Elimination of middle size molecules by the FXCorDiax 60 in relation to the FX 60-Dialyzer

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Introduction and Objectives

Hemodiafiltration (HDF) is a dialysis therapy mode with increasing acceptance because of its efficiency in the elimination of a broad spectrum of uremic toxins. In contrast to conventional hemodialysis treatments which rely almost solely on diffusion-related mechanisms for solute removal, hemodiafiltration (HDF) allows a more efficient removal of higher-molecular weight toxins due to convective transport mechanisms[1,2,3,4]. Decisive for the removal of these toxins in a HDF-treatment are efficient high-flux dialyzers with a defined steep cut-off characteristic to minimize loss of albumin[5,6]. In order to assess the clinical performance (removal rate, elimination) of different dialyzers (FX- and FXCorDiax-class by Fresenius Medical Care, Bad Homburg, Germany) with polysulfone-based membranes in a clinical setting we selected a set of different marker molecules [7,8,9] with increasing molecular weight and established laboratory tests (urea (60 Da), phosphate (95 Da), ß2-microglobulin (11.8 kDa), myoglobin (17.2 kDa), prolactin (22.9 kDa), α1-microglobulin (33 kDa), α1-acidglycoprotein (41 kDa) and albumin (66 kDa)).

Methods

In an open, randomized, cross-over, prospective clinical study 30 adult chronic hemodialysis patients were treated by post-dilution on-line hemodiafiltration with the FX 60 and with the FX CorDiax60 dialyzer type.
In two consecutive weeks patients were dialyzed thrice weekly each with both dialyzers (membrane surface area of 1.4 m², both); the second or third session of each week was analysed only. All treatments were performed with the 5008 hemodialysis system (by Fresenius Medical Care) without any activated automatic modes of substitution flow rate adjustment. Treatment parameters were kept constant for each patient.
All samples (pre- and postdialytic blood and full dialysate collection) were analysed for urea, phosphate, ß2-microglobulin, myoglobin, prolactin, α1-microglobulin, α1-acidglycoprotein, albumin and total protein (hematocrit was measured for all blood samples as well).
All procedures were performed in accordance with the ethical standards of the responsible ethics committee; patients were included after having given written informed consent. The study registration was *ClinicalTrials.gov: NCT01534741*.

Results

30 patients (18 males, 12 females) with 60.97±12.90 ys were included. Pre- and post-dialytic physiological data like weight, blood pressure and heart rate were very similar for both study treatments. The same holds true for parameters like treatment time, blood, dialysate and substitution flow rate, substitution volume, ultrafiltration rate and volume (see table 1). For FX CorDiax 60 in comparison to FX 60 significantly higher removal ratios (RR) of BUN, ß2-microglobulin, myoglobin, prolactin and α1-microglobulin were observed. There were no significant differences in the RR for phosphate, α1-acid glycoprotein, albumin and total protein (see table 3 and figure 1).
On the dialysate side, with FX CorDiax 60 a significantly higher eliminated mass was found than with FX 60 for ß2-microglobulin, myoglobin, prolactin and albumin respectively (table 2).
Due to dilution effects in the dialysate α1-microglobulin and α1-acidglycoprotein were not measurable by our laboratory technique.

Table 1
Vital and treatment parameters of the study cohort (N=30); data expressed as mean value standard deviation and p-value.

Vital and Treatment Parameters	FX 60	FXCordiax 60	Significance (p-value)
Weight [kg]			
predialysis	**70.2** ± 12.1	**70.4** ± 12.2	**0.14**
postdialysis	**68.2** ± 12.1	**68.3** ± 12.0	**0.18**
Systolic Blood Pressure [mmHg]			
treatment start	**128.2** ± 28.3	**131.6** ± 22.4	**0.37**
treatment end	**124.5** ± 27.6	**122.8** ± 27.1	**0.61**
Diastolic Blood Pressure [mmHg]			
treatment start	**62.4** ± 16.0	**63.5** ± 15.3	**0.28**
treatment end	**64.2** ± 15.0	**61.4** ± 14.3	**0.15**
Heart Rate [min⁻¹]			
treatment start	**75.5** ± 14.3	**81.0** ± 18.1	**<0.01**
treatment end	**72.5** ± 16.9	**74.3** ± 16.4	**0.25**
Treatment Time [h]	**4.90** ± 0.29	**4.89** ± 0.30	**0.76**
Blood Flow Rate [ml/min]			
treatment start	**408.3** ± 32.4	**406.7** ± 38.8	**0.67**
treatment end	**405.0** ± 32.9	**403.7** ± 38.8	**0.71**
Dialysate Flow Rate [ml/min]	**500** ± 0	**500** ± 0	**n.a.**
Substitution Volume [l]	**27.3** 3.1	**27.4** 2.8	**0.78**
Ultrafiltration Volume [l]	**2.38** 1.09	**2.50** 0.90	**0.29**

Table 2
Eliminated masses during treatments with FX and FXCorDiax Dialyzers

	Comparison of Eliminated Masses		
	FX 60	FXCordiax 60	Significance (p-value)
BUN [g]	**13.85** ± 4.72	**13.93** ± 4.79	**0.86**
Phosphate [g]	**1.13** ± 0.47	**1.10** ± 0.40	**0.57**
β-2 Microglobulin [g]	**0.24** ± 0.09	**0.26** ± 0.09	**<0.01**
Myoglobin [mg]	**1.51** ± 0.76	**1.83** ± 0.89	**<0.01**
Prolactin [mg]	**0.14** ± 0.08	**0.17** ± 0.13	**0.02**
Albumin [g]	**3.01** ± 2.37	**4.25** ± 3.49	**0.03**
Total Protein [g]	**8.21** ± 4.03	**9.76** ± 4.50	**0.13**

Table 3
Removal Ratios of FX and FXCorDiax Dialyzers

	Comparison of Removal Ratios		
	FX 60	FXCordiax 60	Significance (p-value)
BUN [%]	**84.89** ± 4.59	**86.23** ± 4.14	**0.015**
Phosphate [%]	**65.30** ± 12.50	**64.02** ± 13.05	**0.30**
β-2 Microglobulin [%]	**81.30** ± 4.82	**84.67** ± 3.79	**<0.01**
Myoglobin [%]	**58.60** ± 12.10	**75.23** ± 10.48	**<0.01**
Prolactin [%]	**56.91** ± 13.06	**72.96** ± 9.68	**<0.01**
α-1 Microglobulin [%]	**13.60** ± 12.50	**20.89** ± 18.27	**0.016**
α-1 Acidglycoprotein [%]	**10.85** ± 10.70	**13.68** ± 14.46	**0.40**
Albumin [%]	**6.89** ± 7.28	**3.46** ± 8.57	**0.11**
Total Protein [%]	**5.42** ± 7.68	**2.93** ± 9.19	**0.22**

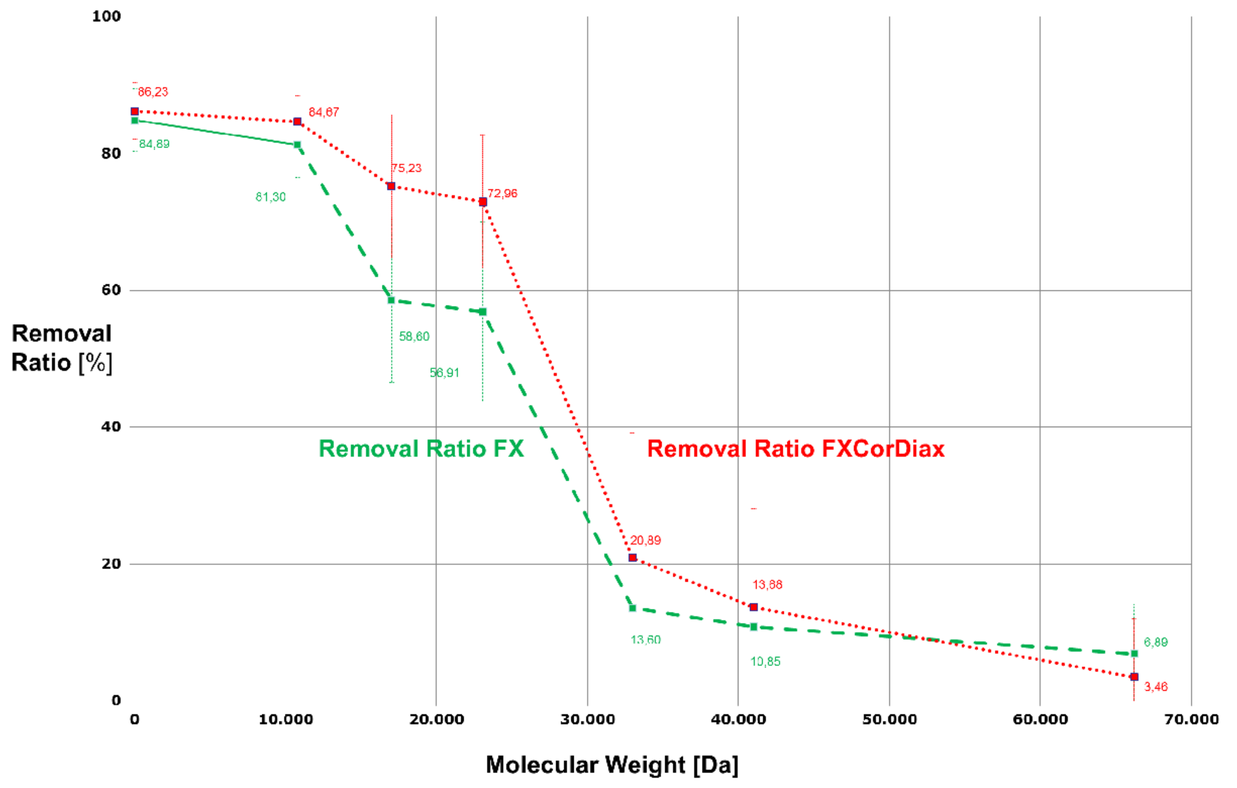

Fig. 1 Removal Ratios of FX and FXCorDiax Dialyzers vs. Molecular Weight [Da]

Discussion

A lot of molecules are known as uremic toxins[10,11] and are removed by convective transport mechanisms in hemodiafiltration (HDF). E. g. phosphate is known to be a risk factor for major cardiovascular events[12] and ß2-microglobulin a predictor for all-cause mortality in HD-patients[13]. Clinical studies employing sets of marker molecules have been performed to characterize pre- and post-hemodiafiltration[8], HDF-systems with on-line regeneration of ultrafiltrate[9] or dialyzers[14] .
There is only little evidence focusing on the relation of removal ratios on the blood side and the corresponding eliminated molecule masses in the dialysate. Using a setting[14] of marker molecules defined by molecular weight allows characterizing dialyzers based on blood- and dialysate-side laboratory data.
Our results showed an increase of the removal ratios for middle molecules for the FXCorDiax dialyzer compared with FX. Analysis of the dialysate showed in general the same result, though the albumin loss for the FXCorDiax was slightly enhanced, which was found to be statistically significant but the difference was judged to be clinically irrelevant.

Conclusion

This study demonstrated that treating patients with online hemodiafiltration and FX CorDiax 60 dialyzers instead of FX 60 results in significantly increased reduction ratios of middle sized molecules without clinically relevant changes in albumin loss. This improvement in removal capacity of higher-molecular weight uremic toxins enables clinical benefit for the patients.

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