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ORIGINAL ARTICLE

Prevention of hypercholesterolemia and atherosclerosis in the hyperlipidemia- and atherosclerosis-prone Japanese (LAP) quail by taurine supplementation

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Abstract The effects of taurine supplementation on the serum cholesterol levels and the progression of atherosclerosis were investigated in the hyperlipidemia- and atherosclerosis-prone Japanese (LAP) quail. The ingestion of a high-cholesterol diet containing 1% cholesterol by LAP quails for 60 days resulted in a marked elevation in serum non-HDL cholesterol and triglyceride, as well as severe aortic lesions with lipid droplets. An immunohistochemical study showed that the lesion consisted of mainly lipid-rich macrophages and T cells. Sixty-day taurine supplementation (1% in drinking tap water) to LAP quails fed high-cholesterol diet containing 1% cholesterol significantly reduced serum non-HDL cholesterol from 4,549 to 2,350 mg/dl. The serum triglyceride level also decreased after taurine supplementation from 703 to 392 mg/dl. Although the HDL cholesterol level significantly decreased due to the high-cholesterol diet, it recovered to the control level fed a regular diet in response to taurine. Bile acid production was stimulated and hepatic cholesterol was reduced by taurine supplementation. A quantitative analysis using aortic cross-sections showed that areas of oil-red O positive lipid accumulation significantly decreased by 74% after taurine supplementation. These results demonstrated the lipid-lowering and anti-atherosclerotic effects of taurine in a diet-induced hyperlipidemic LAP quail model. The prevention of atherosclerosis by taurine is mainly attributed to an improvement in the serum cholesterol and triglyceride levels, which may be related to changes in the hepatic cholesterol metabolism.

Keywords Taurine · LAP quail · Atherosclerosis · Hypercholesterolemia

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Introduction

Taurine is a sulfur-containing amino acid that is widely distributed in animal tissues and it is especially abundant in the heart, liver, and kidney. It plays an important role in maintaining physiological homeostasis (Huxtable 1992). Taurine is involved in the catabolism of cholesterol. Cholesterol is converted to bile acids within the liver, which are then conjugated with either taurine or glycine before secretion into the bile. This process represents one of major means for the ultimate excretion of sterols from the body. The beneficial effects of taurine ingestion on the serum cholesterol levels and cardiovascular disease have been demonstrated in humans (Yamori 1996; Zhang 2004). Epidemiological data revealed the taurine intake to negatively correlate with the mortality associated with ischemic heart disease (Mizushima 1997; Yamori 2001).

The effects of taurine supplementation on the blood cholesterol levels and atherosclerosis have been studied in several animal models (Petty 1990; Yokogoshi 1999).

Taurine supplementation retards the progression of atherosclerotic lesions in genetically hyperlipidemic animal models including apolipoprotein E-deficient mice (Kondo 2001) and spontaneously hyperlipidemic (SHL) mice (Matsushima 2001). Taurine reduces serum atherogenic cholesterols and increases HDL cholesterol in diet-induced models of hyperlipidemia such as C57BL/6J mice fed a high-cholesterol diet (Murakami 1999), while the effect of taurine on atherosclerosis is not clear, since rodents are resistant to diet-induced atherosclerosis. Therefore, hyperlipidemia atherosclerosis prone (LAP) quails fed a high-cholesterol diet were used to confirm the anti-atherosclerotic action of taurine in a diet-induced atherosclerosis model.

The beneficial features of the quail as an animal model are their short life cycle, low food consumption and susceptibility to cholesterol loading (Ojerio 1972; Radcliffe and Liebsch 1985; Casale 1992). The LAP quail is a strain of Japanese quail susceptible to hyperlipidemia and atherosclerosis, which was established by repeated breeding of a highly susceptible line (Inoue 1995). LAP quails develop hypercholesterolemia in response to a diet containing 0.5–1% cholesterol and severe atherosclerotic lesions with foam cells and extracellular matrix deposition appear in the aorta within 1 or 2 months (Nagata 1996; Iwasaki 2000). Therefore, the LAP quail is an attractive animal model to study the pathogenesis and prevention of diet-induced atherosclerosis. The present study was conducted to determine the effects of taurine ingestion on serum lipid levels and progression of atherosclerotic lesions in diet-induced LAP quail.

Materials and methods

Animals

All procedures were done in accordance with the "Guiding principle for the care and use of animals in field of physiological sciences" of the Physiological Society of Japan. Male hyperlipidemia- and atherosclerosis-prone Japanese (LAP) quails were hatched by the artificial incubator and bred until 2–3 months of age and were kept under 12-h light/12-h dark conditions at 23–25°C for 60 days at the University of Miyazaki. The quails were divided into three groups: a control group ($n = 6$), cholesterol group ($n = 7$), and cholesterol plus taurine group ($n = 7$). The quails in the control group received a commercial diet that included grain (61%), plant oil cake (20%), rice bran (5%), fish meal (3%) and minerals (11% High-layer M; Minaminihon Foods Co. Ltd, Kagoshima, Japan). The quails in the cholesterol group received a high-cholesterol diet (the commercial diet plus 1% cholesterol and 5% corn oil) for 60 days. The quails in the cholesterol plus taurine group received the high-cholesterol diet and deionized water containing 1% taurine (w/v) for 60 days.

Measurement of blood samples

The blood was collected from the common carotid artery and jugular vein of the bird by decapitation and then was stored at −80°C. The concentrations of serum cholesterol, serum triglyceride, phospholipids, serum HDL cholesterol, and lipid peroxide were determined by use of the corresponding kits (Wako Pure Chemical Industries Co Ltd, Osaka, Japan). Liver lipids were extracted using the method of Folch et al. (Folch 1957) and followed by measurement of cholesterol using the methods described elsewhere (Yamamoto et al. 2000).

Bile acid analysis

The fractionation of bile acids in the bile was carried out according to a method described elsewhere (Ide and Horii 1987). In brief, the bile samples were diluted with 0.05 M phosphate-buffered saline (pH 7.4) and passed through a Sep-Pak C18 cartridge (Waters Corporation, Milford, MA). The cartridge was washed with 5 ml of water and 5 ml of 1.5% ethanol and bile acids were eluted with 5 ml of 90% ethanol. The bile acids in these extracts were then fractionated according to the mode of conjugation using piperdinohydroxypropyl dextran gel (PHP gel, Shimadzu, Kyoto, Japan): non-conjugated, glycine-conjugated, and taurine-conjugated bile acids. Total and individual conjugated bile acid concentrations were measured by a commercially available kit (Wako Pure Chemicals, Osaka, Japan) and the bile acid composition was analyzed by the HPLC method according to the manufacturer's instructions.

Histological examination

The heart along with the systemic aortic arch were removed from animal and fixed in 4% paraformaldehyde and washed with phosphate-buffered saline (PBS). The aortic arch was dissected out and cryoprotected by incubation with 10% sucrose-PBS, transferred into cryo-embedding compound (Microm, Walldorf, Germany) and quick-frozen by immersion in isopentene cooled with liquid nitrogen. Five-micrometer sections were made from these frozen samples with a cryostat and stained with Hematoxylin–Eosin (H&E), Elastica van Gieson (EVG) and Oil red O, for histological study. Five sections at 100-μm intervals were examined using light microscopy, photographed with a CCD camera XC-007 (SONY, Tokyo, Japan). The oil-red O positive area was measured using

image analysis software Ultimage (Graftek, Yokohama, Japan). The average areas of five sections were calculated (Shih 1983). For the immunohistochemical study, frozen sections were pre-incubated in 1% bovine serum albumin-PBS for 30 min at room temperature and rinsed with PBS. Thereafter, the sections were incubated with primary antibody, QH1 (x500, Developmental Studies Hybridoma Bank, Iowa City, Iowa) for macrophages or endothelial cells, LFA-1α (10 μg/ml, Upstate Biotechnology Inc., Lake Placid, NY) for lymphocytes, 1A4 (ready to use, DAKO, Glostrup, Denmark) for smooth muscle actin, respectively. After washing with PBS, these sections were incubated with the secondary antibody (biotinylated goat anti-mouse IgG, Vector Laboratories Inc, Burlingame, CA) for 1 h at room temperature and rinsed with PBS. The sections were immersed in methanol/hydrogen peroxide solution for 30 min at room temperature to inactivate the endogenous peroxidase activity and incubated in avidin-biotinylated peroxidase complex (Vector Laboratories Inc) for 1 h at room temperature. Finally, the peroxidase activity was visualized with the ABC Chromogen Kit (Sigma-Aldrich, St. Louis, MO).

Statistical analysis

The data are expressed as the mean ± SEM. The statistical significance of the differences was evaluated using a 1-way analysis of variance followed by a Bonferroni post test. A P value of less than 0.05 was considered to be significant.

Results

Body weight

There were no significant differences between the body weights of each group. The body weights at the termination of the experiment were 98.4 ± 2.5 g (control group), 102.6 ± 2.4 g (cholesterol group) and 108.9 ± 2.2 g (cholesterol plus taurine group).

Serum and liver lipids

The serum total cholesterol level was markedly elevated from 246 to 4,631 mg/dl after 60 days treatment of LAP quail with the high-cholesterol diet (Fig. 1a). The increase in total cholesterol was attributed to an increase in non-HDL cholesterol (Fig. 1b). In contrast, serum HDL cholesterol was significantly decreased by the high-cholesterol diet (Fig. 1c). Serum triglyceride was also markedly elevated by ingestion of the high-cholesterol diet (Fig. 1d). Taurine supplementation significantly reduced the serum non-HDL cholesterol (Fig. 1b) and triglyceride (Fig. 1d) by 49 and 52%, respectively. The decreased HDL cholesterol level recovered to the control level in response to taurine (Fig. 1c). The hepatic total cholesterol level increased after the quails consume a high-cholesterol diet for 60 days (control group 3.64 ± 0.13; cholesterol group 61.2 ± 7.1 mg/g liver, $P < 0.05$), which was lower in the taurine-treated quails (46.7 ± 2.2 mg/g liver, $P < 0.05$ vs. cholesterol group).

Bile acids

The high-cholesterol diet increased the total bile acid by 44%. Taurine treatment further increased total bile acid by 27%. In LAP quails, most of the cholesterol was conjugated with taurine (Table 1). Taurine ingestion tended to increase the amount of taurine-conjugated bile acids. Taurochenodeoxycholic acid increased by 32% in response to taurine supplementation in the bile acid composition.

Atherosclerotic lesions in aorta

There were no atherosclerotic lesions or lipid accumulation in the LAP quail fed a regular diet, as evaluated by a histological analysis of the aorta. The lumen of the aorta was extremely narrowed and severe intimal hyperplasia with lipid accumulation was seen in animals fed a high-cholesterol diet for 60 days (Fig. 2). Almost completely occlusive lesions were noted in three animals. An immunohistochemical analysis showed that the aortic lesions consisted of macrophages with lipid droplets (Fig. 3). T cells were also detected in regions of severe lipid accumulation. Consistent with the Oil-red O staining, lipid-rich macrophages were decreased in the intima of taurine-treated animals. The severity of atherosclerosis was evaluated quantitatively in aortic sections using an image analyzer. The aortic lesion area was markedly reduced by the treatment with taurine. Lipid accumulation also significantly decreased after taurine administration in both the intima (Fig. 4a) and media (Fig. 4b). In contrast to the animals fed a high-cholesterol diet, no occlusive lesions were noted in the aorta of the taurine-treated group.

Discussion

The present study showed that taurine ingestion improves serum lipid profiles and suppresses the progression of atherosclerosis induced by a high-cholesterol diet in LAP quail. This is a first finding that taurine ingestion clearly suppresses the formation of atherosclerotic lesions in diet-induced atherosclerosis, although there are several studies showing the anti-atherosclerotic effect of taurine in genetically hyperlipidemic animal models. The aortic

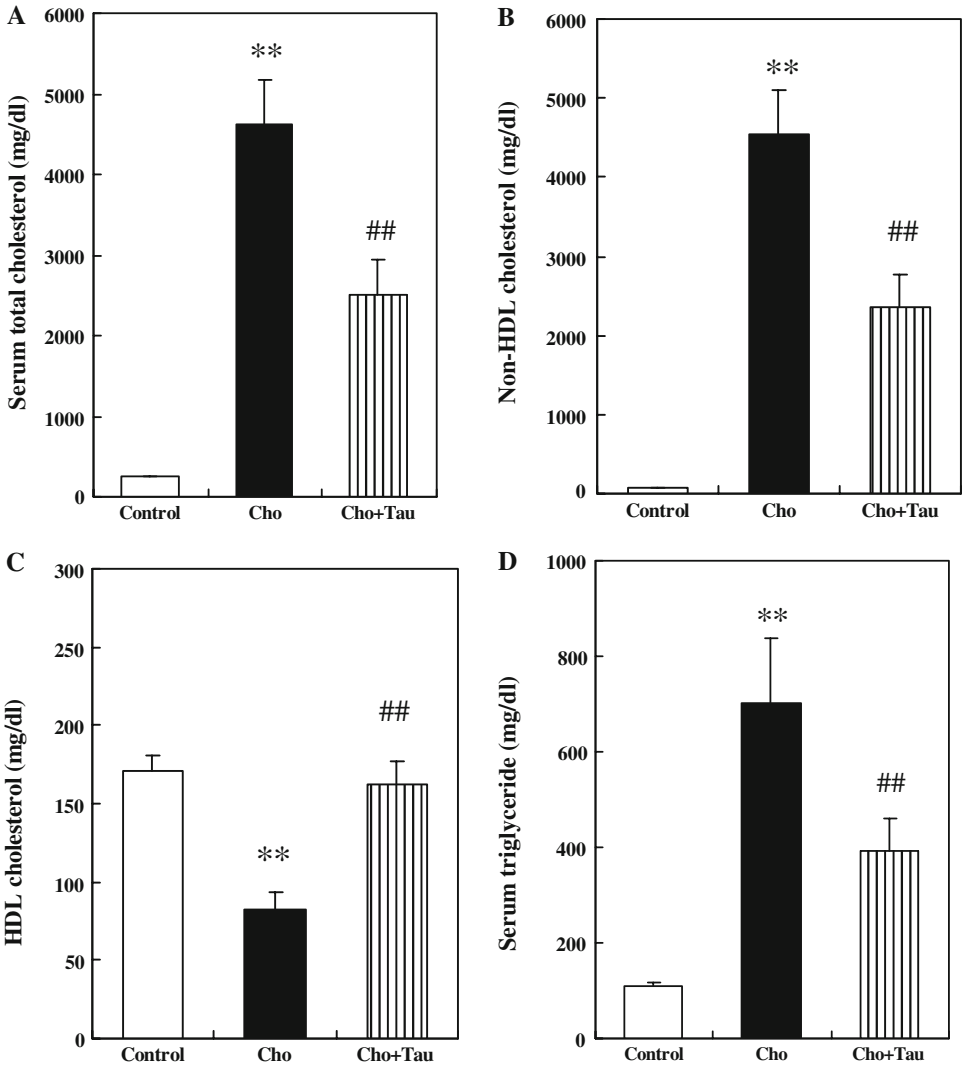

Fig. 1 Effects of a high-cholesterol diet (*Cho*) and high-cholesterol diet plus taurine supplementation (*Cho + Tau*) on serum total cholesterol (**a**), non-HDL cholesterol (**b**), HDL cholesterol (**c**) and triglyceride (**d**) in the LAP quail. The serum lipids levels were determined after the 60-day ingestion of a high-cholesterol diet and/or 1% taurine in drinking tap water. Values represent the means ± SEM ($n = 6$-7). ** $P < 0.01$ (vs. Control), $^{\#\#}P < 0.01$ (vs. Cho)

lesion develops more rapidly in the LAP quail than any other models of hyperlipidemia and atherosclerosis. In addition, the occlusive aortic lesions observed in LAP quails are never seen in other animal models. Among the factors which influence the progression of atherosclerosis in animals fed a high-cholesterol or high-fat diet are the magnitude and duration of hypercholesterolemia. Accelerated progression of atherosclerosis in LAP quails is presumably due to the high response of these animals to a high-cholesterol diet and subsequent extremely high levels of serum atherogenic cholesterols in contrast to rodents. Serum total cholesterol exceeded 4,500 mg/dl in LAP quails, which was far higher than other animal models. These serum cholesterol levels are also two or three times higher in LAP quail in comparison to Japanese quail (Ojerio 1972; Radcliffe and Liebsch 1985; Fann 1989). The present study revealed that stenotic lesions were inducible in LAP quails by ingesting a diet containing 1% cholesterol after only 60 days. The lesions were distributed throughout the entire aorta, similar to apolipoprotein E-deficient mice (Nakashima 1994) and Watanabe heritable hyperlipidemic (WHHL) rabbits (Ito et al. 1994). The complexity and composition of the atherosclerotic lesions that develop in LAP quails is similar to those in other species including humans. Ingestion of taurine by LAP quails fed high-cholesterol diet reduced serum non-HDL cholesterol by 49% and the HDL cholesterol recovered to the level of control quails fed a regular diet. This suggests that the improvement in the cholesterol metabolism accounts for the suppression of atherosclerosis.

The increase in bile acid synthesis from cholesterol is thought to be the major mechanism by which taurine lowers serum atherogenic cholesterol levels (Murakami 1996). Ingestion of taurine by mice, rats, and hamsters increases mRNA expression and enzymatic activity of 7α-hydroxylase, a rate-limiting enzyme of bile acid synthesis, which is accompanied by the reduction in elevated serum cholesterol. The taurine ingestion increased the total

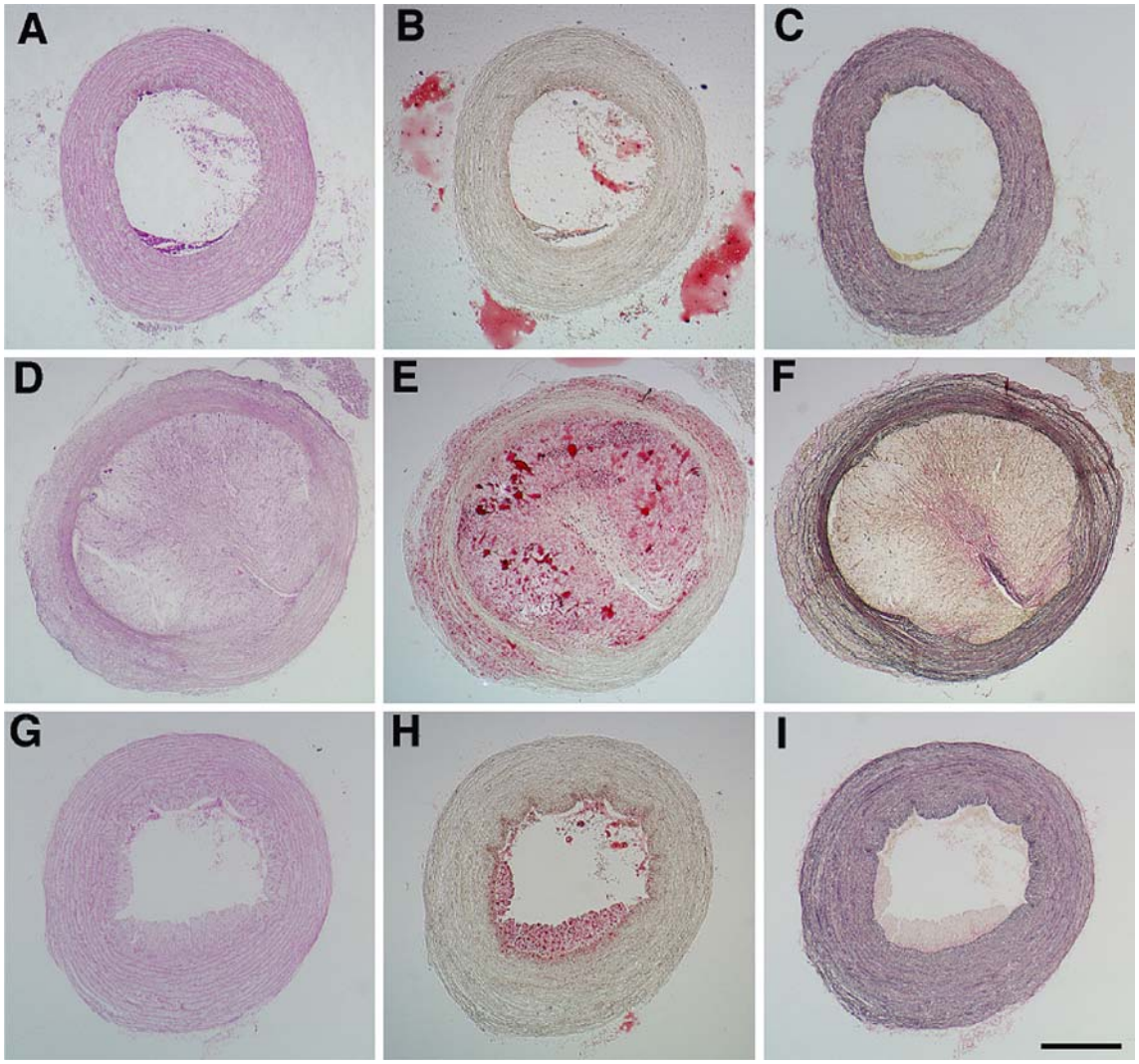

Fig. 2 Representative cross-sections of the LAP quail aorta stained with H&E, Oil red O and Elastica van Gieson (EVG). **a** LAP quail fed a standard diet (HE stain). **b** LAP quail fed a standard diet (Oil red O stain). **c** LAP quail fed a standard diet (EVG stain). **d** LAP quail fed a high-cholesterol diet (HE stain). **e** LAP quail fed a cholesterol diet (Oil red O stain). **f** LAP quail fed a cholesterol diet (EVG stain). **g** Taurine supplemented LAP quail fed a high-cholesterol diet (HE stain). **h** Taurine supplemented LAP quail fed a high-cholesterol diet (Oil red O stain). **i** Taurine supplemented LAP quail fed a high-cholesterol diet (EVG stain). *Bars* = 500 μm

bile acid content in LAP quails parallel to the reduced hepatic cholesterol, thus suggesting that a similar mechanism may be involved in the cholesterol-lowering effect of taurine. There is a significant decrease in the intestinal acyl-CoA:cholesterol acyltransferase (ACAT) activity following taurine ingestion (Murakami 1996). Since ACAT is responsible for cholesterol absorption in the intestine (Suckling and Stange 1985), the inhibition of intestinal cholesterol absorption might to be involved in the hypocholesteremic action of taurine (Murakami 1996). The increased intestinal cholesterol absorption is thought to be the major mechanism responsible for the severe hypercholesterolemia induced by a high-cholesterol diet in the LAP quail (Iwasaki 2000). The inhibition of dietary cholesterol absorption may be related to the cholesterol-lowering effect of taurine in part, in addition to the increased cholesterol catabolism to bile acid.

In contrast to diet-induced hyperlipidemic animals, taurine suppresses the occurrence of aortic lesions without reducing the serum atherogenic cholesterol levels in genetically hyperlipidemic animals including apolipoprotein E-deficient mice (Kondo 2001), SHL mice (Matsushima 2001) and WHHL rabbits (Murakami 2002). Since oxidative stress is closely associated with the initiation and progression of vascular diseases (Schulze and Lee 2005) and the serum and tissue levels of oxidative substances are reduced

Table 1 Effect of taurine supplementation on bile acid composition

	Control	Cholesterol	Cholesterol + taurine
Total bile acid (mg/gallbladder)	3.45 ± 0.54[a]	4.98 ± 1.28[ab]	6.34 ± 0.88[b]
Non-conjugated bile acid	0.07 ± 0.03[a]	0.04 ± 0.02[ab]	0.01 ± 0.01[b]
Glycine-conjugated bile acid	0.04 ± 0.01[ab]	0.08 ± 0.02[a]	0.02 ± 0.01[b]
Taurine-conjugated bile acid	3.49 ± 0.63	5.02 ± 1.48	5.85 ± 1.01
Tauroursocholic acid	0.12 ± 0.03	0.08 ± 0.03	0.08 ± 0.04
Taurocholic acid	0.44 ± 0.10	0.31 ± 0.13	0.33 ± 0.13
Taurochenodeoxycholic acid	0.07 ± 0.01[a]	0.19 ± 0.04[ab]	0.25 ± 0.05[b]
Taurodeoxycholic acid	2.86 ± 0.55	4.44 ± 1.29	5.19 ± 0.93
Taurolithocholic acid	0	0	0

Data are expressed as the mean ± SEM of 6–7 animals. Values not sharing a common superscript letter are significantly different ($P < 0.05$)

Control, LAP quail given a standard diet for 60 days; Cholesterol, LAP quail given a high-cholesterol diet without taurine supplementation for 60 days; Cholesterol + taurine, LAP quail given a high-cholesterol diet with taurine supplementation (1% in drinking tap water) for 60 days

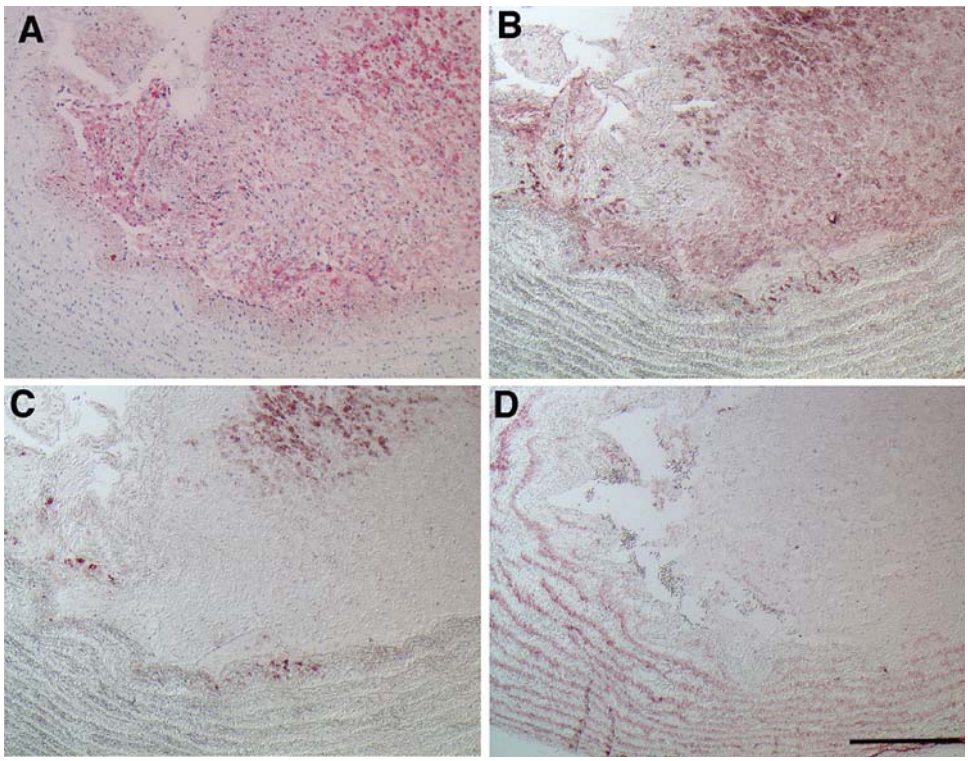

Fig. 3 Immunohistochemical localization of macrophages, smooth muscle cells and T cells in the aorta from LAP quail fed a high-cholesterol diet for 60 days. **a** Oil red O stain. **b** Immunostaining with antibody to macrophages and endothelial cells (QH1). **c** Immunostaining with antibody to T lymphocytes (LFA-1α). **d** Immunostaining with antibody to smooth muscle actin (1A4). *Bars* = 200 μm

by taurine treatment (Kondo 2001; Matsushima 2001; Murakami 2002), the anti-atherosclerotic effect of taurine in these species may thus be attributed to the antioxidative action of taurine. To investigate the contribution of antioxidative action of taurine in the LAP quail, the serum content of thiobarbituric acid-reactive substances (TBARSs) was determined. The serum TBARSs increased by 63% following the ingestion of the high-cholesterol diet. However, taurine had no significant effect on the serum TBARSs level, thus suggesting that antioxidative action is not related to the prevention of atherosclerosis by taurine, at least in the LAP quails.

In summary, the ingestion of taurine by LAP quails fed a high-cholesterol diet markedly suppressed the formation of aortic lesions. This is attributed to the improved serum lipid levels; a decrease in the atherogenic cholesterol and triglyceride levels and an increase in the HDL cholesterol level. An improvement in the hepatic cholesterol metabolism may be responsible for the cholesterol-lowering effect of taurine in LAP quail fed a high-cholesterol diet.

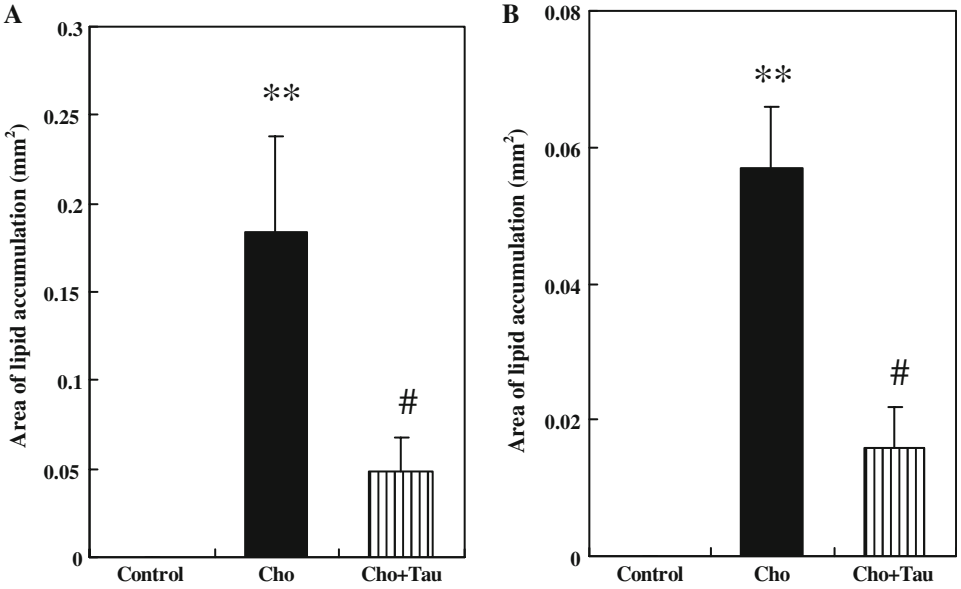

Fig. 4 Effects of a high-cholesterol diet (*Cho*) and a high-cholesterol diet plus taurine supplementation (*Cho* + *Tau*) on the area of aortic lipid accumulation. Aortic cross-sections were stained with H&E and Oil red O. The lesion area was determined quantitatively in the intima (**a**) and media (**b**), using an image analyzer. Values represent the mean ± SEM of 6–7 animals. ** $P < 0.01$ (vs. Control), $^{\#}P < 0.05$ (vs. *Cho*)

References

Casale EN, Qureshi MA, Shih JCH (1992) Immunocytochemical and scanning electron microscopic studies of atherosclerosis in Japanese quail. Poult Sci 71:141–150

Fann JI, Angell SK, Cahill PD, Kosek JC, Miller DC (1989) Effects of fish oil on arteriosclerosis in the Japanese quail. Cardiovasc Res 23:631–638

Folch J, Lees M, Sloane-Stanley GH (1957) A simple method for the isolation and purification of total lipids from animal tissues. J Biol Chem 226:497–509

Huxtable RJ (1992) Physiological actions of taurine. Physiol Rev 72:101–163

Ide T, Horii M (1987) A simple method for the extraction and determination of non-conjugated and conjugated luminal bile acids in rats. Agric Biol Chem 51:3155–3157

Inoue Y, Toda T, Igawa T, Tani T, Kimura Y (1995) The response of serum and hepatic lipids and the aortic wall to different levels of dietary cholesterol: a comparative study between hyperlipidemia-and-atherosclerosis-prone quail and commercially available quail. Tohoku J Exp Med 175:1–13

Ito T, Tsukada T, Ueda M, Wanibuchi H, Shiomi M (1994) Immunohistochemical and quantitative analysis of cellular and extracellular components of aortic atherosclerosis in WHHL rabbits. J Atheroscler Thromb 1:45–52

Iwasaki H, Oku H, Toda T, Nasu T, Miyagi T, Chinen I (2000) Increased cholesterol absorption by hyperlipidemia atherosclerosis prone (LAP) Japanese quail. J Nutr Sci Vitaminol 46:235–239

Kondo Y, Toda Y, Kitajima H, Oda H, Nagate T, Kameo K, Murakami S (2001) Taurine inhibits development of atherosclerotic lesions in apolipoprotein E-deficient mice. Clin Exp Pharmacol Physiol 28:809–815

Matsushima Y, Sekine T, Kondo Y, Sakurai T, Kameo K, Tachibana M, Murakami S (2001) Effects of taurine on serum cholesterol levels and development of atherosclerosis in spontaneously hyperlipidemic (SHL) mice. Clin Exp Pharmacol Physiol 30:295–299

Mizushima S, Moriguchi EH, Ishikawa P, Hekman P, Nara Y, Miura G, Moriguchi Y, Yamori Y (1997) Fish intake and cardiovascular risk among middle-aged Japanese in Japan and Brazil. J Cardiovasc Risk 4:191–199

Murakami S, Yamagishi I, Asami Y, Ohta Y, Toda Y, Nara Y, Yamori Y (1996) Hypolipidemic effect of taurine in stroke-prone spontaneously hypertensive rats. Pharmacology 52:303–313

Murakami S, Kondo-Ohta Y, Tomisawa K (1999) Improvement in cholesterol metabolism in mice given chronic treatment of taurine and fed a high-fat diet. Life Sci 64:83–91

Murakami S, Kondo Y, Sakurai T, Kitajima H, Nagate T (2002) Taurine suppresses development of atherosclerosis in Watanabe heritable hyperlipidemic (WHHL) rabbits. Atherosclerosis 163:79–87

Nagata J, Oku H, Toda T, Chinen I (1996) Effect of dietary cholesterol on the activities of key enzymes of cholesterol metabolism in hyperlipidemia- and atherosclerosis-prone Japanese quail. J Nutr Sci Vitaminol 42:287–300

Nakashima Y, Plump AS, Raines EW, Breslow JL, Ross R (1994) ApoE-deficient mice develop lesions of all phases of atherosclerosis throughout the arterial tree. Arterioscler Thromb 14:133–140

Ojerio AD, Pucak GJ, Clarkson TB, Bullock BC (1972) Diet-induced atherosclerosis and myocardial infarction in Japanese quail. Lab Anim Sci 22:33–39

Petty MA, Kintz J, DiFrancesco GF (1990) The effects of taurine on atherosclerosis development in cholesterol-fed rabbits. Eur J Pharmacol 180:119–127

Radcliffe JD, Liebsch KS (1985) Dietary induction of hypercholesterolemia and atherosclerosis in Japanese quail of strain SEA. J Nutr 115:1154–1161

Schulze PC, Lee RT (2005) Oxidative stress and atherosclerosis. Curr Atheroscler Rep 7:242–248

Shih JC, Pullman EP, Kao KJ (1983) Genetic selection, general characterization, and histology of atherosclerosis-susceptible and resistant quail. Atherosclerosis 49:41–53

Suckling KE, Stange EF (1985) Role of acyl-CoA:cholesterol acyltransferase in cellular cholesterol metabolism. J Lipid Res 26:647–671

Yamamoto K, Yoshitani A, Sakono M, Nasu T, Murakami S, Fukuda N (2000) Dietary taurine decreases hepatic secretion of cholesterol ester in rats fed a high-cholesterol diet. Pharmacology 60:27–33

Yamori Y, Nara Y, Ikeda K, Mizushima S (1996) Is taurine a preventive nutritional factor of cardiovascular diseases or just a

biological marker of nutrition? Adv Exp Med Biol 403:623–629

Yamori Y, Liu L, Ikeda K, Miura A, Mizushima S, Miki T, Nara Y (2001) Distribution of twenty-four hour urinary taurine excretion and association with ischemic heart disease mortality in 24 populations of 16 countries: results from the WHO-CARDIAC study. Hypertens Res 24:453–457

Yokogoshi H, Mochizuki H, Nanami K, Hida Y, Miyachi F, Oda H (1999) Dietary taurine enhances cholesterol degradation and reduces serum and liver cholesterol concentrations in rats fed a high-cholesterol diet. J Nutr 129:1705–1712

Zhang M, Bi LF, Fang JH, Su XL, Da GL, Kuwamori T, Kagamimori S (2004) Beneficial effects of taurine on serum lipids in overweight or obese non-diabetic subjects. Amino Acids 26:267–271