NONALCOHOLIC FATTY LIVER DISEASE AND FIBROSIS ASSOCIATED WITH INCREASED RISK OF CARDIOVASCULAR EVENTS IN A PROSPECTIVE STUDY

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Background and Aims. Patients with non-alcoholic fatty liver disease (NAFLD) are at increased chance for cardiovascular events (CVEs). Severity of liver fibrosis is used to determine prognosis for patients with NAFLD, but little is known about the relationship between liver fibrosis and CVEs in the real world.
Methods. We analyzed data from the prospective observational progression of liver damage and cardiometabolic disorders in non-alcoholic fatty liver disease study, comprising 898 consecutive outpatients screened for liver steatosis by ultrasound. Liver fibrosis was defined as FIB-4 score greater than 2.67 and NAFLD fibrosis score greater than 0.676. Patients were followed by phone every 6 months and examined every 12 months in the outpatient clinic. CVEs were recorded (fatal or nonfatal ischemic stroke and myocardial infarction, cardiac or peripheral revascularization, new-onset arterial fibrillation and cardiovascular death). The primary outcomes were incidence rate of CVEs in patients with vs without NAFLD and factors associated with CVEs in patients with NAFLD.
Results. Over a median follow-up time of 41.4 months (3044.4 patient-years), 58 CVEs (1.9%/year) were registered. The rate of CVEs was higher in patients with (n=643, 2.1%/year) vs without NAFLD (n=255, 1.0%/year) (P=.066). In multivariable Cox proportional regression analysis, NAFLD increased risk for CVEs (hazard ratio [HR], 2.41; 95% CI, 1.06-5.47; P=.036), after adjustment for metabolic syndrome. Among patients with NAFLD, male sex, previous CVEs, metabolic syndrome and FIB-4 scores greater than 2.67 (HR, 4.02; 95% CI, 1.21-13.38; P=.023) were independently associated with risk of incident CVEs. NFS scores greater than 0.676 were also independently associated with risk of incident CVEs (HR, 2.35; 95% CI, 1.05-5.27; P=.038).
Conclusions. NAFLD patients had more than a 2-fold increase in risk of CVEs. In patients with NAFLD, liver fibrosis indexes were independently associated with a 4-fold increased risk for incident CVEs.

CHRONIC RUPATADINE TREATMENT WORSENS ATHEROSCLEROSIS PROGRESSION IN APOLIPOPROTEIN E KNOCKOUT MICE FED WESTERN-TYPE DIET

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Aim. Rupatadine is an N-alkyl pyridine derivative exerting anti-inflammatory properties through the inhibition of a range of mediators. Its primary mechanism of action is through the histamine H1 receptor, with an additional antagonist activity towards PAF. The potent anti-inflammatory effects displayed by rupatadine could be exploited against atherosclerosis development.
Methods. Apolipoprotein E-deficient (EKO) mice (n=15 per group) were fed Western-type diet, with (Rupa) or without (Ctrl) 0.17 g/kg rupatadine for 12 weeks (~16 mg/kg/die).
Results. Weight gain, food/water intake, organ weights were similar in both groups. Plasma total cholesterol and triglyceride levels were also comparable. No difference in inflammatory infiltrates was detected in liver, kidney and lungs. Atherosclerotic plaque extent in arch, thoracic and abdominal segments of aorta (en-face) was comparable between groups. Ctrl and Rupa plaques were remarkably similar in the macrophage content (anti-Galectin3), necrotic core and plaque matrix content (Masson's trichrome). However, plaque area at the aortic sinus (H&E) was higher in Rupa (+14.8%, p=0.02).
Conclusions. Rupatadine treatment in apoE-KO mice fed Western diet resulted in a moderate worsening of atherosclerosis development. Shedding light on controversial in vitro results, our findings are in line with evidences from other related molecules (cetirizine, fexofenadine). While the molecular mechanism is still under investigation, it would be worthwhile to assess the impact of rupatadine treatment on human health, especially in chronically treated patients.