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## **Effect of dialysate acidification with citrate in hemodialysis patients**

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The introduction of bicarbonate-based dialysate in 1980s was one of great steps in the development of dialysis fluid. It decreased hemodynamic instability during hemodialysis (HD) and improved acidosis compared with the previous acetate-based dialysate (41 mmol/L of acetate). However, it still contains small amounts of acetate (3–8 mmol/L) to balance pH and prevent the precipitation of calcium and magnesium. During the last decade, citrate has been introduced as another acidifying agent with a number of beneficial effects: improvement in inflammation, dialysis efficiency, anemia, malnutrition, metabolic acidosis, and reduction of heparin dose.

Acetate-free dialysis lowered cytokine production and brought less neutrophil and monocyte activation than conventional HD, indicating that even small amounts of acetate can promote microinflammation. In addition, in vitro studies exhibited that citrate resulted in less complement and neutrophil activation and reduced endothelial apoptosis and necrosis under hyperglycemia. Moreover, regional citrate anticoagulation showed similar beneficial effects such as decreased degranulation of neutrophil and platelet and reduced oxidative stress.

Citrate dialysis abolished cellular damage observed with acetate dialysis, reflected by steady state of cell-free mtDNA during HD. Given the previous findings of its increase during HD through apoptosis of leukocyte, it is worth highlighting the absence of intradialytic rise of cell-free mtDNA with citrate dialysis in contrast to acetate one. Since complement and blood cell activation is considered as calcium-dependent process, leukocyte activation was diminished with citrate dialysate by decreasing available free calcium, thereby leading to reduced generation of cell-free DNA. Citrate dialysis improved hsCRP in patients undergoing maintenance HD. It is conceivable that constant level of cell-free mtDNA over citrate period may result in an improvement of hsCRP. Citrate dialysis marginally improved dialytic removal of indoxyl sulfate. In addition, citrate dialysate allowed the reduction of heparin dose without a difference in aPTT as compared with acetate one