Abstract

Increased triglyceride (TG) concentration has been generally accepted as a risk factor for ischemic heart disease and, therefore, lowering TG is therapeutic target that should reduce cardiovascular disease risk. Traditionally, concentration of TG is measured in the fasting state (8–12 hours after an overnight fasting) mainly because the rise in TG levels after meal leads to the high variation in TG values. However, human beings spend larger portion of the day in a postprandial state and postprandial hypertriglyceridemia may then play a substantial role in determination of cardiovascular disease risk. The increased and prolonged postprandial lipemia has been found in patients with coronary heart disease. Moreover, recent data from Copenhagen Heart Study point out that the non-fasting TG concentration is associated with cardiovascular disease risk more tightly than the fasting TG concentration. Importantly, concentration of non-fasting TG is substantially affected by individual behavioural habits such as diet composition and physical activity. It remains to be determined whether it would be appropriate to identify individuals at higher risk of cardiovascular disease due to increased postprandial TG using tolerance test analogous to glucose tolerance test. The protocol of standardized fat tolerance test (FTT) that can be used for such a purpose was proposed by an Expert Panel group in 2010. The test is carried out after min. 8 hour fast, subjects receive the liquid meal that consists of 75 g of fat, 25 g of carbohydrates and 10 g of protein, and triglyceridemia is determined before and 4 hours after meal (Kolovou et al., 2011).

First aim of my thesis was to determine how insulin secretion induced by administration of carbohydrate affects the course of postprandial lipemia after fat load administration. The study was carried out in 30 healthy male volunteers. Men consumed an experimental meal containing either 75 g of fat + 25 g of glucose or 75 g of fat in a control experiment. Blood was taken before the meal and at selected time points within the following 8 hours. The addition of glucose did not affect the magnitude of postprandial triglyceridemia and triglyceride-rich lipoprotein-cholesterol and triglyceride (TRL-C and TRL-TG, respectively) concentrations (evaluated as areas under curves) but stimulated a faster response of chylomicrons to the test meal, evaluated as changes in apolipoprotein B-48 concentrations. Glucose added to a fat load induced an increase of glycemia and insulinemia and, surprisingly, a 20% lower
response of both total and active glucagon-like peptide-1 (GLP-1) concentrations compared to the test in which only fat was given to subjects.

Second aim of my thesis was to determine in the same group of volunteers whether polymorphisms -1131T>C (rs662799) and 56C>G (rs3135506) of the APOA5 gene have an impact on the course of postprandial lipemia induced by a fat load and a fat load with added glucose. Apolipoprotein A-V plays an important role in the determination of plasma triglyceride (TG) concentration. In the group of 30 volunteers seven subjects were heterozygous for the -1131C variant and three for the 56G variant (HT carriers), twenty were wild-type carriers (WT carriers). HT carriers had a 42 % higher postprandial response after fat load than WT carriers. Glucose added to the test meal suppressed such a difference. These findings suggest that the meal composition modulates the effect of these polymorphisms on the magnitude of postprandial lipemia.

Third aim of my thesis was to determine whether magnitude of postprandial lipemia evaluated by FTT can improve prediction of atherosclerotic injury that was assessed by four non-invasive clinical methods (ultrasound examination of intima-media thickness, arterial stiffness and endothelial dysfunction and CT calcium scan). The study was carried out in 73 postmenopausal women using standard FTT as recommended by Kolovou et al., 2011. There were no associations between postprandial triglyceridemia and atherosclerotic injury as evaluated using these methods. Interestingly, women with increased triglyceridemia and waist (hypertriglyceridemic waist, EWET) had increased intima-media thickness and Belcaro score. Our data do not support the idea that the use of FTT can significantly improve the prediction of atherosclerotic injury in clinical practice.