

Differential effects of moderate and excess alcohol consumption on the atheroprotective process of the reverse cholesterol transport in vivo

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Epidemiological studies worldwide revealed that light to moderate alcohol consumption is inversely correlated with cardiovascular morbidity and mortality, whereas consumption above recommended limits causes the loss and even the reversal of this beneficial activity. Cardiovascular disease (CVD) and atherosclerosis can be prevented or retarded by the process of reverse cholesterol transport (RCT), in which high density lipoproteins drive the removal of excess cholesterol from the macrophages of the artery wall. Recent studies in vivo established the inverse relationship between RCT efficiency and atherosclerotic CVD.

The aim of the present study was to evaluate whether moderate and heavy consumption of alcohol may differently impact RCT in an animal model of atherosclerosis-prone mice. For this purpose, RCT was measured with a standardized, radioisotope-based technique in 3 groups of apolipoprotein E knock out mice: group I (n=10), receiving placebo, mimicking the abstainers;

group II (n=10), receiving 0.8g/kg alcohol/day for 28 days, mimicking a moderate intake of ethanol; group III (n=10), receiving 0.8g/kg alcohol/day for 26 days, followed by the administration of 2.8g/kg alcohol/day for 2 days, mimicking a heavy intake. Two days before the sacrifice, mice were injected with a suspension of ³H-cholesterol loaded macrophages and the radioactivity was quantified in plasma, liver and feces in the following 48h.

Alcohol intake caused a dose-dependent increase in plasma total cholesterol (272mg/dl±59, 283mg/dl±53, 374mg/dl±86 in group I, II and III respectively) and HDL-cholesterol (124mg/dl±27, 154mg/dl±37, 179mg/dl±38 in group I, II and III respectively). Interestingly, excess alcohol consumption significantly increased plasma LDL cholesterol (126mg/dl±40, 113mg/dl±25, 165mg/dl±65; in group I, II and III respectively) and triglycerides (110mg/dl±36, 88mg/dl±16, 136mg/dl±30; in group I, II and III respectively).

The amount of radioactivity in plasma (1.7%±0.6, 2.6%±1.9; 2.0%±0.5; in group I, II and III respectively) and liver (2.4%±0.7, 4.2%±0.8, 3.4%±1.0 in group I, II and III) was higher in the moderate alcohol group. On the contrary, the elimination of radioactivity as fecal neutral sterols and bile acids was similar in all groups: 5.3%±2.3, 4.9%±2.3, 4.1%±0.9; in group I, II and III respectively. Overall, the removal of radioactivity from macrophages along the RCT pathway was higher in animals treated with moderate dose of alcohol: 12.2%±3.1, 15.1%±3.7; 13.3%±2.4; in group I, II and III respectively.

In conclusion, moderate alcohol consumption may promote the mobilization of radioactive cholesterol from macrophages, along the RCT pathway, thus suggesting the amelioration of this process. Differently, excess alcohol consumption seems not to significantly affect the process, but it exerts deleterious effects on plasma lipoprotein profile.