REDUCTION OF HEPAIN DOSE IN ROUTINELY DIALYSIS WITH CITRATE CONCENTRATE AND HEPARIN-GRAFTED MEMBRANE

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INTRODUCTION / AIM

Heparin is the most common anticoagulant drug used in chronic dialysis, but a number of side-effects are well-known. Recent trials have shown, in routinely practices, that citrate enriched concentrate could be able to decrease 33% of heparin dose in 92% of the population [1] and heparin-grafted membrane (Evodial-membrane HeprAN, Gambro, Meyzieu) of 45% in the 67% of the study population [2].

Our **Aim** was to evaluate the feasibility of heparin reduction (unfractionated -UFH- and low molecular-weight –LMWH- ones) in routinely practices using citrate enriched concentrate and heparin-grafted membrane and its effect on dialysis dose.

METHODS

19 stable ESRD patients (16/3 FAV/CVC, Hb 11.4±1.0 g/dl, Ht 34.5±3.1%) were enrolled in a 7-week, prospective, non-randomized, longitudinal, controlled study. Each patient was her/his control and, according to anticoagulant type used, was assigned to one of 2 groups: UFH or LMWH group (tab. I and II). At the baseline, the patients were treated with HD high-flux polysulfone membrane and regular concentrate (Ac-bicarbonate) for 1 week; then each patient was switched to HD high-flux with citrate concentrate and Evodial for 1 month, decreasing the heparin dose (UFH: two reduction steps, -30% and -50%, of 2 weeks; LMWH: one reduction step: -30%). Finally the last two weeks all patients were treated by Evodial and Ac-bicarbonate concentrate (Phase 3 for UFH and Phase 2 for LMWH). The following variables were measured: number of clotting sessions, Kt/V, visual clotting score for dialyzer (ranged from 0 to 4, fig.1) and bloodlines (ranged from 0 to 4, fig.2). The pre-dialytic values of PTH were measured at baseline and Phase1 in both groups.

Statistics: The descriptive analysis was based on the mean ± standard deviation. Inferential statistics included two tailed t-test for paired data, considering a probability value of less than 0.05 as significant.

UFH Group	Baseline	Phase 1	Phase 2	Phase 3
Treatment Type	High-flux HD	High-flux HD	High-flux HD	High-flux HD
Dialyzer Membrane	Polysulphone	HeprAN	HeprAN	HeprAN
Concentrate Type	Ac-bicarbonate based buffer, Ca=1.50 mM	Cit-bicarbonate based buffer, Ca=1.65 mM	Cit-bicarbonate based buffer, Ca=1.65 mM	Ac-bicarbonate based buffer, Ca=1.50 mM
Heparin dose (UI/Kg)	64 20	44 13	36 7	64 20

Table I:
Study design UFH Group

Figure 1:
Dialyzer Clotting Score

LMWH Group	Baseline	Phase 1	Phase 2
Treatment Type	High-flux HD	High-flux HD	High-flux HD
Dialyzer Membrane	Polysulphone	HeprAN	HeprAN
Concentrate Type	Ac-bicarbonate based buffer, Ca=1.50 mM	Cit-bicarbonate based buffer, Ca=1.50 mM	Ac-bicarbonate based buffer, Ca=1.50 mM
Heparin dose (UI/Kg)	71 16	49 9	71 16

Table II:
Study design LMWH Group

Figure 2:
Bloodline Clotting Score

RESULTS

All patients completed the study in both groups. The percentages of clotting sessions were reported in table III. The Kt/V were not different between the phases on LMWH Group (baseline 1,14±0.2, Phase 1 1,17±0.1, Phase 2 1,16±0.2, p=n.s.), while it decreased on both heparin reduction steps on UFH Group (baseline 1,22±0.2, Phase 1 1,12±0.2, Phase 2 1,12±0.2, Phase 3 1,29±0.2, p<0.01). The visual clotting score for dialyzer did not show any difference on LMWH Group (baseline 1,0±0.0, Phase 1 1,2±0.4, Phase 2 1,3±0.4, p=n.s.), while it increased on UFH Group, but still remaining below any safety threshold (baseline 0,1±0.2, Phase 1 0,5±0.4, Phase 2 0,6±0.5, Phase 3 0,1±0.2, p<0.01). The visual clotting score for bloodlines did not show any difference on LMWH Group (baseline 0,8±0.6, Phase 1 0,8±0.6, Phase 2 0,8±0.6, p=n.s.) and on UFH Group (baseline 0,7±0.5, Phase 1 0,8±0.6, Phase 2 0,7±0.5).

The pre-dialytic values of PTH were affected by 1 mM of Citrate on LMWH group (Baseline: 215±196 vs Phase 1: 315±229, p<0.05; fig.3), while it did not happen on UFH group due to the increase of the Calcium concentrate content of 0.15 mM (Baseline: 290±36 vs Phase 1: 330±48, p=0.160; fig.4).

Session with clotting	Baseline	Phase 1	Phase 2	Phase 3
UFH Group	0/30	0/60	1/60	0/30
LMWH Group	0/30	1/120	0/30	

Table III: *Session with clotting on UFH and LMWH Groups*

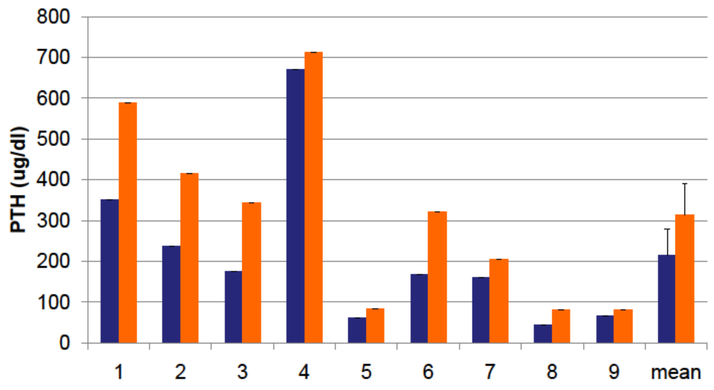

Figure 3: *pre-dialytic PTH level of patients in LMWH group (baseline in blue columns, Phase 1 in orange columns)*

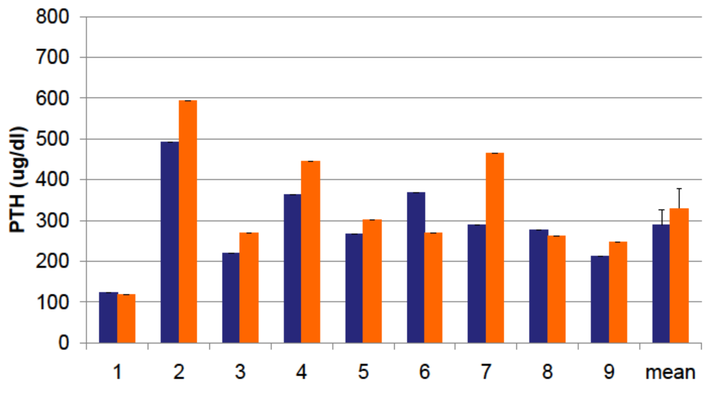

Figure 4: *pre-dialytic PTH level of patients in UFH group (baseline in blue columns, Phase 1 in orange columns)*

CONCLUSIONS

The Heparin is a risk factor in dialysis patients, particularly in those with hemorrhagic diathesis, anticoagulant therapy or with a long hemostasis time at the end of HD treatment. Combining Citrate in dialysis fluid and heparin-grafted membrane could, based on our preliminary data, routinely halve the heparin dose in the 100% of ESRD patients treated with UFH and decrease of 30% the heparin dose in patients treated with LMWH. Further studies to validate our data and to investigate further decrease in the dose of heparin are required.

REFERENCES

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510--MP
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Ugo Teatini
DOI: 10.3252/pso.eu.51era.2014
Poster presented at: 51 ERA-EDTA CONGRESS AMSTERDAM 2014
PosterSessionOnline.com