Urinary calprotectin, NGAL, and KIM-1 in a large cohort of patients with branched-chain organic acidurias

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Introduction

The development of chronic tubulointerstitial nephritis (cTIN) is a severe long-term complication of especially mut⁰ methylmalonic aciduria (MMA) and to a much lesser extent of propionic aciduria (PA, Fig. 1). We now investigate whether tubular or proinflammatory urinary markers like urinary neutrophil gelatinase-associated lipocalin (NGAL), kidney injury molecule (KIM-1) and calprotectin reflect the development of kidney disease in these patients in comparison to conventional parameters such as microglobulinuria.

Fig. 1 Relationship between cTIN and excretion of urinary biomarkers in branched-chain organic acidurias.
The occurrence of cTIN especially in mut⁰ MMA may increase urinary excretion of proinflammatory and tubular biomarkers such as calprotectin, kidney injury molecule 1 (KIM-1) and gelatinase-associated lipocalin (NGAL).

Method

Fig. 2 Analyzing of KIM-1, NGAL and calprotectin.
Using commercial kits based on sandwich elisa technique. Capture and detection antibodies bind to non-overlapping epitopes on the protein to sandwich the protein. A chemical substrate is added to produce a colometric signal which can be read by a plate reader.
Fig. 3 Characterization of patient cohort. (a) Frequency of different CKD stages across different age groups. (b) Distribution of different CKD stages in MMA and PA patients. (c) Breakdown of the analyzed groups in this study.

Results I

Fig. 4. Beta 2-microglobulin (B2MG) as predictor for CKD stage
(a) Effect plot for B2MG as predictor for CKD stage over time. (b) B2MG in different CKD stages of patients at last visit
Results II

The urinary biomarkers calprotectin, NGAL, and KIM-1 have no additional diagnostic value beyond beta 2-microglobulin (B2MG) alone in our patient cohort. However, it cannot be excluded, that there is a diagnostic potency of these urinary biomarkers in the progression of CKD. More patients in respective CKD stages have to be included over a long-term observation period.

**Conclusion**

The urinary biomarkers calprotectin, NGAL, KIM-1 have no additional diagnostic value beyond beta 2-microglobulin (B2MG) alone in our patient cohort. However, it cannot be excluded, that there is a diagnostic potency of these urinary biomarkers in the progression of CKD. More patients in respective CKD stages have to be included over a long-term observation period.

**Fig. 5** Levels of KIM-1, NGAL and calprotectin at different CKD stages and gender differences

Effect plot of KIM-1 (a), NGAL (b) and calprotectin (c) in different CKD stages of patients at last visit.

(d) Urinary calprotectin levels vary between male and female.

****: $p \leq 0.0001$