



Editorial

Dietary deep seawater and hepatic steatosis

Fatty liver disease is a growing health concern in western and other developed countries. The cause of fatty liver can be broken down into two categories: (1) alcoholic fatty liver disease and (2) nonalcoholic fatty liver disease (NAFLD). The abnormal retention of fat as vacuole in hepatocytes is more commonly known as steatosis and can progress further to steatohepatitis, possibly resulting in hepatocytic damage. According to the latest practice guidelines for the diagnosis and management of NAFLD,¹ a patient with NAFLD typically has histological or imaging evidence of hepatic steatosis, with no history of significant alcohol consumption or steatogenic drug use. NAFLD is often linked with risk factors such as obesity, diabetes mellitus, and dyslipidemia. Worldwide, its estimated prevalence ranges from 6.3% to 33%, with a median of 20% in the general population.

Hepatic steatosis is an important change that is related to chronic inflammation of the liver. It has been reported that alcohol intake stimulates the production of proinflammatory cytokine interleukin-12 (IL-12), leading to an increased serum level of IL-12 in patients with alcoholic liver disease. However, the IL-12 level in the hepatic steatosis group was similar to that in the control group after the patients stopped using alcohol for 9 months, suggesting that hepatic steatosis is reversible.² By contrast, it was reported that 52% of Chinese patients with chronic hepatitis C had hepatic steatosis. This correlation is observed frequently in patients with chronic hepatitis C virus infection³ and also presents an increased risk factor for the development of hepatocellular carcinoma.⁴ Recently, it was reported that mice lacking miR-122a (Mir122a) might develop steatohepatitis, fibrosis, and hepatocellular carcinoma. Steatosis was the result of an impaired expression of microsomal triglyceride transfer protein.⁵ However, the detailed mechanism underlying the development for hepatic steatosis in relation to changes in intracellular signaling pathways and extracellular microenvironment still requires further investigation.

Eicosanoids are lipid signaling molecules that play important roles in the regulation of inflammation in the body. The eicosanoids derived from omega-6 (n-6) polyunsaturated fatty acids (n-6 PUFA) and omega-3 PUFA (n-3 PUFA) are proinflammatory and anti-inflammatory functional molecules, respectively. The ratio of n-6 PUFA to n-3 PUFA has increased significantly in recent years, which has corresponded well with the observed increases in obesity, cardiovascular disease, and

NAFLD.⁶ Consequently, in order to maximize patient benefits, it is important for clinicians to also treat the associated metabolic syndrome customarily seen in NAFLD patients, such as obesity and hyperlipidemia. Increased exercise, combined with reduced caloric intake, can result in weight loss and reduced hepatic steatosis.¹

In the February 2013 issue of the *Journal of the Chinese Medical Association*, Chen et al⁷ examined the effects of deep seawater drinking water on high-fat-diet-induced oxidation and lipid accumulation in hepatocytes of hamsters. Their results clearly showed that hamsters that consumed 300–1500 ppm deep seawater drinking water, undergoing a 6-week high-fat diet, had reduced serum cholesterol and triglyceride levels significantly, in a dose-dependent manner. In addition, cholesterol and triglyceride levels in the liver were also decreased significantly, along with an increase in the levels of fecal bile acid, cholesterol, and triglyceride in a dose-dependent manner. These results suggest that drinking deep seawater may have decreased the uptake of cholesterol and butter in the high-fat diet and/or increased the excretion of triglyceride and cholesterol through bile and feces. Moreover, similar results were found by these authors using the same model of hamsters fed on a high-fat/high-cholesterol diet, reaching the conclusion that 300–1500 ppm deep seawater drinking water has a cardiovascular protective effect.⁸ It is interesting that when rabbits that had been fed a high-fat diet and drinking 28, 300, or 1200 ppm desalinated deep seawater reverted back to their normal diet, the decrease in total cholesterol and low-density lipoprotein cholesterol levels was higher than that of the control rabbits.⁹ Furthermore, Lee et al¹⁰ used deep ocean water to culture red mold dioscorea (RMD) and compared its hypolipidemic effect to that of the reverse osmosis water-cultured RMD in hyperlipidemic hamsters. It was found that deep-ocean-water-cultured RMD had a higher level of magnesium (Mg^{2+}) ion because of its mineral richness, and displayed a greater effect on lowering cholesterol levels and lipid peroxidation in serum. These *in vivo* results together suggest that the reduction of hyperlipidemic effect by drinking deep seawater is closely related to the high levels of mineral ions such as Mg^{2+} , and may have resulted more from an increased excretion of steroids in the feces than from the inhibition of uptake of dietary fat.

Several studies have examined whether cardiovascular disease mortality is, in any way, related to dietary water

hardness. Yang et al¹¹ examined the calcium(Ca) and Mg²⁺ levels in drinking water of 10,094 cases of Taiwan residents with acute myocardial infarction as well as of 10,094 matched control without acute myocardial infarction. Based on the data from the Taiwan Water Supply Corporation on Ca and Mg²⁺ levels in drinking water throughout Taiwan, it was found that higher Ca level, but not Mg²⁺ level, in drinking water had a significant protective effect on the risk of death from acute myocardial infarction. A recent study further examined the effect of drinking deep seawater with high levels of Mg²⁺ (Mg: 395 mg/L, hardness 1410 ppm) on blood lipids and its antioxidant capacity in 42 hypercholesterolemic volunteers. It was found that drinking 1050 mL deep seawater per day for 6 weeks resulted in a time-dependent decrease in blood cholesterol levels and serum low-density lipoprotein cholesterol. Moreover, drinking deep seawater also lowered serum lipid peroxidation in these hypercholesterolemic individuals.¹² These results clearly indicate that mineral ions in the drinking water are important components in the proper maintenance and regulation of lipid metabolism. Drinking water or deep seawater with high levels of Ca and/or Mg²⁺ ions appears to beneficially attenuate the serum cholesterol and low-density lipoprotein cholesterol levels in individuals with acute myocardial infarction and hypercholesterolemia. The detailed mechanism of this correlation and its potential long-term side effects merit further investigation.

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