Lipid Metabolism Abnormalities Secondary to Alcohol Administration in Cholesterol-Fed Rabbits - A Morphometric and Hematologic Study -

INTRODUCTION

Nontraumatic osteonecrosis (ON) has been proven to be associated with alcohol abuse in many published reports (1). However, the pathogenesis of alcohol-induced ON remains unclear. Some reports suggested that pathologic changes in steroid- and alcohol-induced ON are similar (1). Several possible factors in the pathogenesis of steroid-induced ON have been suggested based on human and animal studies, including hyperlipidemia and coagulation abnormalities (2). In addition, an experimental study showed the potential hyperlipidemia is one of the risk factors in steroid-induced ON (3).

Therefore, we evaluated morphological changes of bone marrow fat cells and serum lipid level changes secondary to alcohol administration in rabbits with hyperlipidemia.

METHODS

All Rabbits (n = 11) were fed 100 g/day of a high cholesterol diet (RC-4 containing 1% cholesterol, Oriental Y east Co., Ltd., Tokyo) for 6 weeks, which were divided randomly into 2 groups (experimental group: n = 6, control group: n = 5). Alcohol (Korean shochu: containing 25% ethanol) at a dose of 20 ml/kg body weight per day was intragastrically administered in the experimental group once daily for 4 weeks, starting from 2 weeks after a high cholesterol diet.

Six weeks after the start of high cholesterol diet (4 weeks after the initial alcohol administration), both femora and humeri were histopathologically examined for the changes of bone marrow fat cell morphologically. We calculated the size of bone marrow fat cells as the average of the maximal diameters of 100 fat cells in randomly selected fields (1 field = 4 x 10^-8 meters^2), using NIH Image software, as previously described (4).

Blood alcohol concentrations (BACs) at 1 hour after alcohol administration were measured in rabbits with the experimental group. Every week, we examined the serum lipid levels (total cholesterol, triglycerides, low-density lipoprotein [LDL] cholesterol, free fatty acid, and hepatic enzyme [alanine aminotransferase [ALT] and aspartate aminotransferase [AST]]) morphologically. Although the present study showed the lipid metabolism abnormality, these findings were moderate in comparison with those in steroid-induced ON. The average size of bone marrow fat cells in the experimental group was 57.4 ± 6.3 µm, which is smaller than those in the steroid-induced ON rabbits (63.5 ± 5.8 µm) as previously reported (4). Hematologically, a recent study reported the mean level of triglycerides 2 weeks after the injection of methylprednisolone (20mg/kg) in rabbits was approximately 800 mg/dl, which is three times higher than those in experimental group (3).

We consider the abnormal lipid metabolism to be one of the important factors considering the pathogenesis of ON, however, drastic changes of lipid status both morphologically and histopathologically after alcohol administration might be necessary to lead to the ON in animals.

RESULTS

Fig. 1 The average size of bone marrow fat cells was significantly larger in the experimental group (57.4 ± 6.3 µm) than in the Group C (49.7 ± 5.4 µm) (*p = 0.0001, the one-way analysis of variance (ANOVA) with Scheffe’s post-hoc test).

Fig. 2 Levels of total cholesterol, triglycerides, and free fatty acid in the experimental group (high cholesterol diet + alcohol administration) and the control group (high cholesterol diet only) are shown. Alcohol administration was started at 2 weeks after a high cholesterol diet. (A) The total cholesterol levels in the experimental group were significantly higher (p < 0.01) than those in the control group throughout the experimental period. (B) The levels of triglyceride in the experimental group were significantly higher (p < 0.05) than those in the control group throughout the experimental period. (C) The experimental group exhibited a higher (p < 0.05) than the average free fatty acid across the experimental period in comparison to the control group.

REFERENCES