CITRIC ACID AND ACETATE FREE BASED DIALYSATE IN ONLINE HEMODIAFILTRATION POST-DILUTION ALLOWS HEPARIN FREE SESSIONS

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INTRODUCTION AND AIM

Up to now, heparin is the simplest mean to realize OnLine HemoDiaFiltration Post-Dilution (OL-HDF) without clotting, however it induces several adverse events (increased bleeding risk, bone metabolism disorders, dyslipidemia) and exposes nurses to patients' blood. Citric acid based concentrate has been yet studied in order to stop heparin injection during dialysis sessions (J. Aniort, Blood purif. 2012) but this dialysate contains a small proportion of acetate (citric acid 0.8mM, acetate 0.3mM) with its own side effects (per-dialytic hypotension, cramps, inflammation). The aim of our study is to determine if citric acid and acetate free fluid (citric acid 1mM, acetate 0mM) is safe in HDF-OL and can allow heparin removal.

PATIENTS AND METHODS

All stable patients treated by OL-HDF with 3mM acetate dialysate on machines accepting the studied concentrate (Select Bag Citrate®, Gambro) were prospectively included (***Fig. 1***). Patients treated with antiplatelets and/or antivitamin K drugs were not excluded. Study patients received citrate concentrate and have been randomly assigned to either the control group (nadroparin as usual at the beginning of the OL-HDF session) or study group (nadroparin slow withdrawal, 0.1ml per week until discontinuation) for a 3 months period. Dialysis fluids contained 0.10 or 0.15mEq/l calcium more than usual (1.60 or 1.65mEq/l) in order to avoid hypocalcemia. Other dialysis parameters remained unchanged (blood flow rate, dialysis flow rate, …). Substitution was always achieved by Ultra-Control® system. The blood calcium concentration (total or ionized) was checked weekly for 4 weeks. All the hemorrhagic or clotting events were thorough noted as well as online dialysance and total convective volumes at each session. Same data were extracted from the sessions realized 3 months before the prospective study to evaluate the stability of calcium and epuration by comparison with acetate concentrate. Statistical analyses were performed with Statview® software and non parametric tests were applied.

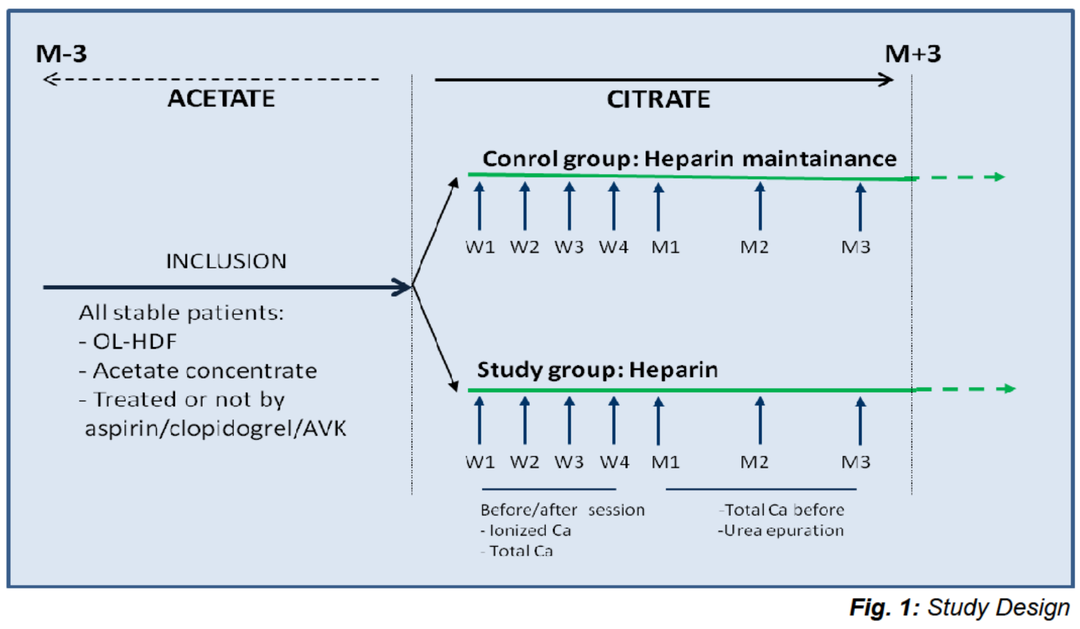

Fig. 1: *Study Design*

RESULTS

PATIENTS AND SESSIONS:

17 patients (16 male/ 1 female, mean age 71.8 years +/- 18.7) were enrolled in the study. 9 patients were randomly assigned to the control group and 8 to the study group (fraxiparin discontinuation). 589 sessions were analyzed, 306 in the control group and 283 in the study group (***Fig. 2***).

All the HDF-OL sessions realized (n=538) during the 3 months period before citrate introduction on study patients have been analyzed so that calcium balance and the quality of OL-HDF has been compared.

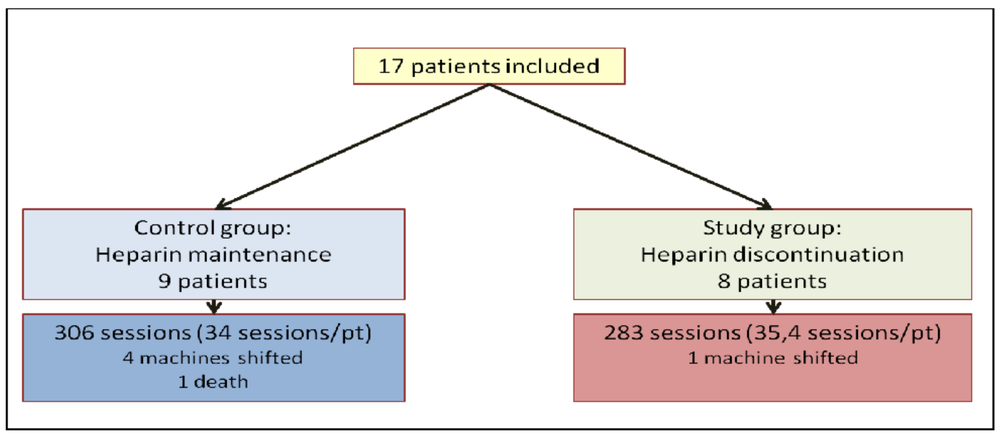

Fig.2: *Flow Chart*

COAGULATION:

In the study group, no more clotting events were observed (13 in each group, control patients: 4.25% - Study patients: 4.59%, p=0.94). No more loss of blood circuits was also observed (Control group: 3 events, 0.98% - Study group: 5 events, 1.77%) (***Fig. 3***).

Nadroparin was discontinued by 5 out 8 patients in the study group and 0 out 9 in the control group (p=0.009) with 0.075ml mean dose in study group *vs.* 0.41 ml in control group (p=0.018) (***Table 1***).

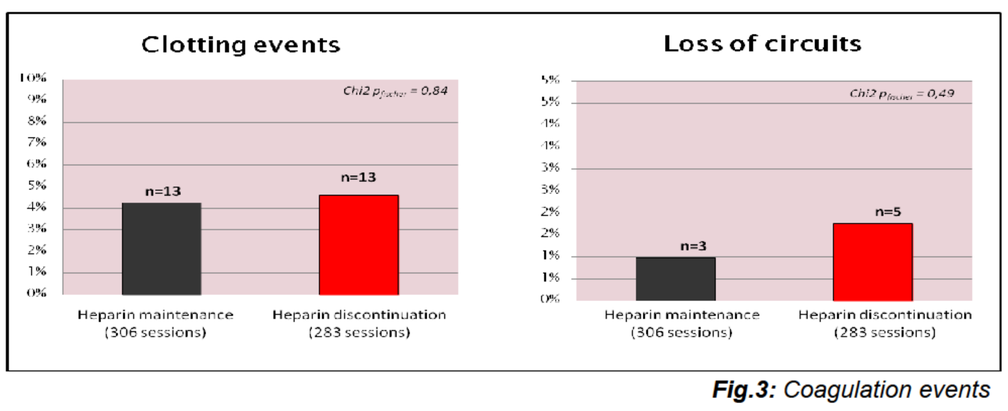

Fig.3: *Coagulation events*

Table 1: *Heparin use*

	Control Group Heparin maintenance	Study group Heparin discontinuation	p
Mean dose of nadroparin at baseline	0.41 ml (+/- 0.18 ml)	0.40 ml (+/- 0.12 ml)	0.93 (Wilcoxon)
Mean dose of nadroparin at the end of study	0.41 ml (+/- 0.18 ml)	0.075 ml (+/- 0.12ml)	0.018 (Wilcoxon)
Number of patients without nadroparin at the end of the sutdy	0/9 (no delivery change during the study)	5/8 Pt n°1 0.5 =>0.3 (no discontinuation) Pt n°3 0.3 => 0.1 (disc. failure) Pt n°8 0.6 => 0.2 (no discontinuation)	0.009 (Chi2)

CLINICAL TOLERANCE:

No bleeding, no paresthesia, no arrhythmia, no seizure were observed during the study period with the citrate dialysate. Blood pressure, before and after sessions, also remained unchanged with citrate fluid compared to acetate concentrate. Hemoglobin was not different in the control group (11.9 g/dl +/- 1.1 g/dl) and in the study group (11.5g/dl +/- 0.5g/dl) (Wilcoxon test, p=0.27) as well as erythropoietin resistance index (Control group 9.1 +/- 5.9 UI/kg/week, study group: 8.0 +/- 1.8UI/kg/week) (Wilcoxon test, p=0.86).

CALCIUM BALANCE:

No difference in total calcemia was observed between acetate dialysate and citrate dialysate (global Friedman test, p=0.19) (***Fig. 4***). Same results were obtained for PTH concentration (p=0.55). Total and ionized calcium concentration also remained stable during the first 4 weeks of the citrate use (***Fig. 4***).

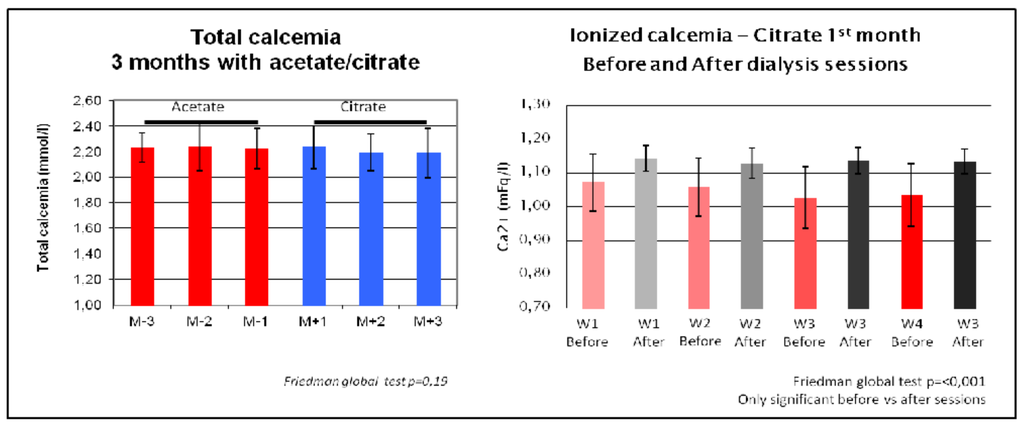

Fig.4 *Calcium balance*

DIALYSIS ADEQUACY:

The dialysis dose did not differ among the two groups (Kt/V Daugirdas 2: control group 1.81 *vs.* 1.72 study group, Wilcoxon p=0.68 and On-line Kt 51.64 *vs.* 50.53, Wilcoxon p=0.40) as well as total convective volumes (26.45l in control group *vs.* 26.50l in study group, Wilcoxon p=0.94) (***Fig. 5***). No difference was emphasized during acetate and citrate period.

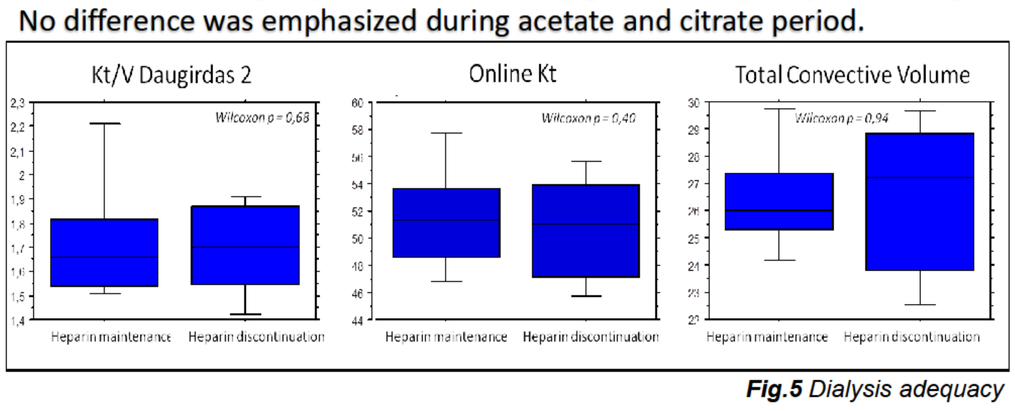

Fig.5 *Dialysis adequacy*

CONCLUSION

Heparin free OL-HDF is achievable with the use of citrate based and acetate free concentrates. Dialysis parameters and performances remain stable. Nevertheless, not all the patients can benefit from this technique and the reasons should be determined by a larger and longer trial.

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M) Dialysis. M1) Extracorporeal dialysis: techniques and adequacy.
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