

# Targeting microbiota-derived uremic retention solutes with antibiotics

Ruben Poesen, Bert Bammens, Patrick Augustijns, Pieter Evenepoel, Björn Meijers

Division of Nephrology, Department of Microbiology and Immunology, University Hospitals Leuven, Leuven, Belgium

## INTRODUCTION AND OBJECTIVES

The gut microbial metabolism contributes substantially to uremic retention solutes accumulating in chronic kidney disease. Both *p*-cresyl sulfate and indoxyl sulfate are representatives of this group of solutes and have been associated with adverse outcomes in patients with renal dysfunction. Whether antimicrobial therapy has a direct and sustained effect on generation of these solutes in patients with chronic kidney disease has not been studied to date.

## METHODS

Serum levels and generation rates of indoxyl sulfate and *p*-cresyl sulfate were prospectively measured in chronic kidney disease patients receiving antibiotics. To minimize the effects of systemic infection, we studied a homogenous population of peritoneal dialysis patients receiving flucloxacillin for exit site infection. We collected serum, urine and peritoneal dialysate at baseline, as well as immediately and 6 weeks after treatment. Total removal rate, a surrogate of intestinal generation, was calculated using 24h urinary collection and dialysate. Differences were compared using the Wilcoxon signed rank test.

## RESULTS

In this ongoing trial, 11 peritoneal dialysis patients (mean age 55y, dialysis vintage 11.8 months, weekly Kt/V 2.32) have already been included. Serum levels of *p*-cresyl sulfate significantly decreased during antimicrobial therapy (median decrease of 46%, P 0.03), also accompanied by a trend of lower total removal rates (-60%, P 0.08). For indoxyl sulfate, we observed a trend of lower serum levels (-33%, P 0.12), and concomitant significant decreases in total removal rate (-21%, P 0.04) following antimicrobial therapy. However, there were no significant changes when comparing baseline serum levels and total removal rates of both solutes with those obtained 6 weeks after treatment.

## CONCLUSIONS

Antibiotics decrease intestinal generation of microbiota-derived uremic retention solutes in patients with chronic kidney disease. Therefore, antimicrobial therapy should be taken into account when interpreting solute levels in observational and intervention trials. Although single and short-term antibiotic exposure had no sustained solute-decreasing effect, probably due to recovery of the gut microbiota, the long-term effects of frequent antimicrobial treatment remains unknown.