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## Citrate in dialysate – The standard for the next decade in hemodialysis?



**MICHAEL SCHMITZ**  
Solingen, Germany

The primary buffer substance that is supplied to the patient in the context of hemodialysis treatment is bicarbonate. However, since calcium and magnesium must also be added to the dialysate, these two components cannot be stored together in a concentrated solution without precipitating in the form of sparingly soluble calcium and magnesium carbonate. Therefore bicarbonate is mixed with the dialysis concentrate and pure water within the dialysis machine. In addition, the concentrate contains a small amount of a salt of a weak acid, usually acetate, which can to a certain extent prevent precipitation of calcium carbonate.

The idea of using citrate as a component in the dialysate is less based on its anticoagulative property, than on its greater biocompatibility compared to the otherwise used acetate. The concentration of citrate in the dialysate of about 1 mmol/L is clearly below the 3–4 mmol/L that is necessary to reduce ionized calcium to a level sufficient for anticoagulation. However, local anticoagulatory effects are seen that can also con-

tribute to a more effective dialysis. It is also suggested that the indirect citrate buffer can help to control uremic acidosis due to the slow metabolism of citrate to bicarbonate. In addition, acetate in higher concentration causes hypotension, nausea, vomiting, headache and angina pectoris. The low concentrations usually used in hemodialysis are also considered potentially dangerous for hypotonic patients.

The safety of a citrate-containing dialysate in various dialysis forms (hemodialysis, pre- and post-hemodiafiltration) was demonstrated in a prospective, randomized study including 92 patients. [1] The observed mild side effects (especially cramps), which only occurred during the first two weeks of therapy, can be explained by the fact that when a citrate-containing dialysate is used, a calcium concentration of approximately 0.2 mmol/L higher than the corresponding acetate solution is required in order to obtain a comparable net calcium supply. An advantage was that post-dialysis alkalosis was significantly less frequent, similar to a study by Nunez. [2] In the latter study, less inflammation and dialysis efficiency was also observed. Other authors report an increased biocompatibility. [3,4] However, many authors report a slight postdialytic calcium drop of about 0.1 mmol/L with consecutive increases in iPTH. The clinical significance of this observation is still unclear. A recently published study showed for the first time that dialysis patients who were older than 70 years and were never exposed to acetate dialysate showed a sig-

nificantly improved survival (HR 0.79). [5] Unfortunately, in this study other techniques of acetate-free dialysis than citrate were investigated (i.e. HCl and acetate-free biofiltration).

### Citrate-containing dialysate and heparin reduction

Due to possible local anticoagulative effects even with the low citrate concentration used in citrate-containing dialysate, studies have been conducted to investigate whether a citrate-containing dialysate is able to spare heparin during the dialysis treatment. The results are inconsistent. In some studies, heparin reduction was possible; in other studies, this could not be demonstrated. Therefore, it seems reasonable to combine the properties of the citrate-containing dialysate with heparin-coated hemofilter membranes, which alone also resulted in unsatisfactory heparin reductions. In one recent study, comparable treatment success rates of approximately 95 % were found similar to regional citrate anticoagulation with calcium-containing dialysate. [6]

In all these efforts, however, it must be considered that even if dialysis treatment can be achieved without complete clotting of the extracorporeal circuit, it leads to a considerable activation of the coagulation system. Richtrova reports that using citrate-containing dialysate in predilution mode without systemic heparin dialysis was successful, but with an increased formation of clots in the extracorporeal system and activation of various coagulation factors. He con-

cluded that this procedure is an option for single applications, but should not be used as a permanent therapy. [7]

In conclusion, when used as part of the effort of improving biocompatibility of the hemodialysis procedure, citrate in the dialysate is a safe and well-tolerated option with potential benefits for patients that have to be determined by larger randomized studies. Its particular role in heparin-free dialysis has yet to be defined. ■

### References

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**Session 5.6**  
**Hemodialysis anticoagulation: present and future**  
**Sunday, 17.00–18.30, Hall N105–106**