PRELIMINARY RESULTS OF HIGH-EFFICIENCY ON-LINE MIXED HEMODIAFILTRATION IN A DIALYSIS CENTRE NETWORK IN ITALY (NEPHROCARE)

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INTRODUCTION

Recent large trials (ESHOL, CONTRAST, and TURKISH Studies) have strongly suggested that survival of chronic dialysis patients may be significantly improved on post-dilution haemodiafiltration (post-HDF) provided that high volume exchange is performed. However, this goal requires high blood flow rates, hardly to be achieved in a large cohort of patients with failing vascular access, central venous catheters, high haematocrit, hyperviscosity/ coagulability, or conditions of scarce plasma refilling (diabetics, authonomic disfunction, cardiax failure, old age, etc).

Mixed HDF is an advanced on-line infusion modality in HDF, in which substitution fluid is simultaneously infused at the inlet and outlet port of the dialyzer, at a rate and site partition modulated on the trans-membrane pressure (TMP) by means of a feedback system which is sensitive to the patient and operating conditions (flow rates, haemoconcentration, membrane surface and permeability) (Fig.1-2).

Preliminary studies (Pedrini et al. Kidney Int. 2000-2003-2006) have shown that Mixed HDF may safely achieve high convective removal of small and middle molecular uremic toxins while avoiding the drawbacks of the more traditional post-HDF.

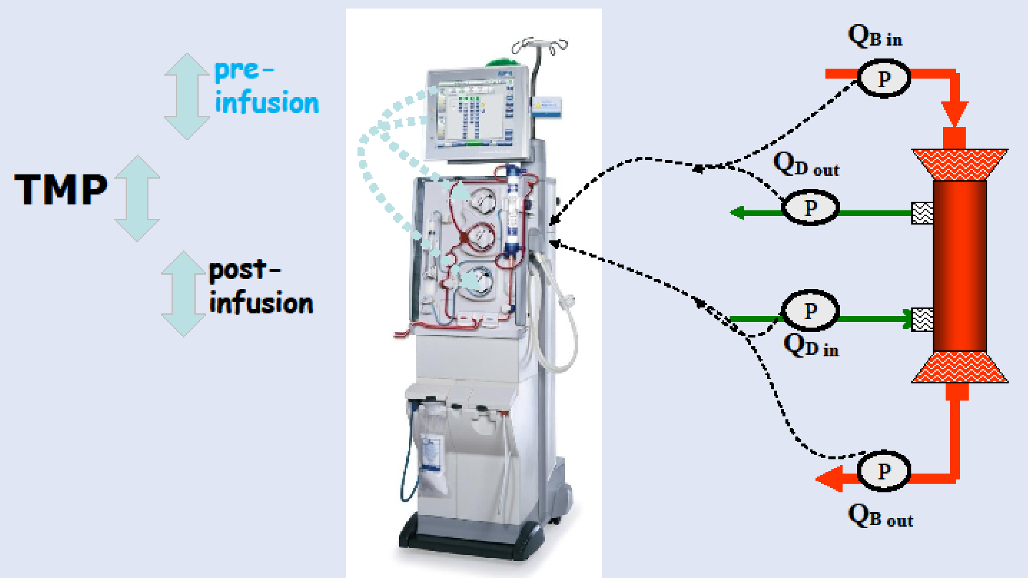

Figure 1. Schematic representation of the on-line system for mixed HDF with the TMP feedback control device. Four pressure transducers (P), placed at the inlet and outlet blood and dialysate ports of the filter send continuous signals (dotted black lines) to the machine software, which calculates and monitors the mean trans-membrane pressure (TMP). The rate of the total infusion and the ratio of post- to pre-filter infusion are regulated by the TMP values through modulation of the speed of the two infusion pumps.

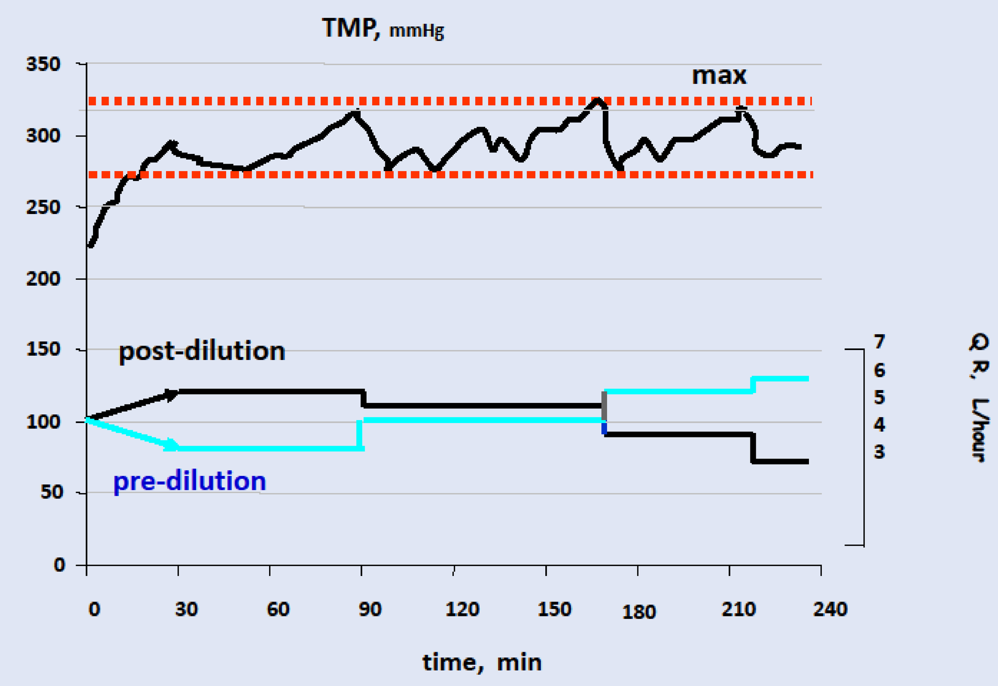

Figure 2. The Mixed HDF feedback : At the start of the treatment the total infusion rate is rapidly increased in order to establish the TMP within a safe range of values (260–320 mmHg). Subsequently, the system self-regulated the ratio of pre- to post infusion in order to maintain the TMP within the set range without affecting the total infusion nor the planned ultrafiltration. If TMP falls below the lowest value of the range, a small amount of fluid (5-10 ml/min) is diverted from pre- to post-infusion, with the result of increasing the filtration fraction FF (and thusTMP). Vice versa, the same amount of fluid is diverted from post- to pre-dilution, thus reducing FF, whenever the TMP rises beyond its maximum tolerated value. In short, the feedback is able to ensure the highest FF compatible with the progressive hemoconcentration and loss of hydraulic permeability of the membrane throughout the sessions, while avoiding dangerous increase inTMP.

AIM OF THE STUDY

To evaluate the efficiency and safety of Mixed HDF 3-6 months after its implementation in 13 facilities of an international Dialysis Centre Network (NephroCare).

METHODS

Efficiency of Mixed HDF in terms of small and middle molecular solute removal was evaluated in 125 chronic dialysis patients of 13 Centres as a mean of a 3-months period, and compared with that obtained by the same patients in a previous length-matched period on post-HDF.
Mean age of the patients was 63.1±13.2 years, (range 26-87). 10 out of 125 patients had central venous catheter. The remaining had native or prosthetic A-V fistula. High-flux helixone dialyzers 1.8-2.2 m^2 were used on 5008 HDF dialysis systems (Fresenius Medical Care, Bad Homburg, Germany)
The efficiency of the technique in removing small toxins was evaluated with urea Kt/V calculated from on-line ionic dialysance K, (conductivity method, OCM), effective treatment time, and urea volume measured with bio-impedance method (BCM). Beta2-microglobulin (β2-M) was used as a marker of middle molecular toxins and its basal level and reduction ratio RR were calculated .
Student's t test for paired data was used in comparisons.

RESULTS

Patients and treatment parameters as a mean of values recorded during the three-monts periods of observation in all patients are shown in Table 1.

TABLE 1		Ht %	T.Proteins g/dl	Albumin g/dl	Dry BW kg	QB Eff ml/min	time min
Mixed HDF	mean	36.7	6.5	3.7	75.3	400	239
	SD	4.2	0.5	0.2	3.5	32	7
Post-HDF	mean	35.4	6.7	3.8	75.4	386	236
	SD	4.1	0.5	0.3	3.3	20	4
	P	0.02	0.07	0.3	0.8	0.03	0.09

Larger amount of substitution fluid was infused (as expected) in Mixed HDF and the amount infused post-filter (~ 50%) matched the total infusion in post-HDF (Table 2). Besides higher small molecules removal, Mixed HDF ensured higher β2-m removal and a slightly lower β2-m basal level in the medium-term.

TABLE 2		Infusion , L. total	Infusion , L. post-dil.	OCM Kt/V	β2-M , mg/L pre-HD mg/L	β2-M , mg/L post-HD mg/L	β2-M , mg/L RR % *	Phosphate mg/dl
Mixed HDF	mean	40.2	20.5	1.88	22.4	4.3	80.9	4.4
	SD	4.9	1.9	0.38	4.8	1.4	3.9	1.1
Post-HDF	mean	21.8	21.8	1.61	24.4	5.7	76.2	4.5
	SD	3.0	3.0	0.26	5.0	1.7	5.7	1.2
	P	<0.001	0.07	<0.001	0.6	0.02	0.03	0.64

*comparison of 57 available paired data .

The results of a Mixed Linear Model showed that blood flow exerted the most significant effect on β2-m level (est.=-0.09, 95%CI, 0.16/-0.02, p<0.01). Treatment modality (post-HDF vs Mixed HDF) exerted additional significant effect (est. -0.16, 95%CI, -0.23/-0.10, p<0.05). Age, sex, vintage, session duration, infusion volume, membrane surface area, dry BW, intra-dialytic weight loss and residual diuresis were also evaluated.

A sub-group of 10 patients failing to achieve an adequate volume exchange on post-HDF (n.7, scarce refilling and hemoconcentration, n.3, low blood flow rate) were shifted to Mixed HDF and evaluated over the same period and with the same criteria as the whole group. Their parameters and efficiency indexes are reported in Tables 3-4.

TABLE 3		Ht %	T.Proteins g/dl	Dry BW kg	QB Eff ml/min	Time min
Mixed HDF	mean	37.3	6.4	70.7	329	242
	SD	5.1	0.6	6.1	28	11
Post-HDF	mean	38.1	6.5	71.1	317	241
	SD	4.6	0.7	5.8	24	14
	P	0.2	0.1	0.8	0.05	0.4

TABLE 4		Infusion , L. total	Infusion , L. post-dil.	OCM Kt/V	β2-M , mg/L pre-HD mg/L	β2-M , mg/L post-HD mg/L	β2-M , mg/L RR % *	Phosphate mg/dl
Mixed HDF	mean	30.8	16.4	1.41	25.3	5.7	77.5	4.9
	SD	5.5	2.4	0.22	5.1	1.4	4.2	1.3
Post-HDF	mean	14.4	14.4	1.27	26.7	6.4	76.0	4.8
	SD	4.1	4.1	0.26	6.9	1.9	5.7	1.4
	P	<0.001	0.04	<0.01	0.08	0.03	0.04	0.4

CONCLUSIONS

These promising preliminary results indicate that Mixed HDF may be a highly efficient and versatile technique to achieve the highest removal of toxic uremic substances of different molecular weight. The feedback system working in Mixed HDF adapts infusion flow and filtration pressure to the patient- and operating conditions, thus allowing to perform HDF and to extend its benefits also to critical patients who can hardly be treated on post-HDF for different reasons. More extensive application of Mixed HDF is needed to confirm the present results and, possibly, to provide new insight in the potential of this technique.

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