

REDUCTION OF HEPARIN AND OXIDATIVE STRESS USING CITRATE ENRICHED DIALYSATE IN HIGH-FLUX DIALYSIS

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OBJECTIVES

Citrate containing dialysate (Citrasate®) has been reported to have anti-coagulant properties, which allow to reduce the Heparin dosage (1,5). If the heparin dosage was reduced by 50%, additionally a significant decrease of myeloperoxidase (MPO) plasma level was also found recently (5). It was the aim of this study to clarify the question, if the heparin or the Calcium-binding effect of citrate causes mainly the decrease of MPO level, which means a reduction of oxidative stress during high-flux-dialysis.

METHODS

14 stable ESRD-patients were treated with high-flux dialysis and included in the trial running 14 weeks. The trial was divided in the following 4 study periods:

- Weeks 1+2: Baseline with standard concentrate and customary Heparin dose.
- Weeks 3-6: Change over to Citrasate® with unchanged treatment conditions.
- Weeks 7-10: Reduction of the Heparin bolus by 50 %.
- Weeks 11-14: Reduction of both, Heparin bolus and continuous dose, by 50 %.

Measured parameters: iCa, total Ca, HCO₃⁻, electrolytes, spKt/V, activated clotting time (ACT) and myeloperoxidase (MPO) plasma concentration.

Treatment parameters: Blood flow: 300-320 ml/min, dialysate flow: 500 ml/min. The treatments were performed with FMC 5008 machines and FX high-flux-dialyzers.

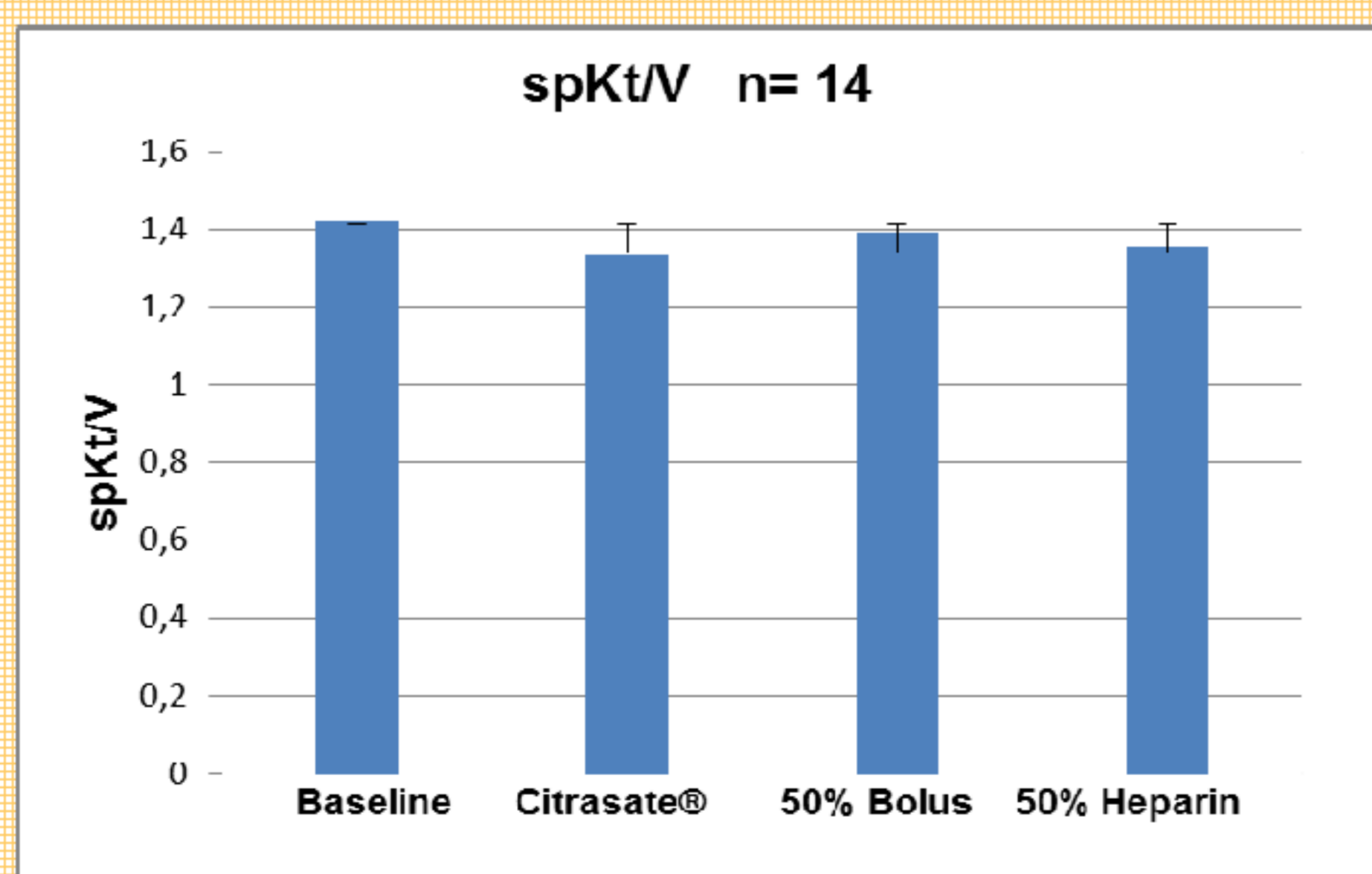
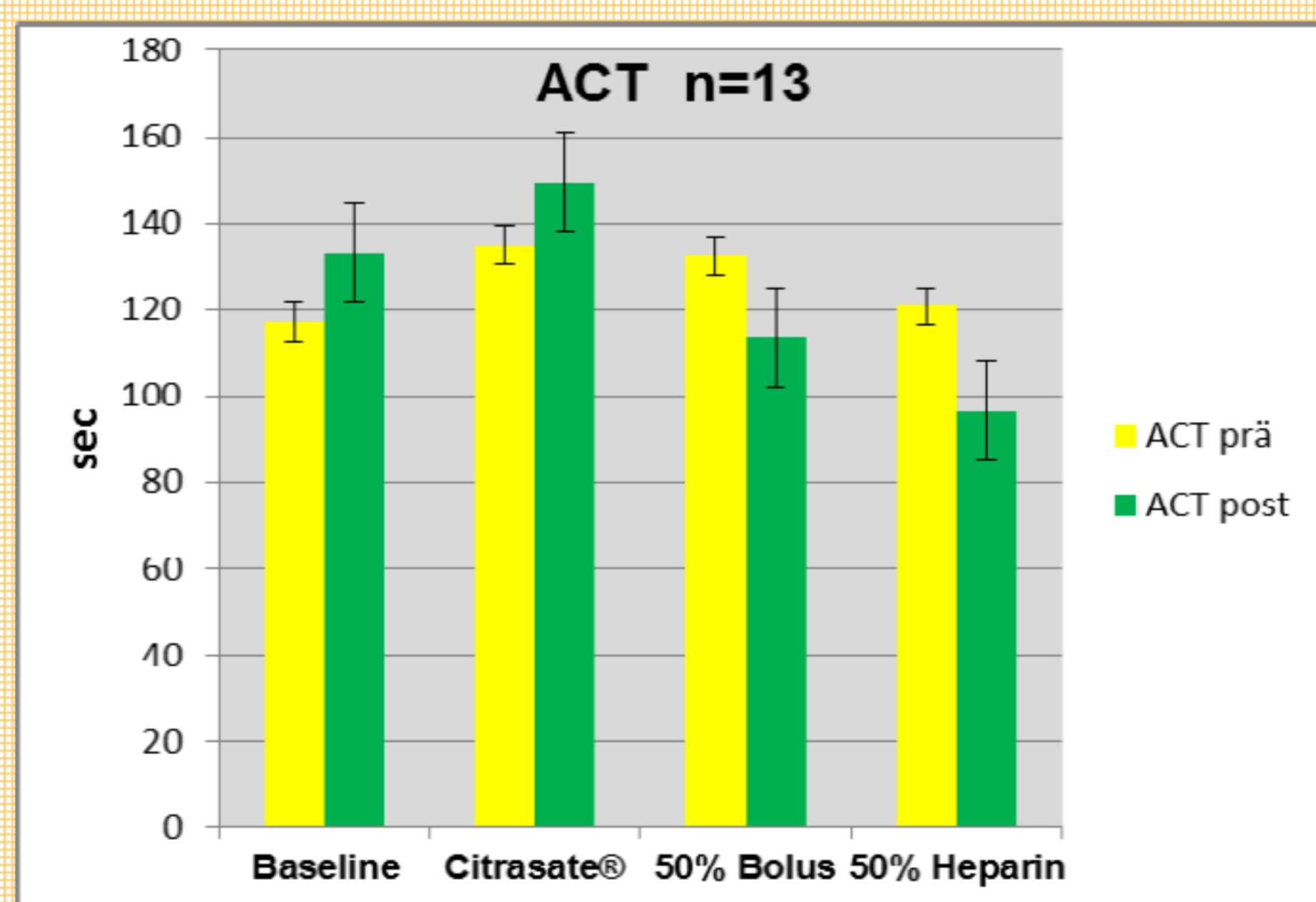
Used concentrates:

Type	Na ⁺ mmol/L	K ⁺ mmol/L	Ca ²⁺ mmol/L	Mg ²⁺ mmol/L	Cl ⁻ mmol/L	Acetate mmol/L	Citrate mmol/L	HCO ₃ ⁻ mmol/L	Glucose g/L
standard	138.0	2.0/3.0	1.25	0.50	108,5/ 109,5	3.00	-	32.0	1.0
Citrasate®	135.3	2.0/3.0	1.50	0.50	106/107	0.30	0.80	32.6	1.0

RESULTS

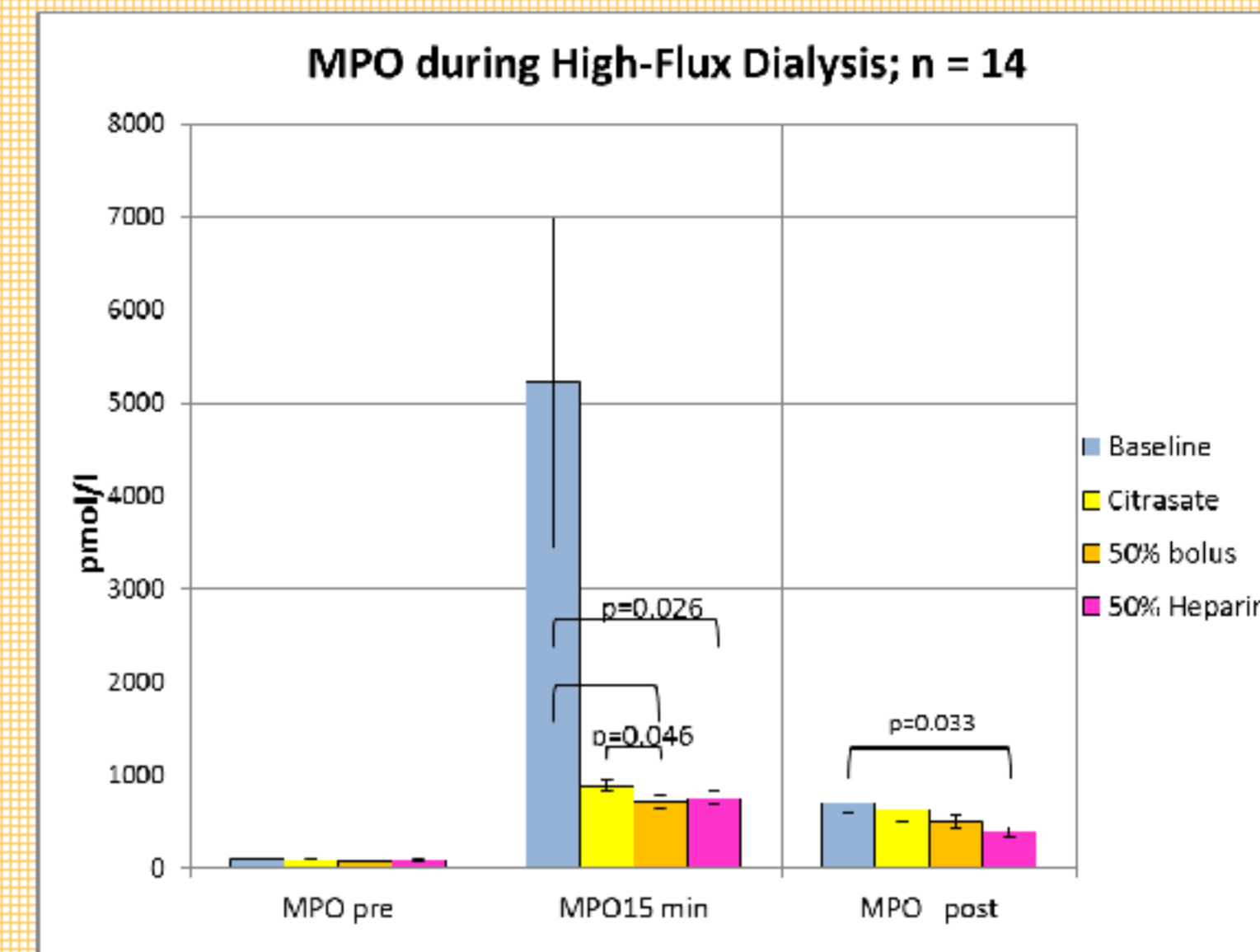
Impact on the treatment effectivity:

In agreement with previous results (1,4) the stepwise reduction of the Heparin dose did not lead to any clotting in the extracorporeal circuit or dialyzers, despite the mean post-treatment values of ACT decreased by approx. 20%. After a reduction of the total Heparin dose by 50 % there was no drop of the efficacy judged by spKt/V. An increase of spKt/V observed by Ahmad et al. (2) could not be confirmed by us.



Impact on the biocompatibility:

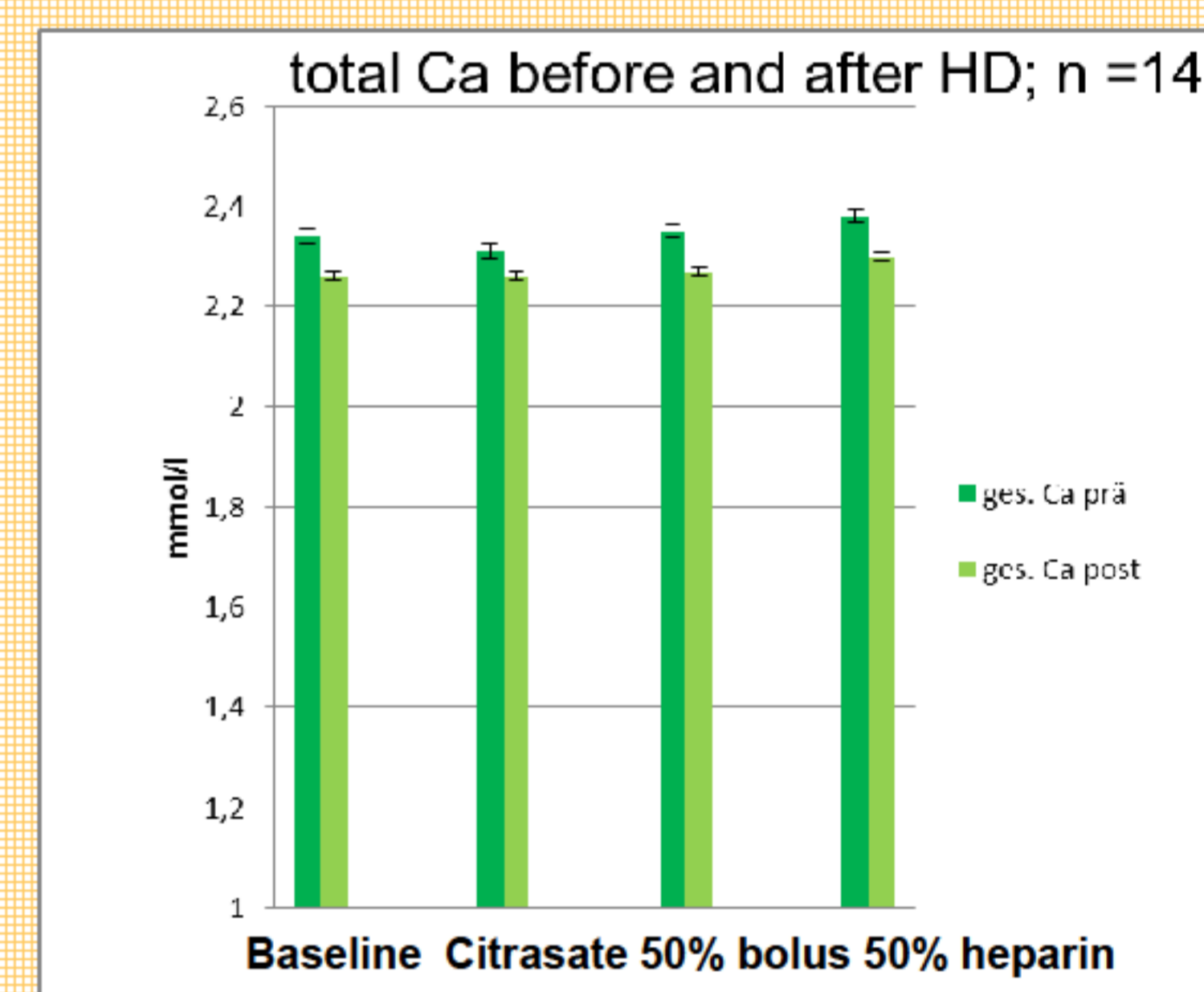
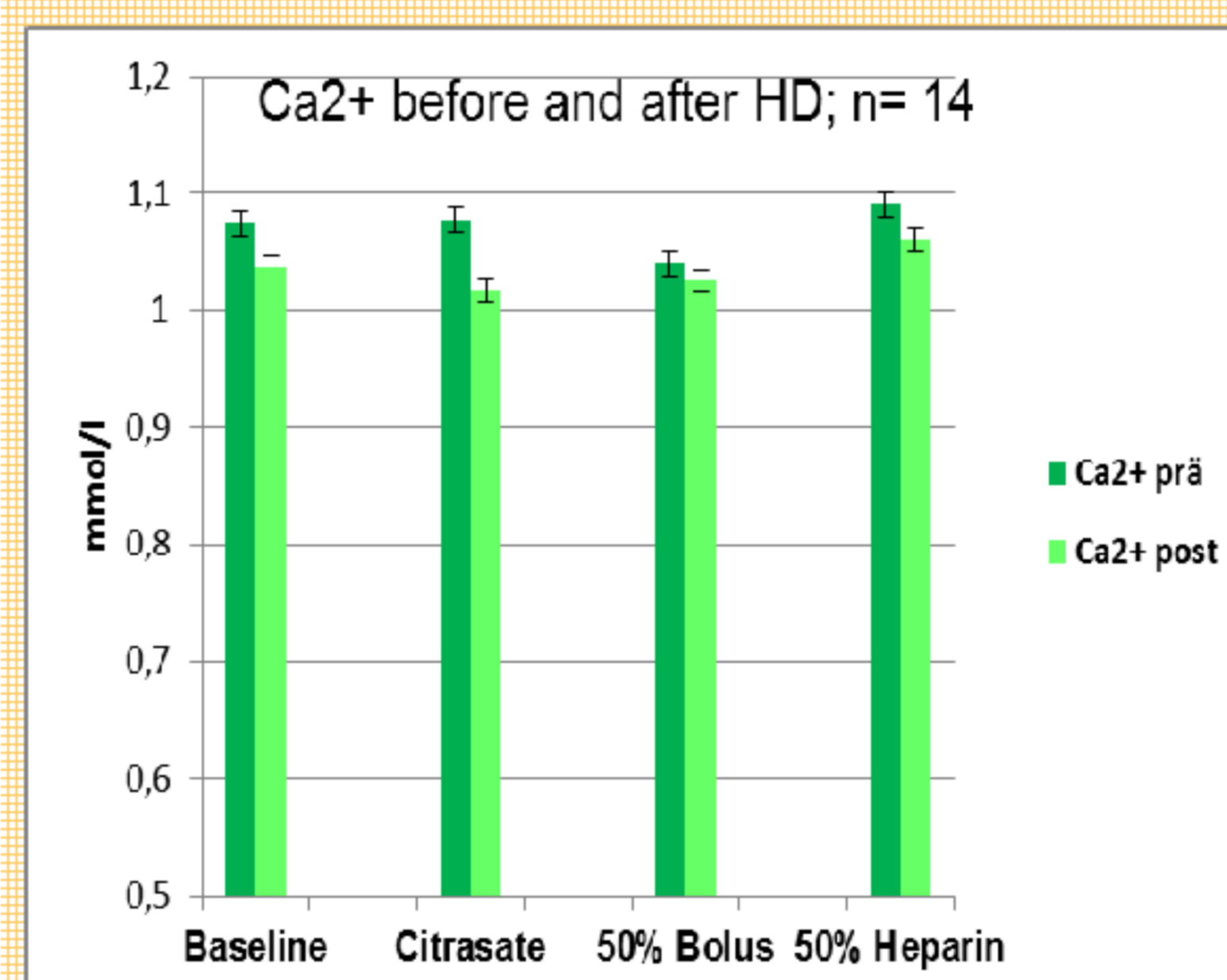
MPO counts as a marker of oxidative stress and inflammation during extracorporeal therapies. Plasma MPO is known to be associated with atherosclerotic complications and mortality of dialysis patients. HD treatments with standard concentrate are typically connected with a steep MPO increase (3).



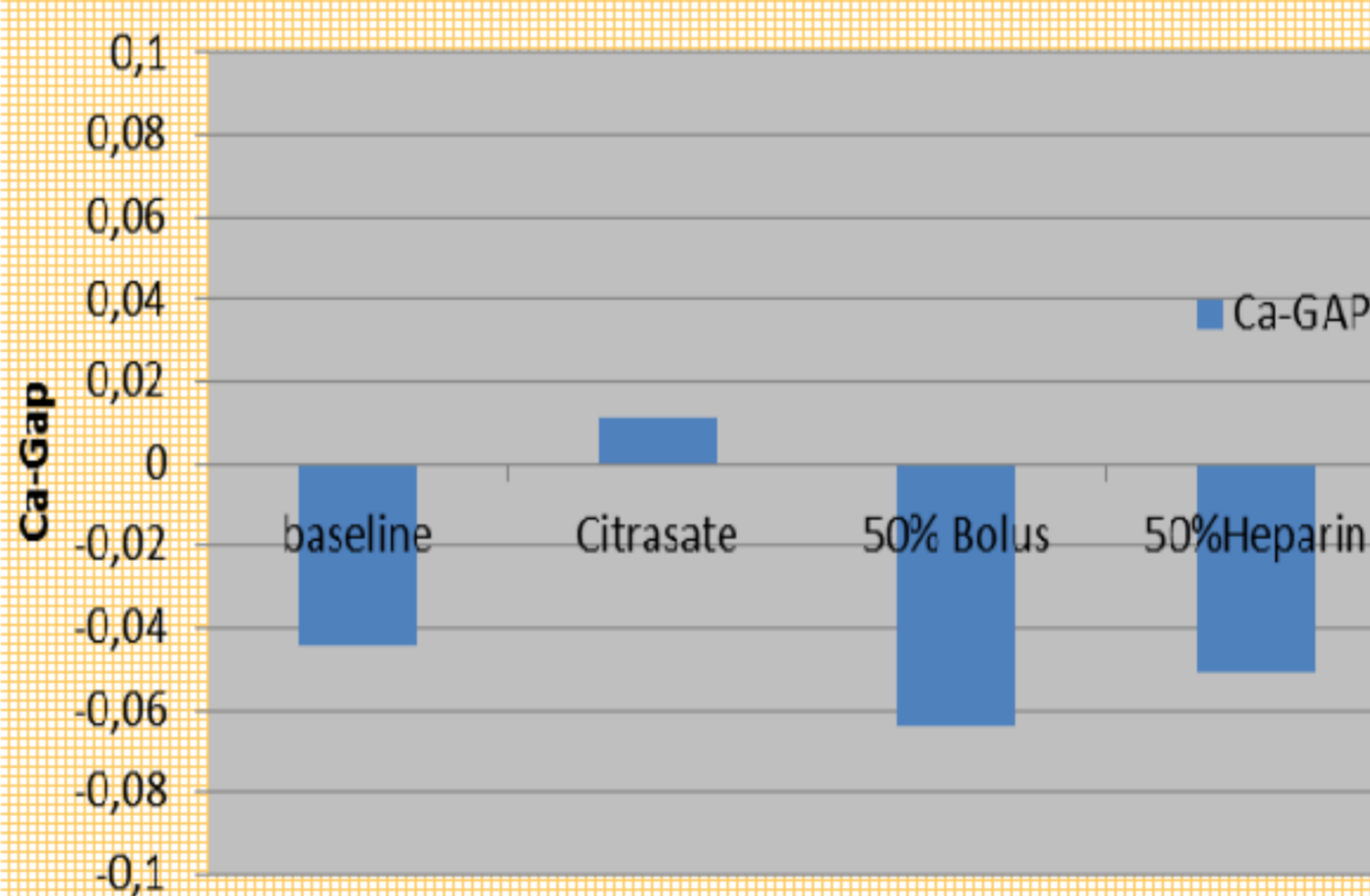
The MPO plasma concentration rose tremendously after 15 min dialysis time with standard concentrate and dropped down strongly after switch to citrate-containing dialysate. The influence of following stepwise heparin reduction on the MPO level using citrate-containing dialysate, however, was found to be very small and not significantly.

Impact on the calcium levels:

Ionized Ca (iCa) and total Ca were slightly reduced by about 5-7 %. A Ca²⁺ - decrease to unphysiological plasma values could be avoided by applying Citrasate® with 1.5 mmol/l Ca²⁺ instead of 1.25 mmol/l Ca²⁺ in standard concentrate.



Ca-GAP; n=14



The citrate accumulation can be calculated due to Gabutti et al (4) from the following equation : **Ca-GAP = (totalCa post - totalCa pre) - (iCa post - iCa pre)** In our study the Ca-GAP was <0.2 in any cases, which means, there was a sufficient rapid metabolism of citrate .

CONCLUSIONS

- Citrasate® allows a Heparin reduction of totally by 50 % without additional clotting events and reduction of dialyzer performance.
- Because iCa and total Ca were slightly reduced, 1.5mmol/l Ca²⁺ should be used for High-Flux Dialysis with Citrasate®.
- Since the MPO plasma level was decreased strongly after switching to Citrasate®, whereas the additional stepwise reduction of heparin dosage results in a very small effect, it was concluded that the main reason for the reduction of oxidative stress seems to be the Calcium-chelating property of citrate ions.

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