Role of HFR cartridge in the removal of mediators of inflammation and p-cresol in hemodialysis patients

Eleonora Riccio[1], Maristella Minco[1], Gennaro Argentino[1], Andrea Memoli[1], Bruna Guida[2], Mauro Cataldi[2], Bruno Memoli[1]

[1]Department of Nephrology, and of [2]Department of Neuroscience, University Federico II, Naples, Italy.

INTRODUCTION

A major limitation of standard hemodialysis is that it does not clear the plasma from interleukin-6 (IL-6) and p-cresol, two uremic toxins responsible for the high cardiovascular risk in end stage renal disease (ESRD)[1,2]. Alternative dialysis strategies have been developed to more efficiently remove protein-bound compounds, such as p-cresol and IL-6, from plasma either by their absorption on resin cartridges incorporated in the dialysis apparatus[3], or by altering the strength of protein binding in the plasma[4]. One of the most promising among them is HFR, a double-chamber hemodiafiltration system that combines the processes of diffusion, convection and adsorption[5], in which the ultrafiltrate (UF) eturns to the patient after its regeneration through a resin cartridge.

AIM OF STUDY

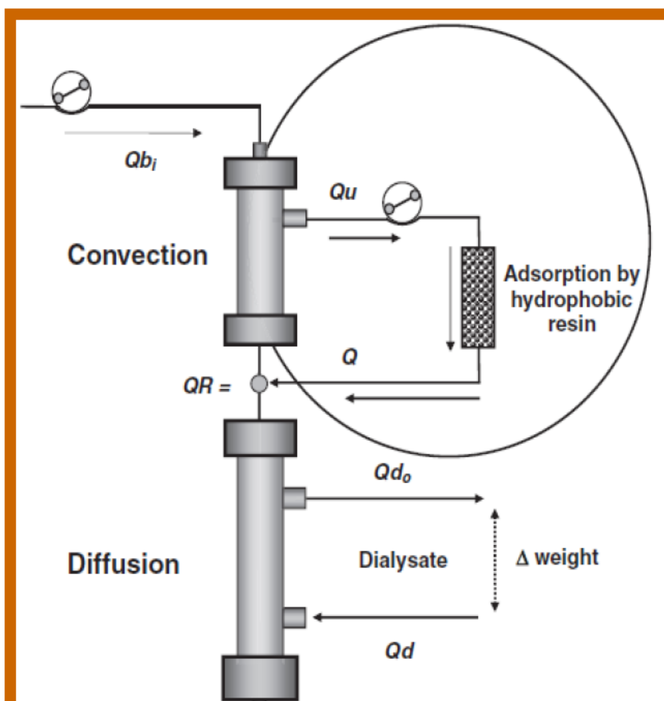
The aim of our study was to evaluate whether online HFR ameliorates the inflammatory status of chronic hemodialysis patients by decreasing the circulating concentrations of proinflammatory molecules, such as IL-6 and p-cresol.

METHODS

We selected 8 inflamed chronic HD patients, which underwent a single 240 minutes HFR session. To establish whether HFR is effective in lowering IL-6 and p-cresol serum concentrations, we compared their circulating levels in blood samples collected before and following the HFR dialysis session. Then, to explore the hypothesis that IL-6 and p-cresol were removed because they were retained on the HFR cartridge, we compared their concentrations in UF entering (UF_{in}) and UF exiting (UF_{out}) from the cartridge, collected 15 minutes after the start (start-15 min) and 15 minutes before the end (end-225 min) of the HFR session. Finally, to test the hypothesis that this dialysis technique could lower the overall proinflammatory activity of the UF, we compared the inflammatory response, in terms of IL-6 gene expression and release, induced by the UF_{in} (at 15 min) with that induced by UF_{out} (at 225 min) addition to peripheral blood mononuclear cells (PBMCs) drawn from 8 healthy subjects.

RESULTS

HFR caused a decrease in p-cresol but not in IL-6 serum concentrations (A). Both p-cresol and IL-6 were lower in UF_{out} than in UF_{in} either at the start or at the end of the HFR session, suggesting that they were largely retained by the cartridge (B). IL-6 mRNA expression (C) and release (D) were lower in PBMC incubated with UF_{out} collected at the end than with UF_{in} collected at the start of the session, suggesting that passage through the cartridge reduced UF proinflammatory activity.



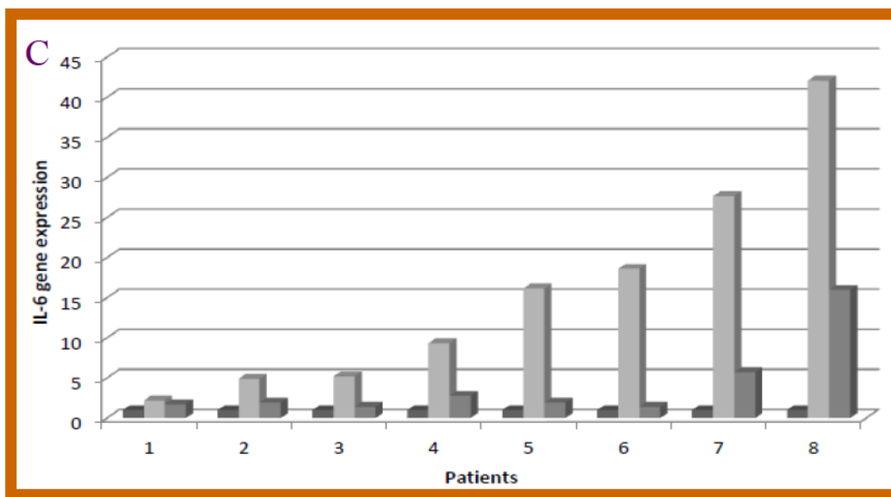
HFR

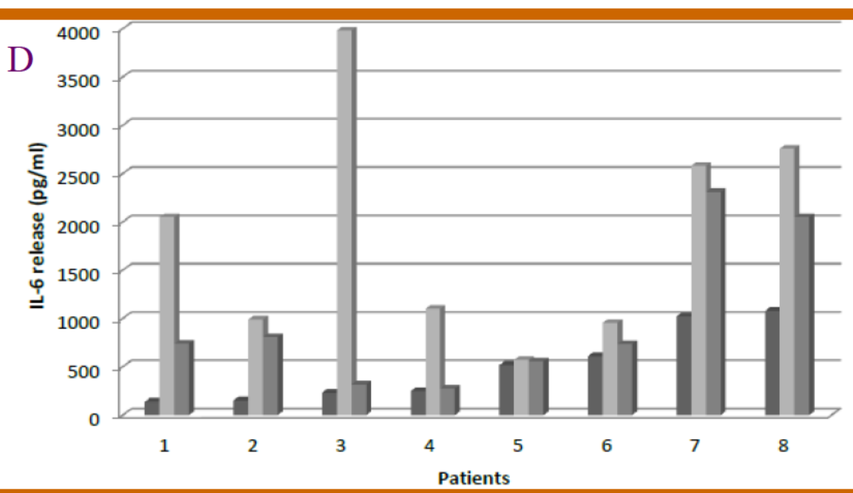
A	Before HFR	After HFR	P
Albumin (g/dl)	3.66 ± 0.199	4.25 ± 0.16	<0.001
p-cresol (mg/l)	11.54 ± 7.82	5.94 ± 3.4	0.018
IL-6 (pg/ml)	57.74 ± 73.14	56.32 ± 77.56	0.883

Serum level of albumin, p-cresol and IL-6 in pre- and post-HFR specimens.

B	15 minutes			225 minutes		
	Pre-cartridge	Post-cartridge	P	Pre-cartridge	Post-cartridge	P
IL-6 (pg/ml)	10.28 ± 12.79	0	0.05	11.82 ± 13.98	0.93 ± 1.27	0.046
p-cresol (mg/l)	6.66 ± 3.6	2.29 ± 2.06	0.015	4.09 ± 3.92	0.72 ± 0.59	0.05

Levels of IL-6, p-cresol and albumin in UF collected pre- and post-cartridge at the start and at the end of the HFR session.





Individual values of IL-6 gene expression (C) and release (D) in PBMC cultures of 8 healthy volunteers after incubation for 24 h with saline (basal condition, black), UF_{in} collected at the start of HFR session (light gray), or UF_{out} collected at the end of the HFR session (dark gray)

RESULTS

CONCLUSIONS

This study shows that HFR-Supra is effective in removing p-cresol and inflammatory mediators in ESRD patients. Considering the role of these toxins in the genesis of ESRD cardiovascular complications, our results suggest that HFR-Supra could favorably affect cardiovascular risk in ESRD patients.

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