Effect of Higher Convection on the chronic inflammatory markers: comparison between middilution vs post-dilution hemodiafiltration.

Borrelli S[1,2], De Simone E[3], Laurino S[2], De Simone A[2], Covotta L[2], Sereni L[4], **De Simone W[2]**

[1]Second University of Naples ; [2]" San Giuseppe Moscati" Hospital of Avellino; [3]University of Bologna; [4]Bellco Scientific affairs.

INTRODUCTION

Background

Chronic inflammation is widely diffuse in maintenance haemodialysis (HD) patients and is associated with poor survival [1-3].

Middilution (MID) is a novel highly efficient convective-mixed technique that combining pre-dilution and post-dilution, improves removal capacity and have been shown of additional benefit for large middle molecules by higher convective clearance [4]

Whether this convective mixed technique could improve inflammatory status of these patients is unknown too.

Aims:

The aim of this prospective cross-over study was to compare the effect of MID with convectional post-dilution HDF on inflammatory biomarkers in HD patients.

METHODS

After a 1 month run-in period of bicarbonate dialysis, chronic HD patients were shifted with a cross-over design to a higher convection treatment by Middilution (MID) or a lower convection treatment by post-dilution hemodiafiltration (HDF). In reverse MD-HDF with the MD-220 dialyser, post-dilution occurs in the core region of the fibre bundle (1.0 m^2) through which blood first flows, then pre-dilution is performed in the annular region (1.2 m^2) with co-current dialysate flow (figure 1).

It has been calculated that about 2/3 of convection volume is in post-dilution and 1/3 in pre-dilution [4].

Each study period of 4 months was followed by 1 month of HD and the total duration of the study was 9 months.

Primary outcome was the change of serum levels of C reactive Protein (CRP), IL-6, IL-1, IL-10, TGF-β, TNF-α, β2-Microglobulin, albumin and prealbumin, monthly assessed, during four months of each treatment.

RESULTS

Ten HD patients were enrolled (age:64.9 12.6 years; dialytic vintage: 10.6(2.7-16.2) years; 70% males). Mean convection volume was 40.6 2.6 L/session (of which 26.5 1.7 L/session in post-dilution) in MID and 16.8 2.1 L/session in HDF. As shown in table 1, in MID we registered a reduction of CRP from 11.3 [3.2-31.0] to 3.1[1.4-14.4] mg/L (P=0.007), IL-6 from 12.7 [5.0-29.7] to 8.3 [4.4-14.0] pg/mL (P=0.003), TGF-β from 10.6[7.4-15.6] to 7.4[5.9-9.3] ng/mL (P=0.001) and β2-Microglobulin from 39.0 9.4 to 30.1 9.1 mg/L (P<0.0001). However, in post-dilution HDF (table 2) a significant reduction of CRP from 8.5 [3.2-31.0] to 4.6 [3.2-31.0] mg/L (p=0.037) and β2-Microglobulin from 39.4 9.3 to 30.1 9.1 mg/L was detected (P<0.0001). In MID the percentage changes of serum CRP and IL-6 were correlated with post-dilutional convective volume [R=0.73 (P=0.018) and R=0.71 (P=0.022) respectively].

Figure 1. Reverse configuration of filter in MID

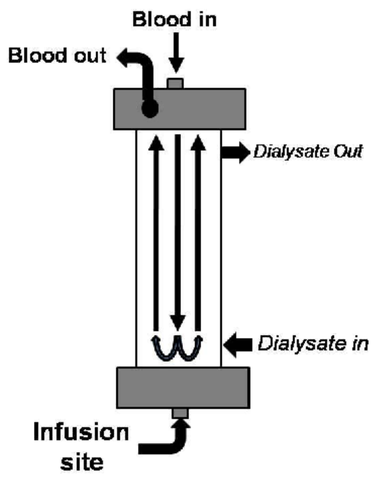

Table 1. Effect of middilution on inflammation

	Baseline	1° mo	2° mo.	3° mo	4° mo	p
CRP *(mg/L)*	11.3(3.2-31.0)	3.6(1.3-6.4)	3.1(1.3-6.4)	6.7(2.7-9.6)	3.1(1.4-14.4)	0.007
IL-6 *(pg/ml)*	12.7(5.0-29.7)	6.9(4.7-9.1)	5.6 (4.0-10.1)	8.5(4.4-11.1)	8.3(4.4-14.0)	0.003
IL-1 *(pg/ml)*	0.0(0.0-0.1)	0.0(0.0-0.2)	0.0(0.0-0.1)	0.0(0.0-0.1)	0.0(0.0-0.2)	0.463
IL-10 *(pg/ml)*	6.0(2.8-10.0)	9.7(4.0-13.5)	5.4(3.0-10.3)	8.1(3.9-14.5)	6.9(3.0-18.0)	0.648
TNF-α *(pg/ml)*	12.0(3.5-17.0)	8.6(4.4-13.4)	9.4(7.9-14.5)	16.6(11.1-18.3)	12.5(9.5-15.7)	0.107
TGF-β *(pg/ml)*	10.6(7.4-15.7)	11.0(6.3-15.6)	12.6(10.4-15.0)	10.1(8.0-12.5)	7.4(5.9-9.3)	0.001
Albumin *(g/dl)*	4.0(3.8-4.5)	4.4(3.8-4.7)	4.0(3.8-4.4)	4.0(3.8-4.2)	4.0(3.7-4.2)	0.266
Prealb. *(g/dl)*	2.9(2.6-3.8)	3.3(2.8-4.3)	3.5(2.9-4.3)	3.4(2.4-3.7)	3.2(2.9-4.0)	0.045

Table 2. Effect of HDF on the inflammation

	Baseline	1° mo	2° mo.	3° mo	4° mo	p
CRP *(mg/L)*	8.5(3.1-23.2)	7.5(2.9-13.2)	8.3(2.2-15.6)	10.4(2.5-19.8)	4.6(1.2-8.6)	0.037
IL-6 *(pg/ml)*	9.7(3.3-15.9)	8.0(3.0-14.3)	10.2(4.2-18.9)	8.0(4.6-22.0)	7.7(4.0-12.6)	0.147
IL-1 *(pg/ml)*	0.0(0.0-0.1)	0.0(0.0-0.2)	0.0(0.0-0.1)	0.0(0.0-0.1)	0.0(0.0-0.2)	0.514
IL-10 *(pg/ml)*	6.0(4.2-12.3)	11.1(8.7-15.4)	9.3(7.3-14.1)	6.1(5.1-9.4)	8.2(5.4-10.4)	0.104
TNF-α *(pg/ml)*	10.0(5.0-14.9)	9.8(4.9-12.9)	8.0(4.5-18.8)	10.0(4.4-13.7)	12.0(7.9-17.2)	0.374
TGF-β *(pg/ml)*	10.0(6.4-11.9)	9.5(6.1-15.5)	11.1(8.3-13.1)	10.8(6.8-15.5)	9.2(6.6-11.0)	0.095
Albumin *(g/dl)*	4.1(3.9-4.5)	4.0(3.5-4.5)	4.0(3.8-4.3)	4.0(3.7-4.2)	4.0(3.8-4.3)	0.144
Prealb. *(g/dl)*	3.3(2.5-3.6)	3.0(2.5-3.6)	3.0(2.5-3.9)	3.3(2.6-4.0)	3.1(2.4-4.0)	0.997

CONCLUSIONS

MID is associated with an attenuation of inflammatory pattern that seems to be correlated with higher convective volume. Our study is limited by little sample size and no randomized nature of study that does not allow interpretation of results in causal terms. We are waiting the results of Milestone trials on effect of MID on mortality.

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