European Respiratory Society
Annual Congress 2012

Abstract Number: 2168
Publication Number: P1886

Abstract Group: 4.2. Sleep and Control of Breathing
Keyword 1: Sleep disorders **Keyword 2:** Genetics **Keyword 3:** Hypoxia

Title: Effects of CETP and APOE polymorphisms on lipoprotein levels in patients with obstructive sleep apnea

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Body: Rationale. Cholesterol ester transfer protein (CETP) and apoliprotein E (APOE) polymorphisms were related to serum lipids in association studies. In a mouse model of obstructive sleep apnea (OSA) hypoxia inhibited clearance of triglyceride-rich lipoproteins. Since hypoxia might interfere with genetic background to affect lipid levels, we examined effects of interactions between CETP and APOE variants and hypoxia on serum lipids in OSA patients. Methods. 634 adult subjects evaluated for suspected OSA underwent overnight polysomnography. The association of HDL-cholesterol (HDLC), triglycerides (TG) and LDL-cholesterol (LDLC) with OSA-related hypoxia reflected by oxygen desaturation index (ODI) was examined and adjusted for relevant covariates. Findings. Patients were 69.1% male (age 51.1±11.2 years, apnoea-hypopnoea index 30.4±29.9). In univariate analyses, HDLC was related to the both ODI and CETP polymorphism ($R=-0.196$, $p<0.001$; $R=0.123$, $p=0.002$). In multivariate analysis only CETP genotype remained associated with HDLC ($R^2=0.185$, $p=0.002$) and no interaction between CETP variant and ODI was observed. In contrast, TG were related to ODI and APOE polymorphism in the univariate analyses ($R=0.284$, $p<0.001$; $R=0.100$, $p=0.013$), and also after adjustments ($R^2=0.382$, $p=0.046$, $p=0.002$). Significant interaction between APOE genotype and ODI was observed with respect to TG levels ($p=0.010$ for the interaction term APOE*ODI). Conclusion. Our findings support the role of CETP and APOE polymorphisms in atherogenic dyslipidaemia in OSA patients, and suggest the presence of an interaction between hypoxia and APOE genotype to affect TG levels. Funding. APVV-0134-11, VEGA 1/0111/12, Slovakia.