irrespective of the type of chains.

Based on this assumption, a linear relationship between rate of removal and treatment duration should be expected. In our observation, the limited variation in length of the sessions did not enable us to detect a significant correlation, although a difference between mean removal in 3-hour vs.4-hour sessions (46.4% ± 15.7% vs. 57.0% ± 16.0%, p=0.08) may become significant for a larger sample or broader differences in treatment length. This effect of timing of the treatment sessions could be explained both by the bicompartmental kinetics of FLC, which tend to refill plasma from extravascular deposits, and by the dual convective and adsorptive processes of depuration.

From a prognostic point of view, the recovery of renal function is a key factor [2, 9]. In our limited cohort, 50% (3/6) of patients achieved a complete recovery of renal function. Our less favourable results, compared to Hutchinson's experience (67%), are attributable to a later diagnosis and treatment initiation, rather than to the technique of FLC removal itself. Indeed, a certain degree of removal was achieved in all of our patients. On the other hand, patients who remained HD-dependent were older and had a longer history of misdiagnosed or untreated MM symptoms, while patients who recovered from AKI had lower serum creatinine levels at the beginning of treatment. All of our patients had HD-dependent AKI. It is conceivable that an earlier institution of extracorporeal therapies in patients with AKI could improve renal prognosis. Evidence is still lacking in the literature to guide timing of treatment of AKI patients with extracorporeal therapies in monoclonal gammopathies.

Our experience confirmed that failure of the kidney to recover portends a worse prognosis. About 75 % of patients who remained HD-dependent died shortly thereafter. This poor prognosis could be either caused by renal failure itself, HD-related complications such as catether infections, or represent a consequence of a more severe haematological disease, of which AKI resistant to therapy is a manifestation.

On the other hand, our patients who recovered from HD received pharmacologic treatment and showed a stable remission of kidney disease. In our cohort, only one patient was eligible to an autologous PBSC transplantation-graft of stem cells. This woman, 46-y.o., with a micromolecolar κ myeloma, developed bone pain and almost simultaneously a rapidly progressive renal failure. She was immediately hospitalized and a renal biopsy was performed, showing a "cast nephropathy" in the context of LCDD. Upon such finding, she was immediately started on a HFR-SUPRA protocol (when sCr was still 4 mg/dl), along with

chemotherapy. Complete recovery of renal function and an initial haematological response to therapy allowed to perform the autologous PBSC transplantation. Eighteen months after the onset of MM and 12 months following PBSC transplantation, the patient still maintains a completely normal kidney function. This case outlines the importance of starting therapy in combination with HD as soon as possible. On the other hand, it underscores once more that younger age and a lower serum creatinine at the onset are favourable prognostic factors.

Conclusion

Our pilot study demonstrates that HFR-SUPRA provides substantial reduction in plasma FLC levels in patients with MM and AKI, with good tolerance and minimal loss of albumin. When started early in combination with chemotherapy, HFR-SUPRA enhances recovery of renal function, as occurred in three cases of this small series. We suggest that this technology might be tested in a larger scale, randomized trial on MM patients eligible for chemotherapy with AKI treated with conventional HDF vs. HFR-SUPRA. Renal recovery, clinical outcomes of chemotherapy, and overall survival rates could be sensitive endpoints to be explored. Based on our proof-of-concept experience with HFR-SUPRA, such approach might offer practical and clinical advantages over more conventional high cut-off membranes in terms of lower costs and negligible loss of albumin.

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Disclosure Statement

No conflict of interest is declared by any of the authors.

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