Improvement of ESA responsiveness in HD patients treated by high cut-off hemodialysis – pilot study (CIEPO-Pilot)

Giorgio Romei Longhena [1], Werner Beck [2], Ariane Liebchen 2, Ugo Teatini 1

1 Bollate Hospital; AO Garbagnate M.se, Milan, Italy; 2 Gambro Dialysatoren GmbH, Hechingen, Germany

INTRODUCTION & AIMS

Chronic inflammation in HD patients is caused by multiple inflammatory stimuli and linked to clinical signs and symptoms and cardiovascular mortality. Inflamed dialysis patients also show an impaired response to erythropoiesis-stimulating agents (ESAs).
Aim of this pilot study was to investigate if HD treatment with a membrane having a high molecular permeability in a broad molecular weight range improves ESA responsiveness (ESA resistance index, ERI) and attenuates the chronic inflammatory state.

METHODS

24 ESRD patients (6 women, 65 16 years, 70 11 kg) on 3x per week chronic high-flux HD or HDF (for ≥3 months) with adequate iron status (TSAT > 20%, ferritin > 100 ng/mL) were randomized into a study group (Theralite high cut-off membrane (Gambro) alternating with routine treatment high-flux HD or HDF) or control group (only routine treatment high-flux HD or HDF) and treated for 12 weeks. ESA dose was adapted according to guidelines to maintain Hb levels in the range of 10-12 g/dL. CRP, IL-6, IL-10, hepcidin (ELISA), κ- and λ-FLCs (nephelometry), ESA dose, Hb and albumin were analyzed during the study period.

RESULTS

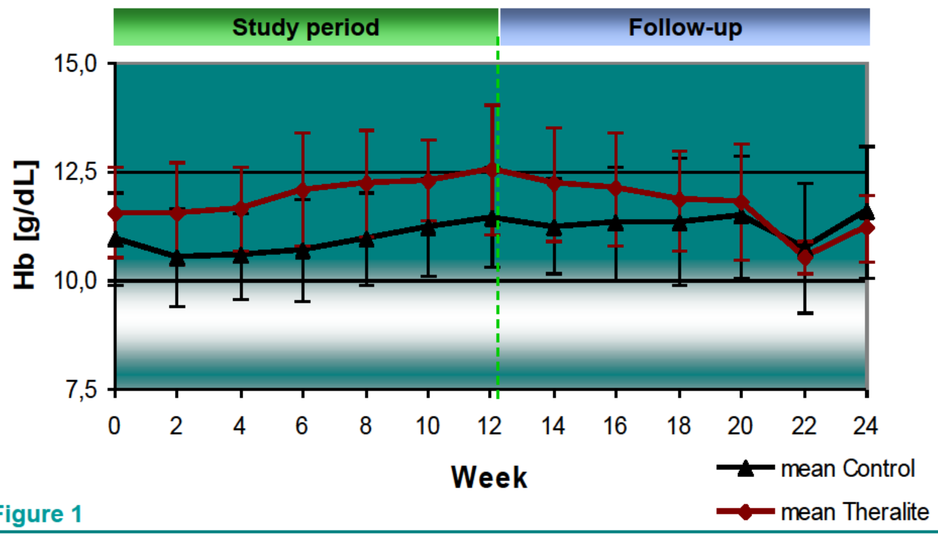

Figure 1

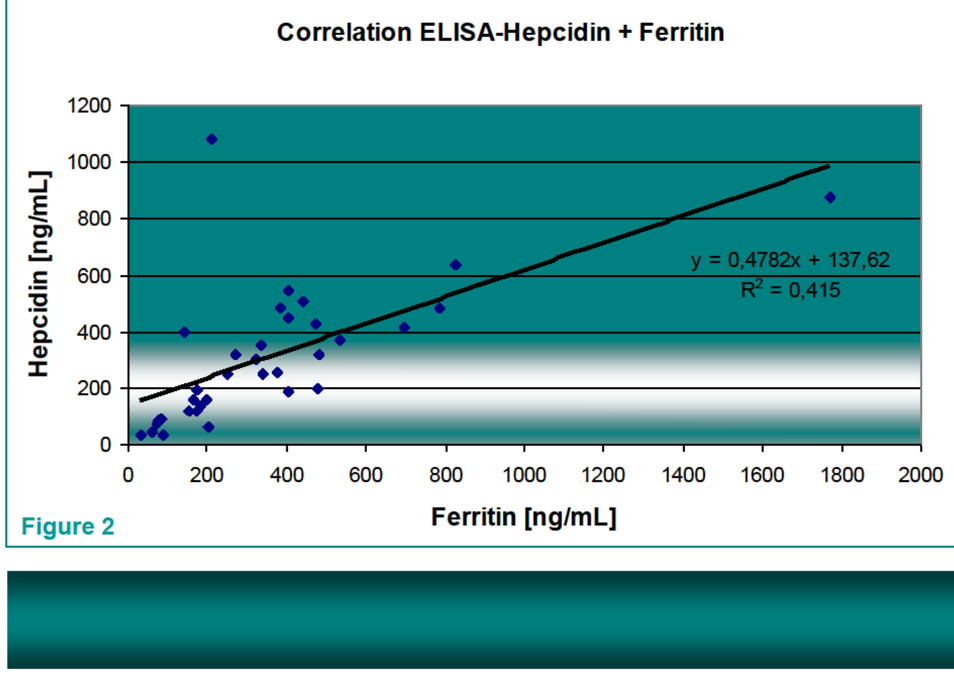

Figure 2

Group	Time point	ERI [IU/kg/weeek/g/dL]	Hb [g/dL]	CRP [mg/L]	Hepcidin [ng/mL]	Albumin [g/dL]
Control (n=10)	T0	14.6 ± 5.1	11.0 ± 1.1	2.9 ± 3.5	324 ± 309	3.9 ± 0.2
	T12	13.3 ± 4.8	11.5 ± 1.1	4.1 ± 3.9	370 ± 250	4.1 ± 0.2
	T24	12.2 ± 5.3	11.6 ± 1.5	-	-	4.0 ± 0.3
Theralite (n=7)	T0	11.3 ± 3.4	11.6 ± 1.0	4.3 ± 5.5	303 ± 189	4.0 ± 0.3
	T12	10.4 ± 2.8	12.5 ± 1.5 *	3.6 ± 3.3	157 ± 83 *°	3.4 ± 0.4 *°
	T24	11.7 ± 4.2	11.2 ± 0.8	-	-	3.9 ± 0.3

* p<0,05 vs T0; p<0,05 vs T12 control

- 6 patients dropped out during the 12 weeks study period. One patient was excluded due to unusual high ferritin values. Data from patients who completed the 12 weeks study period are shown.
- ERI reduction in both groups (non-significant, see table for results)
- Significant increase in hemoglobin (Hb) levels in the study group with a peak after 12 weeks in contrast to the control group (table and figure 1)
- Significantly lower hepcidin levels were measured in the study group, while an increase has been detected in the control group.
- Significant correlation of ferritin with hepcidin (p<0.0001; figure 2)
- A drop of albumin was detectable in the study group; the levels stabilized after about 2 weeks at the lower level
- The intradialytic reduction ratios of κ and λ FLCs (24 kDa and 45 kDa respectively) had been higher in the study group compared to the controls (80 7% and 72 9% vs. 47 9% and 12 8% (p<0.005))

CONCLUSIONS

The data of this pilot study shows that high cut-off dialysis allows a significant better removal of large uremic toxins (λ FLCs) and points to an improved ESA responsiveness (indicated by a rise in Hb levels and a fall in hepcidin). Larger studies with strict control of ESA dose adjustment are needed to confirm if regular treatment with high permeability membranes leads to an improvement in anemia of chronic inflammation in HD patients.

50ERA-EDTA
545--SP
Anaemia in CKD 5D
Ugo Teatini
Poster presented at: ERA-EDTA 50th Congress Istanbul, Turkey May 15-21, 2013