THE CLOSED LOOP CONTROL OF BLOOD VOLUME (BV) IN ON-LINE HEMODIAFILTRATION (OL-HDF)

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Alessandro Surace[1], Paolo Rovatti[1], Denis Steckiph[2], Elena Mancini[3], Antonio Santoro[3]

[1]Gambro Dasco S.p.A.*, Medolla, Italy; [2]Gambro Hospal S.p.A.*, Bologna, Italy; [3]U.O. Nephrology Dialysis and Hypertension, S.Orsola-Malpighi Teaching Hospital, Bologna, Italy.

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Objectives

The European Best Practice Guidelines on hemodynamic instability [1] propose, among the possible strategies to prevent intradialysis hypotension (IDH), the use of convective treatments and the application of individualized BV controlled feedbacks.

High volume convective treatments offer different advantages, even from the cardiovascular standpoint [2].

Furthermore, numerous studies demonstrated that the **HemoControl™** (HC) biofeedback system on Blood Volume reduces IDH and improves cardiovascular stability [3, 4].

However, this system has never been used in On-Line Hemodiafiltration treatments (OL-HDF): the combination of HC benefits with those of high-volume convective treatments could be of major clinical interest.

Since HC continuously modifies the dialysate conductivity, the **aim** of this study was to verify performance and safety of HC system in OL-HDF treatments in terms of dialysis efficiency and sodium balance.

Methods

A **new Na^+ kinetic model** was developed to take into account, apart from dialysate Na^+, both the infused Na^+ and that removed by convective transport.

This model was tested in a prospective, randomized, cross-over, pilot study (**SOCRATHE**, NCT01582867).

Six patients (4 male, 2 female) were treated on 2 different modalities, i.e. HD+HC and OL-HDF with HC (HDF+HC). For each modality a first Run-In phase consisted of 6 HD (or OL-HDF) treatments has been executed, followed by 12 treatments with HC system activated. Each patient acted as his/her own control. Patients' characteristics are summarized in Table 1.

Plasma Na^+ concentrations (Na_p, measured every hour by ion selective sodium electrode), interdialytic weight gain (IDWG), systolic and diastolic blood pressures (BP) pre and post-dialysis, relative BV changes (ΔBV%), dialysis dose (KT/V) and thirst scores reported by the patients (TS, Likert type scales from 1=never to 5=always thirsty) were collected. Furthermore, eventual detrimental effects on treatment efficacy, due to the mutual interaction of HC system with OL-HDF therapy, have been assessed.

HC prescription was the same in both the modalities.

Statistical analysis was conducted considering the mean value calculated for each primary endpoint of each patient in HD+HC and HDF+HC phases.

Paired t-test was used for analysing differences between the two treatments given to the same patient.

For time dependent variables **ANOVA for repeated measures** was used.

Table 1: Patients' characteristics (Mean ± SD)

Age	73±12
Dry Weight [Kg]	67.5±12.3
Years on HD	5±6
Pre-dialysis Na^+ (before the study)	135.5±5.4
Haemoglobin [g/dl]	10.7±1.4
Diagnoses of renal disease	Hypertensive Nephropathy (3) Diabetic nephropathy (3)

Results

Statistical differences on primary endpoints between HD+HC and HDF+HC treatment modalities are summarized in Table 2.

Table 2: Evaluation of statistical differences between HD+HC and HDF+HC

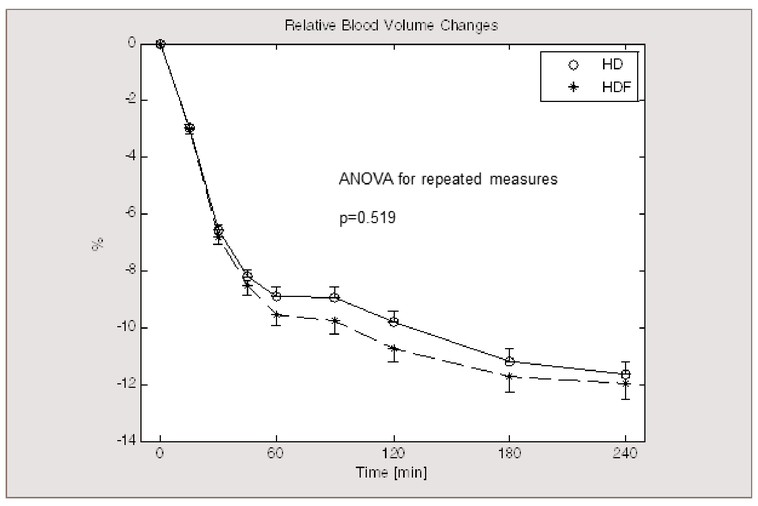
	IDWG [Kg]	Initial Nap [mmol/L]	Final Nap [mmol/L]	KT/V
HD+HC	3,02 ± 0,47	134,8 ± 4,2	135,4 ± 2,2	1.29 ± 0.20
HDF+HC	3,07 ± 0,56	135,8 ± 3,9	136,5 ± 2,1	1.37 ± 0.25
p-value (Paired t)	p=0,503	p=0,114	p=0,028*	p=0.020*

	Pre-dialysis BP [mmHg]	Post-dialysis BP [mmHg]	Thirst Score
HD+HC	Systolic (S): 130 ± 23 Diastolic (D): 67 ± 18	S: 121 ± 13 D: 67 ± 17	7,3 ± 2,5
HDF+HC	S: 128 ± 19 D: 67 ± 17	S: 122 ± 13 D: 65 ± 13	9,0 ± 2,5
p-value (Paired t)	S: p=0,580 D: p=0,768	S: p=0,936 D: p=0,489	p=0,049*

No significant difference was found in terms of IDWG, BP values and ΔBV% (Figure 1).

The infusion volume achieved in HDF+HC was comparable with the OL-HDF one (20.6±2.8 vs 20.2±3.9 l, p=0.845).

Figure 1: Average ΔBV% in HD+HC and HDF+HC



Achieved Dialysis Dose resulted higher in HDF+HC treatments (see Table 2).

The HC system with the new Na^+ kinetic model working in OL-HDF was as accurate as in HD treatments to reach its final targets (ΔBV%, Total Weight Loss and serum sodium) as showed in Table 3.

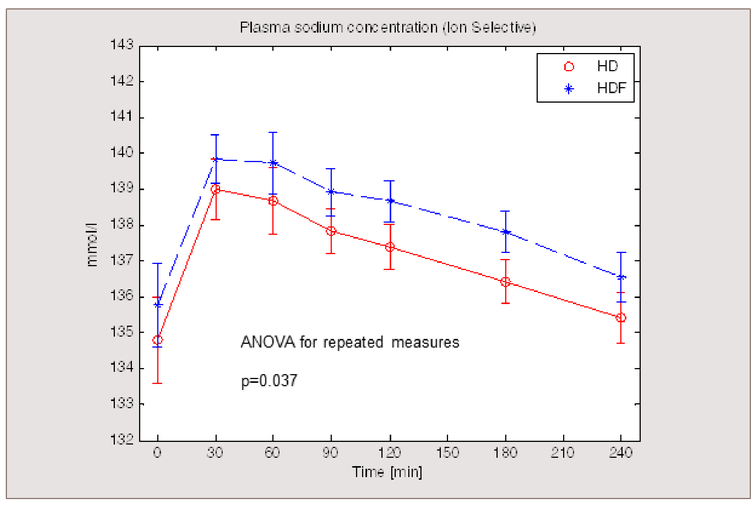
Plasma sodium concentration resulted slightly higher in HDF+HC treatments (about 1 mmol/l for both initial and final Na_p, see Figure 2): however, this Na^+ difference is widely within the instrumentation accuracy (± 3 mmol/l) and

Table 3: Average errors, with respect to desired final targets, for effective TWL, serum sodium and ΔBV/TWL in HD+HC and HDF+HC

	Err_TWL [l]	Err_Na^+ [mmol]	Err_ΔBV/TWL [%/l]
HD+HC	-0.16 ± 0.06	0.94 ± 0.34	-0.08 ± 0.26
HDF+HC	-0.25 ± 0.12	0.61 ± 0.40	0.02 ± 0.44
p-value Paired t-test	0.187	0.159	0.640

can be compensated by lowering of the same amplitude the HC final target sodium.

Figure 2: Average Na_p in HD+HC and HDF+HC



Conclusions

- HDF+HC therapy resulted **safe** and with **performances comparable to HD+HC** in terms of IDWG, BP, ΔBV%.
- The new Na^+ kinetic model implemented in OL-HDF allows to **reach the HC desired targets with the same accuracy obtained in HD.**
- The concurrent use of HC system does **not lower** the effectiveness of OL-HDF treatments in terms of **convective volumes** achieved.
- Na_p slightly higher in HDF+HC (about 1 mmol/l): however, this difference is within the instrumentation accuracy and remains stable during the session highlighting a comparable effect of the HC system when applied in HD or in OL-HDF. Hence, there are **no sufficient evidences to suppose sodium retention effect when combining HC and OL-HDF.**

Further studies will be needed in order to demonstrate if such a system is able to produce relevant clinical benefits in the long term.

References

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