“iFGF23:cFGF23 ratio as a new diagnostic and prognostic marker in acute kidney injury.”

Acute kidney injury (AKI) is severe and common disease. Every year 13.3 million people worldwide are affected by AKI. It is a cause of 1 out of each 7 hospitalizations. More than 30% patients, who are diagnosed with AKI, die. It should be underlined that even small increase in serum creatinine concentration causes 4-fold greater in-hospital mortality. Moreover, for those who survive to hospital discharge, the prognosis remains poor, almost 30% of survivors do not fully recover renal function. It seems, that those pessimistic prognosis might be improved by early administration of appropriate treatment. Unfortunately, currently the diagnosis of AKI is mainly based on the presence of a gradual increase in serum creatinine level, what delays the diagnosis. There are no reliable biomarkers facilitating early diagnosis of AKI and its discrimination from chronic kidney disease (CKD).

Recently, an attention is focused on fibroblast growth factor (FGF23), which may be a potential marker of AKI. It is an osteocyte-derived hormone involved in regulation of calcium-phosphate balance. A study performed on animal model has shown that FGF23 concentration rises 3 hours after kidney injury. Additionally, acute blood loss, inflammation and hypoxia, conditions often met in patients with AKI, also amplify FGF23 production. One of the mechanisms controlling FGF23 concentration is its intracellular degradation. Available FGF23 ELISA assays enable evaluation of FGF23 degradation’s intensity by circulating intact particles (iFGF23) to its C-terminal fragment ratio. We have hypothesised that as a result of factors amplifying FGF23 synthesis in AKI, the secondary activation of intracellular cleavage takes place, and therefore the iFGF23:cFGF23 ratio will be moved toward 0. By contrast, as it is known from previous studies, mainly iFGF23 is increased in CKD, hence, above-mentioned ratio is moved towards 1. Taking above into consideration, we are going to investigate the utility of FGF23 concentration and iFGF23:cFGF23 ratio measurements as a potential marker facilitating early discrimination of acute and chronic disease processes taking place in kidneys. Therefore we are going to study blood samples obtained from patients with AKI and CKD in order to elucidate if there are any relevant differences in intensity of intracellular FGF23 cleavage in those two entities.

Additionally, the project is aimed at determination of prognostic utility of iFGF23:cFGF23 ratio in the degree of renal recovery and the occurrence of adverse outcomes after AKI episode. It is known, that in patients with CKD, elevated FGF23 concentrations predict poor prognosis: faster progression to end-stage renal disease, higher risk of cardiovascular incidents and higher mortality. It will be the first attempt to asses FGF23 concentrations and iFGF23:cFGF23 ratio usefulness in evaluation of AKI prognosis.

Another important aspect of the study is also determination of the mechanisms causing the elevation of FGF23 concentration and its degradation in the course of acute glomerular filtration loss. For this purpose level of known factors influencing on production and degradation of FGF23 will be measured (calcium-phosphate balance disturbances, inflammation or anemia).

It should be stressed, that finding a new biomarker of acute kidney injury will extensively facilitate the diagnosis of AKI among patients with impaired renal function and equivocal clinical picture, what will enable earlier introduction of proper treatment. Demonstrating an association of iFGF23:cFGF23 ratio and patients’ prognosis will enable to distinct a group of patients who require more careful follow-up and early administration of therapeutic interventions to prevent progressive loss of kidney function and development of adverse outcomes. Moreover, determining the exact mechanisms responsible for increase of FGF23 concentration and its intensified cleavage in AKI patients may, in the context of above-mentioned advantages, indicate potential target for new therapies improving outcomes of patients with acute kidney injury.