S-1) Hypocholesterolemic Effect of Taurine in Hypercholesterolemic SHRSP Induced by the Feeding of a High-Fat and High-Cholesterol Diet. Hiroshi Ogawa, Tomoyo Nishikawa and Sukenari Sasagawa, Department of Hygiene, Kinki University School of Medicine, Osaka-fu 589.

Summary:

Taurine showed a strong hypocholesterolemic effect in hypercholesterolemic WKY and SHRSP induced by the feeding of a high-fat and high-cholesterol diet. The hypocholesterolemic effect, which was more remarkable in SHRSP than in WKY, was mainly due to suppression of the marked increase of cholesterol, apo B and apo E in the VLDL and IDL fractions, and to prevention of cholesterol accumulation in the liver. In addition, a recovery in the HDL fraction of SHRSP, associated with increases of cholesterol and apo A-I, was observed after taurine treatment, while, in the HDL fraction of WKY, the decreased apo E content was reduced further and no effective change was observed.

Introduction:

Taurine, a final metabolite of sulfur-containing amino acids, is well known to have an antihypertensive action and to show a hypocholesterolemic effect in experimentally induced hypercholesterolemic animals. In the previous paper (1), we reported the effect of taurine on serum lipoprotein metabolism in hypercholesterolemic SHRSP associated with hypothyroidism. In this study, in order to confirm this hypocholesterolemic effect of taurine and to get further information about the mechanism, we investigated changes in 1) concentrations and distributions of serum lipoproteins and apolipoproteins and 2) cholesterol content in the liver, following taurine administration in hypercholesterolemic SHRSP induced by the feeding of a high-fat and high-cholesterol diet (HFC diet).

Materials and methods:

Male SHRSP at ages of 16-17 weeks and age-matched male WKY were used and divided into three groups, respectively. Control group was fed a regular diet (CE-2, Clea Japan Inc.) and HFC group was fed a HFC diet, prepared as described previously (2), with free access to diet and tap water. Taurine group was fed a HFC diet and given 3% (W/V %) taurine as a drinking water. The experimental duration was 5 weeks. Blood pressure was measured by tail-pulse pickup method. Blood was collected from the jugular vein under light ether anesthesia after fasting overnight. Serum lipoprotein fractions (VLDL:d<1.006, IDL:d;1.006-1.020, LDL:d;1.020-1.063, HDL:d;1.063-1.210 and lipoprotein-free:d>1.210) were separated by stepwisely density-gradient ultracentrifugation. The lipids in the liver were extracted by the method of Folch et al. (3). Cholesterol content was enzymatically determined by commercially available kit (C-II test, Wako Chemicals). Concentrations of apolipoproteins (apo-) A-I, A-IV, B and E were measured by Laurell rocket electroimmunoassay as modified by us (4).

Results:

Effects of taurine on body weight, blood pressure (B.P.), serum concentrations of total cholesterol (T.C.) and apolipoproteins, apo B/apo A-I ratio, liver weight (liver W.) and liver cholesterol content (liver T.C.) in WKY (upper table) and SHRSP (lower table) were shown in Table.

Then, among serum lipoprotein fractions, the large increase of cholesterol, apo B and apo E in the VLDL and IDL fractions were markedly suppressed by taurine treatment in both strains. This effect was more remarkable in SHRSP than in WKY. In the LDL fraction, the increase of native LDL was also suppressed by taurine treatment in both strains. In the HDL fraction, the decreased content of apo E was reduced further and no effective change was observed in WKY, while a recovery in the decreased HDL fraction, due to increases of cholesterol and apo A-I, was observed in SHRSP, although the decreased apo E content remained unchanged. In lipoprotein-free fraction, the increase of apo A-IV was suppressed only in SHRSP.

Table Changes in Body Weight, Blood Pressure (B.P.), Serum Concentrations of Total Cholesterol (T.C.) and Apolipoproteins, Apo B/Apo A-I Ratio, Liver Weight (Liver W.) and Liver Cholesterol Content (Liver T.C.) in WKY and SHRSP¹

	Control diet + Tap water	HFC diet + Tap water	HFC diet + 3%-Taurine
WKY			
Body weight (g)	385 ± 11	390 ± 6	391 ± 6
B.P. (mmHg)	134 ± 4	130 ± 5	140 ± 6*
T.C. (mg/dl)	101 ± 3	169 ± 21 [#]	103 ± 3*
apo A-I (mg/dl)	55.8 ± 1.7	51.1 ± 0.6	51.9 ± 1.2
apo A-IV (mg/dl)	11.8 ± 1.0	13.6 ± 0.3 [#]	12.7 ± 0.6**
apo B (mg/dl)	7.0 ± 0.5	20.6 ± 1.4 ^{##}	14.5 ± 0.5*
apo E (mg/dl)	59.4 ± 3.0	42.2 ± 2.1 ^{##}	35.2 ± 1.0*
apo B/apo A-I	0.13 ± 0.07	0.40 ± 0.03 ^{##}	0.28 ± 0.01**
Liver W. (g/100g B.W.)	3.00 ± 0.05	4.42 ± 0.04 ^{##}	3.80 ± 0.04**
Liver T.C. (mg/wet g)	15.3 ± 0.5	155.9 ± 11.4 ^{##}	78.1 ± 6.7**
SHRSP			
Body weight (g)	310 ± 6	332 ± 10	336 ± 9
B.P. (mmHg)	230 ± 1	216 ± 6 [#]	213 ± 5
T.C. (mg/dl)	88 ± 3	243 ± 16 ^{##}	163 ± 20**
apo A-I (mg/dl)	48.3 ± 1.1	36.8 ± 2.0 ^{##}	42.6 ± 1.4*
apo A-IV (mg/dl)	9.5 ± 0.4	13.5 ± 0.3 ^{##}	12.2 ± 1.0**
apo B (mg/dl)	5.6 ± 0.1	24.0 ± 0.7 ^{##}	15.8 ± 0.5**
apo E (mg/dl)	31.6 ± 0.5	25.3 ± 1.4 ^{##}	16.6 ± 1.3**
apo B/apo A-I	0.12 ± 0.01	0.66 ± 0.02 ^{##}	0.37 ± 0.01**
Liver W. (g/100g B.W.)	3.50 ± 0.14	5.42 ± 0.12 ^{##}	4.59 ± 0.11**
Liver T.C. (mg/wet g)	14.9 ± 0.6	170.6 ± 6.5 ^{##}	41.3 ± 3.4**

! Values were expressed as Means ± S.E. (N=6 in each group)

Significant difference from control group (#:p<0.05, ##:p<0.01)

* Significant difference from HFC group (*:p<0.05, **:p<0.01)

#,* Statistical significance was determined by Student's t-test

Discussion:

The hypocholesterolemic effect of taurine in hypercholesterolemic WKY and SHRSP induced by the feeding of a HFC diet was mainly due to 1) suppression of the marked increase of cholesterol, apo B and apo E in the VLDL and IDL fractions, and 2) prevention of cholesterol accumulation in the liver. The results that this effect was more remarkable in SHRSP than in WKY could be partly explained by the fact that the endogeneous content of taurine in the liver is significantly low in SHRSP compared with WKY (5). Moreover, a recovery in the HDL fraction of SHRSP may be attributed to a recovery in apo A-I HDL.

In contrast, the decreased apo E content in the HDL fraction was not improved by taurine treatment in both strains, indicating a reduction of apo E HDL production. But, apo E HDL is considered to be an anti-atherogenic lipoprotein which may play an important role in reverse transport of cholesterol from peripheral tissues to the liver (6). This discrepancy between hypocholesterolemic effect and the decrease of apo E HDL is an important subject to be resolved in the future.

References:

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