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Significance of Creatinine and Cystatin-S Values in Early Diagnosis of Renal Dysfunction in Cardiorenal Syndrome

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Annotation: It is known that, according to generally accepted principles, early diagnosis of kidney dysfunction in cardiorenal syndrome uses calculated glomerular filtration rate (hCFT) determined on the basis of creatinine and cystatin-S indicators. However, a number of scientific studies have shown that the decrease in hKFT is observed much later than the appearance of tubulo-interstitial changes in the kidneys. From this point of view, it is important to study not only balls, but also markers that show tubulo-interstitial changes early. Because the biological markers used in the early assessment of tubular dysfunction in relation to glomerular changes are not widely used in practice. Therefore, the use of uromodulin for this purpose can be one of the promising laboratory indicators confirming renal tubular dysfunction (regardless of the cause).

Keywords: creatinine, cystatin-S, cardiorenal syndrome, hCFT (calculated glomerular filtration rate), SBK (chronic kidney disease).

Uromodulin or Tamm-Horsfall is the most abundant protein in urine. In recent years, studies have shown that decreased uromodulin levels are a risk factor for end-stage renal disease. The discovery of a direct correlation between this protein and CKD confirmed that its decrease in urine in secondary nephropathies is an ominous sign of impaired renal function.

Some scientific observations have shown that a decrease in uromodulin levels in patients with cardiovascular diseases is an indicator of accelerated development of chronic kidney disease (CKD) and increased overall cardiovascular risk. A rare mutation of the uromodulin gene causes autosomal dominant tubulo-interstitial disorders and changes. In the development of cardiorenal syndrome, the study of not only uromodulin protein, but also polymorphism of its genes is of known importance. Oxidative stress plays a key role in the development of SLE and, as a result, SCD. In the presence of oxidative stress, inflammatory cytokines increase in the human body, leading to systemic inflammatory processes in many organs. In these processes, α-tumor necrosis factor (α-O'NO), interleukin (IL)-1 and 6 take the leading place. From this point of view, it is appropriate to study the relationships between oxidative stress, inflammatory cytokines and uromodulin protein.

According to some literature, the Tamm-Horsfall protein produced in the renal tubules has the property of controlling oxidative stress processes. Although most uromodulin is excreted in the urine, a small amount of the protein passes into the renal interstitium and enters the bloodstream. According to Tarek El-Achkar and co-authors, uromodulin is a protector of renal and systemic homeostasis.

Recent observations have shown that higher levels of circulating uromodulin are associated with reduced mortality and the development of SCD and acute renal failure. To determine the relationship between uromodulin and the presence of oxidative stress, it is necessary to assess the level of malondialdehyde in the blood serum, which is considered a reliable marker of the latter condition. It is known that oxidative stress occurs as a result of an imbalance between the oxidation and antioxidant systems. In this case, the process proceeds with a predominance of the oxidation process, resulting in cell damage.

Uromodulin protein has been shown to be important in predicting not only a number of kidney diseases, but also SCD and cardiovascular events. The relationship between serum protein levels and oxidative stress, which is considered one of the main causes of cardiovascular disease, has been proven in recent studies. However, there is no information in the literature on the role of Tamm-Horsfall protein in the early detection of SCD developing on the basis of SUE, its degree of correlation with malondialdehyde, a reliable marker of oxidative stress, and its antagonist superoxide dismutase. In addition, in a small number of observations, information is provided about the importance of uromodulin gene polymorphism in the occurrence of changes in the kidney. Cell damage due to excess tissue oxidants and oxidative stress plays an important role in the development of acute kidney failure and chronic kidney disease. However, according to data presented by Wellington Caio-Silva et al., several weeks after ischemia/reperfusion injury, there is a decrease in damage and some oxidative substances. This period of renoprotection may be associated with a significant increase in the autophagy process. Some studies have shown that during stress conditions such as acute renal failure, autophagy is activated, which is able to degrade and recycle damaged organelles and macromolecules to maintain cellular homeostasis. Kaushal and Shah also observed that decreased autophagosome formation during acute periods leads to apoptosis. This is consistent with other studies in the renal ischemia/reperfusion model. Of these, 24 hours after ischemic/reperfusion injury, increased cell damage was detected as a result of a decrease in the level of enzymatic activity of SOD and catalase. However, the data presented show that at longer periods, specifically 8 and 15 days after injury, there is a reduction in cellular damage at lipid and protein levels. It confirms that oxidative stress plays a leading role in the development of cardiorenal syndrome. In the rapid development of the process, the imbalance between oxidation and antioxidation markers, i.e. the predominance of the first, causes severe cases of cardiorenal syndrome and ultimately death in most cases. In the available literature, information about the antioxidant system, particularly its more studied marker, superoxide dismutase, is more widely covered. However, data on the oxidative stress inducer malondialdehyde are limited. At the same time, there is insufficient information about the imbalance of representatives of this system (superoxide dismutase and malondialdehyde) in

cardiorenal syndrome that develops on the basis of SUE.

In addition, the relationship between uromodulin and its genes, which is of leading importance in the development of SBK, between the oxidative and antioxidant systems has not been thoroughly studied. The study of the mentioned conditions in relation to each other is important for scientific and practical medicine.

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