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The Importance of Oxidative Stress in the Human Body in the Development of Chronic Heart Failure

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Annotation: It is known that oxidative stress plays a key role in the development of SLE and, as a result, SCD. In a state of oxidative stress, pro-inflammatory cytokines increase in the human body, leading to systemic inflammatory processes in many organs. α-tumor necrosis factor (α-O'NO), interleukin (IL)-1 and 6 take the leading place in the mentioned processes. From this point of view, it is desirable to study the relationship between oxidative stress, inflammatory cytokines and uromodulin protein.

Keywords: uromodulin, cardiorenal syndrome, malondialdehyde (MDA), superoxide dismutase (SOD), α-tumor necrosis factor (α-O'NO), interleukin (IL)-1.

According to some literature, the Tamm-Horsfall protein produced in kidney 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 linked high levels of circulating uromodulin to reduced mortality and the development of SCD and acute renal failure. El-Achkar and colleagues, who have conducted extensive studies on the mechanisms of disease development, studied the molecular signals that uromodulin controls in the kidneys. They concluded that uromodulin inhibits the activation of RAC1–JNK (RAC1-N-terminal kinase c-Jun) in renal proximal tubule cells and that uromodulin deficiency leads to increased systemic and renal oxidative stress.

The development of acute renal failure in mice and liver transplant patients was associated with decreased serum uromodulin and systemic oxidative DNA damage.

In addition, patients with acute renal failure had higher levels of DNA oxidative stress, which was associated with higher mortality rates or the need for dialysis. The authors suggested that the management of oxidative stress may be related to blood uromodulin levels. El-Achkar and co-authors note that if the above findings are confirmed, there is a possibility of choosing therapeutic treatments aimed at increasing systemic levels of this protein in specific clinical conditions characterized by uromodulin deficiency. It is known that oxidative stress plays a leading role in the development of cardiovascular diseases, including CHD and SCD. In this regard, studying the relationship of these complications with uromodulin is of certain scientific and practical importance.

Although studies have shown that elevated serum uromodulin levels are associated with lower mortality rates in older adults and patients with heart disease, the underlying mechanism remains unclear. This observation suggests that Tamm-Horsfall protein inhibits reactive oxygen species in both the kidney and systemic settings. In cases of acute kidney injury resulting from experimental surgical procedures, uromodulin protein has been shown to correlate with systemic oxidative damage. As noted above, the relationship between serum uromodulin levels and cardiovascular disease risk and their potential to predict overall mortality are currently unknown. Leiherer Andreas and co-authors determined uromodulin levels in 529 patients who underwent coronary angiography without acute coronary syndrome but with confirmed or suspected stable coronary artery disease.

The patients were followed for 8 years, and cardiovascular events and deaths were recorded. During this period, 95 deaths and 145 cardiovascular events were recorded among the patients under observation.

Blood Tamm-Horsfall protein was found to be protective against all-cause mortality (relative risk 0.56 [95% confidence interval 0.43-0.72]; $p<0.001$) even after full adjustment for confounders such as CVD, smoking, diabetes mellitus, and coronary heart disease (relative risk 0.57 [95% confidence interval 0.37-0.89]; $p<0.014$). Patients with low serum uromodulin levels had a significantly higher risk of cardiovascular disease compared to those with moderate or high levels (relative risk 1.45 [95% confidence interval 1.04–2.02]; $p=0.027$). It was noted that the studied protein and its ratio to creatinine were significantly correlated with the functional state of the kidneys ($r=-0.322$; $p<0.001$) and showed that this indicator can predict the occurrence of cardiovascular diseases (relative risk – 1.26 [95% confidence interval 1.12–1.41], $p<0.001$). As a result of the study, the authors concluded that uromodulin is a valuable biomarker of overall mortality and morbidity from cardiovascular events. A literature review confirms that the uromodulin protein is 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.

A number of targeted measures are being implemented in our country to raise the medical field to world standards and improve the quality of medical services provided to the population. "....Prophylaxis to prevent, early diagnose, treat and monitor non-communicable diseases and their risk factors, and reduce premature mortality and morbidity of the population..." . The implementation of these tasks will create an opportunity to improve the quality of life and extend the life expectancy of patients with cardiovascular diseases, which are widespread among the population, in particular, patients with chronic obstructive pulmonary disease (COPD), and their severe complications.

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