P 22: Omega-3 polyunsaturated fatty acids alleviates heart pump function in Type 1 diabetic cardiomyopathy

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**Background and aims:** The term ““diabetic cardiomyopathy””, which was first proposed by Rubler in 1972 describes myocardial dysfunction in the absence of coronary heart disease, hypertension or heart valve defects. However, from 70s of previous century is known about the omega-3 polyunsaturated fatty acids (PUFAs), which are potent cardioprotectors. Despite the success of diabetology, the mechanisms of omega-3 PUFAs influence on the heart function in diabetes mellitus remains unresolved. In this study we aimed to evaluate the effects of omega-3 PUFAs on cardiac performance in rats with experimental diabetes.

**Materials and Methods:** Experiments were fulfilled on male Wistar rats, weighing 140-270 g, who were divided into 3 groups: 1 - control, 2 - rats with streptozotocin-induced diabetes (50 mg/kg), 3 - rats with streptozotocin-induced diabetes, which received 45% of omega-3 PUFAs-containing drug Epadol during 4 weeks. Rats were anesthetized with Urethane, fixed and right carotid artery was prepared. Ultramiuitar catheter 2F (Millar Instruments, USA) was injected through the right carotid artery retrograde into the left ventricle. The fatty acids composition in heart homogenates was determined by gas chromatography.

**Results:** We demonstrate that omega-3 fatty acid treatment of diabetic rats modifies fatty acid composition of heart by increasing omega-3 PUFAs content. Additionally, supplemented omega-3 fatty acids significantly prevent body and heart weight loss and reduce blood glucose level, induced by streptozotocin. Our data indicates the impairment of the heart pump function in animals with diabetes. We established that cardiac output declined to 36.78% (P<0.05), ejection fraction fraction to 29.12% (P<0.05), stroke volume to 35.65% (P<0.05), stroke work to 70.13% (P<0.05). Omega-3 PUFAs under similar conditions restores pump function - increases ejection fraction at 35.37% (P<0.05), stroke volume at 40.76% (P<0.05), stroke work at 68.02% (P<0.05) and cardiac output at 15.32%. In 2 group of rats diastolic dysfunction was found - the time constants of active relaxation Tau (Weiss) reduced to 50.63% (P<0.05) and Tau (Glantz) to 59.77%, the minimum rate of myocardial relaxation dP/dtmin slightly increased. Effect omega-3 PUFAs on diastolic function is characterized by the increase of Tau (Weiss) to 64.39% (P<0.05) and Tau (Glantz) to 11.32% (P<0.05) and a slight decrease value of dP/dtmin. Omega-3 PUFAs had almost no impact on the maximum rate of pressure increase in dP/dtmax under diabetes.

**Conclusion:** These novel data indicate that modification of fatty acid composition of cardiac membranes by omega-3 fatty acids prevents the pump, diastolic function alterations induced by streptozotocin. It is assumed that omega-3 PUFAs treatment will lead to a decreased risk of cardiovascular complications in diabetes. These results indicate the prospects of further studies to use omega-3 PUFAs in the treatment of diabetes.
P 24: Non alcoholic fatty liver disease in type 2 diabetes patients

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Non alcoholic fatty liver disease (NAFLD) is observed in up to 80% of type 2 diabetes patients. There is increased evidence that NAFLD is associated with increased cardiovascular risk. In this study we aimed to characterize a group of patients with NAFLD and type 2 diabetes.

In all patients standardized questionnaire, anthropometric measurements and lab tests were performed. NAFLD was diagnosed by ultrasonography. Serum lipids were measured by enzymatic methods, using Roche reagents, glycated hemoglobin HbA1c by high pressure liquid chromatography.

We examined 99 consecutive patients with type 2 diabetes from diabetes clinic, 72 with NAFLD and 29 free of NAFLD. Mean age of patients was 53.1 ±10.4 in NAFLD group and 44.9 ±10.9 years in patients without NAFLD (p<0.001). Mean duration of diabetes was 10±6.3 years in patients with and 15.1±7.8 years in those without NAFLD (p<0.001). Mean values of glycated hemoglobin A1c were similar in both compared groups with and without NAFLD: 9.1 ± 2.0% vs 8.4 ± 2.0% respectively. 86.2% of patients without NAFLD and 72.2% of patients with NAFLD were treated with insulin. Patients with NAFLD were characterized by significantly higher prevalence of coronary angioplasty (20.8% vs 0%, p =0.008), however coronary heart disease prevalence and by-pass surgery were not different between groups. 97.2% of NAFLD patients and 93.1% of patients without fatty liver disease were treated with antihypertensive drugs and blood pressure values did not differ between groups with and without NAFLD. Overweight and obesity were observed in higher percentage of NAFLD patients (p<0.001). NAFLD patients were characterized by significantly higher values of alanine transaminase (p=0.033), and lower serum concentrations of HDL-cholesterol (p<0.001) and creatinine (p=0.034). Logistic regression analysis (p<0.001) revealed that NAFLD was significantly positively associated with waist circumference above norm (women>80cm, men>94cm), (p=0.0083), serum alanine transaminase activity (p=0.0164), and negatively with serum creatinine concentration (p=0.0226). Association of NAFLD with glycemic control, measured by HbA1c was not significant in this model.

The results of this study suggest the higher prevalence of coronary artery disease requiring angioplasty in NAFLD patients. Among coronary risk factors, low HDL-cholesterol was lower and prevalence of obesity higher in NAFLD type 2 diabetic persons, what may be important in development and prevention of coronary artery disease in this group of patients.

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P 25: Effect of metformin on arterial properties, adiponectin, leptin and glucose homeostasis in patients with nonalcoholic fatty liver disease.

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Background: Insulin resistance (IR) is the major driving force behind development and progression of atherosclerosis in patients with nonalcoholic fatty liver disease (NAFLD). Therefore, correction of IR is a relevant therapeutic target. We performed the current trial to evaluate whether 12-month metformin therapy improves vascular stiffness in patients with NAFLD and to assess if this improvement is associated with change in glucose control, insulin resistance or circulating adiponectin.

Methods: In randomized, placebo controlled study, 63 patients with NAFLD were assigned to one of two groups: Group 1 received daily metformin; Group 2 received placebo. Central aortic augmentation index (AI) was performed using SphygmoCor (version 7.1, AtCor Medical, Sydney, Australia) at baseline, at 4-and 12-month treatment period. Metabolic parameters, insulin resistance markers and serum adiponectin levels were determined.

Results: In placebo group: AI did not improve during the treatment period. Liver function and adiponectin levels did not change during the study. In multiple linear regression analysis, the independent predictors of arterial stiffness improvement were metformin treatment and increase in circulating adiponectin levels.

Among metformin treated patients: AI decreased significantly during the study. ALP and ALT decreased during initial 4-month treatment period, however raised to the pretreatment levels after 12 months. Serum adiponectin level tended to increase during treatment period with metformin.

Conclusions: Metformin treatment was associated with significant decrease in AI during one year treatment in NAFLD patients. These beneficial vascular effects was associated with exposure to metformin per se as well as change in adiponectin levels suggesting that metformin may mediate its vascular effects via glycemic control-independent mechanisms.

P 26: Metabolic effects of simvastatin and Omega-3 polyunsaturated fatty acids in type 2 diabetic patients with cardiovascular autonomic neuprophy

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Background and aims: Diabetic neuropathies, including cardio-vascular autonomic neuropathy (CAN), are a common chronic complications of Type 2 diabetes mellitus and confer high morbidity and mortality to diabetic patients. The present study has examined the metabolic effects of simvastatin (SIM), omega-3 polyunsaturated fatty acids (ω-3 PUFA) and their combinations in Type 2 diabetic patients with CAN.

Materials and methods: 76 Type 2 diabetic patients with CAN (54,7±3,6 years), BMI 27,8±2,3 kg/m2, HbA1c 7,1±0,7 % and 15 age-matched controls were observed. Fasting blood glucose,