Abstract

Introduction: Serum uric acid level (SUA) depends on the balance between its production and excretion. SUA is associated with several transmembrane proteins responsible for reabsorption (mainly URAT1 and GLUT9) and secretion (ABCG2) on the apical and basolateral membranes of the proximal tubules in the kidney, and in the case of ABCG2, it also correlates with its significant excretion through the gastrointestinal tract. Gout is a metabolic disease caused by the deposition of urate crystals in the joints and tissues. Chronic hyperuricemia is a primary risk factor for the development of gout; however, gout patients usually have a lower SUA during an acute gout attack than in the intercritical periods. The exact mechanism of this phenomenon is unknown. It has been speculated that the systemic inflammatory response can explain this discrepancy. The aim of the study is to determine whether treatment with specific inhibitors of the proinflammatory cytokine TNF (TNFi) affects SUA in patients with systemic rheumatic disease (SRD), and whether changes in SUA correlate with changes in selected proinflammatory cytokines or with the biomarker of oxidative stress, allantoin. Another aim is to determine the frequency and effect of allelic variants in the *ABCG2* urate transporter gene in patients with primary gout.

Results: In patients with SRD, we observed a significant increase in SUA after initiating TNFi therapy. We did not confirm an association of the magnitude of the change in SUA with changes in any of the 13 pro-inflammatory cytokines, or with allantoin. We identified nine non-synonymous exon variants of the *ABCG2* gene in patients with primary gout in the second project. Overall, patients with non-synonymous allelic variants had an earlier onset of gout and a higher probability of familial occurrence.

Conclusion: In a cohort of patients with SRD, we observed an increase in SUA after the inflammatory response was abrogated. It appears that the actual SUA may be affected by systemic inflammation in addition to known factors. In patients with chronic gout, we have shown that non-synonymous variants of the urate secretory transporter gene *ABCG2* increase the risk of gout, are associated with the early onset and familial occurrence of the disease.