Chronic kidney failure is associated with many kinds of metabolic disorders caused by the kidney disease and also attributable to dialysis treatment. Phenomena such as accumulation or deficit of various substances and dysregulation of metabolic pathways participate in the pathogenesis of these changes.

One of these disorders, which we studied in more detail, is a deficit of carnitine. Carnitine is a substance which plays an essential role in beta-oxidation of fatty acids by catalyzing their transport into the mitochondrial matrix. It enables obtaining of energy, namely in muscle cells including myocardium.

Patients with chronic kidney failure treated by hemodialysis are known to have decreased carnitine concentration in plasma and tissues due to its impaired synthesis in kidneys and the great loss across the hemodialysis membrane during dialysis sessions. A single hemodialysis session reduces plasma free-carnitine concentrations to about one-third of their predialysis values because of small molecule of free-carnitine. On the other hand, renal elimination of acylcarnitine, which is physiologically ineffective, may be impaired in chronic kidney failure, leading to increased blood concentrations of acylcarnitine.

Considerable evidence suggests that carnitine deficiency and abnormalities of carnitine metabolism result in a number of clinical conditions that are associated with dialysis, including muscle weakness, hypotension, fatigue, muscle cramps, poor exercise tolerance, anemia, left ventricular dysfunction, and higher incidence of arrhythmias. Recent studies have demonstrated that carnitine supplementation can restore the abnormal metabolism in dialysis patients and may alleviate some of the symptoms mentioned above.

The main goal of this project was to investigate possible effects of carnitine supplementation on metabolic parameters which could be positively influenced by the support of intramitochondrial beta-oxidation and energy metabolism. These are markers of nutrition, lipid metabolism, red blood cell count and, according to our previous findings, also parameters of oxidative stress and calcium-phosphate metabolism. The purpose is finding ways to prevent from the development of atherosclerosis and renal bone disease in chronically hemodialyzed patients. The consequential goal was to adapt an enzymatic photometric method for free carnitine determination and its automation for the Olympus AU 400 analyzer.

According to our results, a great deal of hemodialyzed patients has carnitine levels comparable with a healthy population. Hence, an effect of supplementation in these persons is questionable, although we realize that serum carnitine concentration may not accurately predicate of tissue saturation. Conversely, positive effects could be expected in patients with decreased carnitine levels.

The supplementation with CAR led to a high increase of serum CAR concentration, so that the values of CAR after HD exceed the lower reference limit for healthy population. The higher CAR concentration remained at least two months after the end of supplementation.

Some authors describe that supplementation with carnitine may positively influence nutritional-inflammation status of hemodialyzed patients. Changes should be happened due to anti-inflammatory effect of carnitine and general improvement of the energy metabolism after its administration. Furthermore, many papers describe positive effects of carnitine on the red blood cell count which manifest by reducing doses of erythropoietin in hemodialyzed patients treated for anemia. This influence should be enabled by increased stability of the erythrocyte membrane and thus reduced degree of hemolysis. These effects were not proved in the current study. We cannot identify causes so exactly, but it seems that a health state of the majority of patients was fairly well-managed at the beginning of the supplementation period and therefore an effect of carnitine on this field of metabolism could not have enforced.

With respect to potential effects of carnitine on lipid metabolism and oxidative stress, we noted a decreasing tendency of serum triglycerides levels in supplemented patients in contrast to controls. Concentration of malondialdehyde, which is considered to be a marker of

oxidative stress, decreased. Decrease of oxidized LDL was more significant in supplemented group than in a placebo group. Other parameters of lipid metabolism, oxidative stress and antioxidative defense did not significantly differ between both groups of patients.

Although we did not prove any significant changes in concentrations of calcium and inorganic phosphate, we did find a tendency to correction of secondary hyperparathyroidism and reduction of bone turnover in the group of patients supplemented with carnitine along with an increasing tendency in controls. Concentration of osteoprotegerin increased significantly after six months of supplementation, while levels of parathormone and osteocalcin had only a decreasing tendency which was not statistically significant. An opposite trend was noted in the control group without carnitine supplementation. As osteoprotegerin is an important factor which suppresses activation of osteoclasts, its increased concentration might play a role in prevention of renal bone disease and osteoporosis in hemodialyzed patients.

To date, the deficit of carnitine in hemodialyzed patients has been diagnosed only on the basis of clinical symptoms defined by the American Kidney Foundation. These symptoms are very important, but cannot serve as exact and objective evidence of carnitine deficiency.