ABSTRAKT (AJ)

Adipose tissue produces numerous adipokines, pro- and antiinflammatory cytokines and hormones which may influence the development of insulin resistance, type 2 diabetes mellitus and other comorbidities of the metabolic syndrome.

The ability of adipose tissue to store lipids and thus protect other organs and tissues from ectopic lipid accumulation and development of insulin resistance (IR) is largely dependent on the adipogenic potential of preadipocytes. The amount and function of these cells may be the key factor in creating "healthy" adipose tissue or on the contrary "unhealthy" adipose tissue eventually leading to metabolic derangements. The regulation of the amount of body fat by converting preadipocytes into mature adipocytes may be crucial in the prevention and treatment of obesity and its comorbidities.

One of the reasons for development of insulin resistance can be the inhibition of the differentiation process of preadipocytes into mature adipocytes with consequent ectopic lipid accumulation caused by the secretion of preadipocyte factor - 1 (Pref – 1). Pref – 1 has been discovered recently as a protein produced by preadipocytes but not by mature adipocytes. Pref – 1 is a member of the protein family sharing similarity with epidermal growth factors which regulate the differentiation of adipocytes and osteoblasts. The inhibition of preadipocyte differentiation may play an important role in determination of the size of adipocytes, their function, expandibility and sensitivity to the potential metabolic disorders.

The aim of this thesis was to explore the changes of Pref – 1 levels in patients with different metabolic diseases such as obesity, type 2 diabetes mellitus, anorexia nervosa and also in healthy lean individuals. Furthermore, we studied the relationship between the serum levels of Pref – 1 and anthropometric and metabolic parameters and the influence of various interventions such as very low-calorie diet (VLCD), acute hyperinsulinemia or chronic fenofibrate treatment in patients with obesity or partial realimentation in anorexia nervosa (AN) patients, respectively, on Pref-1 levels.

The results show that there is a significant difference in serum concentration of Pref-1 among the above described groups of patients, which reflects their nutritional status. Obese diabetic patients had higher Pref-1 levels in comparison with lean individuals, and after three weeks of VLCD the Pref-1 level significantly decreased. A three-hour acute hyperinsulinemia during

hyperinsulinemic-isoglycemic clamp significantly lowered Pref-1 levels in both healthy control group and diabetic patients before and after the treatment with fenofibrate.

On the other hand, a 46-day realimentation program significantly increased the circulating levels of Pref-1 in patients with AN while no difference in Pref-1 levels was found between the control group and patients with AN at baseline.