Antiatherogenic effect of taurine in high fat diet fed rats

S Sethupathy*, C Elanchezhiyan, K Vasudevan & G Rajagopal
Division of Biochemistry, Rajah Muthiah Medical College, Annamalai University, Annamalai Nagar 608 002, India

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The role of taurine on atherogenesis induced by high fat diet in rats, a species which depends entirely on taurine for conjugation of bile acids has been investigated. Wistar male rats were fed on (po) taurine in addition to high fat diet (11% coconut oil w/w) for 6 months. High fat diet caused significant increase of serum total cholesterol (2 fold), serum triglycerides (92.6%), LDL cholesterol (92.3%) and body weight gain (2.8 fold). Taurine administration significantly reduced serum cholesterol (37%), triglycerides (94.5%), LDL cholesterol (34%), body weight (46%). It also significantly reduced aortic cholesterol and thiobarbituric acid reactive substances and there was a significant increase of reduced glutathione. Taurine significantly increased fecal bile acids which may have resulted in significant decrease of serum cholesterol. Aortic lesion index was significantly decreased in the taurine administered group suggesting the antiatherogenic effect of taurine. It is concluded that taurine attenuated the atherogenesis possibly by its hypocholesterolemic and antioxidant property.

Materials and Methods

Wistar male rats of 19±1 weeks age, weighing 225-250 g were obtained from the Department of Experimental Medicine of the College. They were housed in polypropylene cages, 3 per cage and kept at 25±2°C with 12:12 hr light and dark cycle. The animals were maintained on standard chow diet and water ad libitum. They were grouped into following 4 groups of 8 animals each; Group 1 (control) standard chow diet; Group 2 (chow diet plus taurine); Group 3 (high fat diet) Group 4 (high fat diet and plus taurine).

The composition of various diet was as follows:
- Control diet: Wheat flour 22.5%, roasted bengal gram powder 60%, skimmed milk powder 5%, casein 4%; refined oil 4%; salt mixture with starch 4% and vitamin and choline mixture 0.5%. (3700 C/kg of diet).
- High fat diet: Wheat flour 20.5 roasted bengal gram powder 51%, skimmed milk powder 5%, casein 4%, refined oil 4%; coconut oil 11%. Salt mixture with starch 4%, vitamin and choline mixture 0.5% (4000 C/kg of diet).

Rats of Group 2 and Group 4 were on oral administration of taurine (0.5 ml of 2% w/v in water) once daily at the dose 50 mg/kg body weight/day in addition to their respective diets.

At the end of fourth month, all the animals were sacrificed by cervical decapitation after overnight fasting. Animals were given enough care as per the animal ethical committee's recommendations.

Serum total cholesterol, triglycerides, HDL cholesterol, LDL cholesterol, phospholipids were estimated using Boehringer Mannheim kits by Erba Smart Lab analyzer, U.S.A. A portion of aortic tissue was blotted, weighed and homogenized with methanol (3 volumes) and lipid extract was obtained by the method of Folch et al. and the lipid extract was used for estimation of total cholesterol, triglycerides, phospholipids. Ester cholesterol10 and free cholesterol were analyzed using digitonin. Thiobarbituric acid reactive substances (TBARS) in plasma, aortic TBARS12, fecal bile acids, and reduced glutathione (GSH)14.
were estimated. Aortic tissue, plasma and urinary taurine concentrations were analyzed by High Performance Liquid Chromatography. Aortic lesion index was calculated by the method of Newman and Zilversmit.

Statistical analysis — One way anova test was applied in order to evaluate any significant difference in the mean values. All values used in analysis represent the mean±SE of 8 rats in each group. If anova results were significant, Scheffe’s multiple comparison test was applied in order to find out which of the groups was statistically significant at 0.05 level.

Results and Discussion

Results are presented in Tables 1 and 2 and Fig. 1.

The weight gain in high fat diet groups was significantly higher than in control reflecting the influence of high fat diet. But Group 4 showed lesser weight gain even though there was no significant difference in food intake between Group 3 and Group 4 (18.6±1.1 Vs 17.6±0.9 g/day). Oil red O staining of aorta showed extensive lesion in Group 3 and marked reduction of lipid accumulation in Group 4. There were no lesions in the aorta of group 1 and 2 (Fig. 1). Aortic lesion index of Group 3 was significantly higher than Group 4 (16.5±0.53 vs 9.35±0.36, P value < 0.001).

Taurine supplementation significantly reduced serum triglycerides and cholesterol. The significant increase of bile acid excretion by taurine suggests that the effect of taurine was at least in part due to an increase in cholesterol catabolism to bile acids. Previous studies indicate that taurine enhances 7α-hydroxylase enzyme activity, the key enzyme in bile acid synthesis leading to enhanced bile acid synthesis and its excretion. At least a part of excess dietary fat would have been directed towards the formation of bile acids by taurine and this may have caused decrease in serum cholesterol and triglycerides. Therefore in the aorta also there was a significant decrease of cholesterol content. Elevated TBARS and significant decrease of GSH in high fat diet group suggests the enhanced oxidative stress in hyperlipidemic state as reported by the earlier studies. LDL modified by lipid peroxidation by products such as malondialdehyde and 4 hydroxy nonenal are more atherogenic and it has been shown that probucol, an antioxidant decreased the rate of atherogenesis in Watanabe rabbits. Reduction of aortic TBARS and increase in GSH shows that taurine would have acted as antioxi-

<p>| Table 1 — Effect of taurine on body weight changes and lipid profile in rats [Values are mean±SE] |</p>
<table>
<thead>
<tr>
<th>Group</th>
<th>Body weight changes (g)</th>
<th>Serum TGL</th>
<th>Serum HDL-C</th>
<th>Serum LDL-C</th>
<th>Aorta TGL</th>
<th>Aorta HDL-C</th>
<th>Aorta LDL-C</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>15.5±0.22</td>
<td>71.2±2.4</td>
<td>242.4±9.1</td>
<td>51.5±2.7</td>
<td>119.4±4.9</td>
<td>25.1±1.2</td>
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</tr>
<tr>
<td>2</td>
<td>13.7±0.34</td>
<td>66.3±2.90</td>
<td>226.1±10.64</td>
<td>46.8±2.11</td>
<td>107.1±5.89</td>
<td>13.3±0.85</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>43.8±0.69</td>
<td>170.4±1.8</td>
<td>332.2±14.1</td>
<td>108.5±0.39</td>
<td>277.6±6.5</td>
<td>12.4±0.48</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>23.1±0.28</td>
<td>94.7±5.6</td>
<td>292.4±8.34</td>
<td>63.5±2.4</td>
<td>200.5±8.1</td>
<td>12.8±0.3</td>
<td></td>
</tr>
</tbody>
</table>

N.S. Not Significant

Aorta = mg/100 g fresh tissue

P values: * < 0.05 (compared to control); ** < 0.01 (compared to group 3).
Fig. 1—Oil red O staining of aorta. (a) Control (Group 1); (b) Taurine only (Group 2); (c) High fat diet (Group 3); (d) High fat diet + taurine (Group 4). Lipid accumulation indicated by arrow marks × 200

Table 2—Effect of taurine on TBARS, GSH levels and fecal bile acids
(Values are mean ± SE)

<table>
<thead>
<tr>
<th>Groups</th>
<th>Plasma TBARS (nmol/ml)</th>
<th>Aortic TBARS (nmol/mg protein)</th>
<th>Aortic tissue GSH (μmol/100 g fresh tissue)</th>
<th>Plasma taurine (nmol/ml)</th>
<th>Aortic tissue taurine (nmol/mg protein)</th>
<th>Urinary taurine (μmol/mg creatinine)</th>
<th>Total fecal bile acids (mg/rat/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.41 ± 0.14</td>
<td>0.53 ± 0.04</td>
<td>0.86 ± 0.03</td>
<td>82.1 ± 2.4</td>
<td>29.1 ± 3.3</td>
<td>0.38 ± 0.02</td>
<td>12.80 ± 0.26</td>
</tr>
<tr>
<td>2</td>
<td>1.34 ± 0.15&lt;sup&gt;N.S&lt;/sup&gt;</td>
<td>0.49 ± 0.05&lt;sup&gt;NS&lt;/sup&gt;</td>
<td>0.90 ± 0.04&lt;sup&gt;N.S&lt;/sup&gt;</td>
<td>85.4 ± 2.6&lt;sup&gt;N.S&lt;/sup&gt;</td>
<td>37.7 ± 3.9&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.51 ± 0.03&lt;sup&gt;b&lt;/sup&gt;</td>
<td>15.74 ± 0.21&lt;sup&gt;N.S&lt;/sup&gt;</td>
</tr>
<tr>
<td>3</td>
<td>2.4 ± 0.18&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.80 ± 0.06&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.72 ± 0.20&lt;sup&gt;b&lt;/sup&gt;</td>
<td>76.5 ± 2.9&lt;sup:NS&lt;/sup&gt;</td>
<td>41.8 ± 4.3&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.37 ± 0.03&lt;sup&gt;NS&lt;/sup&gt;</td>
<td>23.92 ± 0.36&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>4</td>
<td>1.6 ± 0.15&lt;sup&gt;d&lt;/sup&gt;</td>
<td>0.65 ± 0.06&lt;sup&gt;d&lt;/sup&gt;</td>
<td>0.98±0.05&lt;sup&gt;c&lt;/sup&gt;</td>
<td>86.2 ± 3.7&lt;sup&gt;NS&lt;/sup&gt;</td>
<td>51.4 ± 4.8&lt;sup&gt;d&lt;/sup&gt;</td>
<td>0.40 ± 0.02&lt;sup&gt;NS&lt;/sup&gt;</td>
<td>46.32 ± 0.63&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

N.S. Not Significant
P values: <sup>a</sup><i>P</i> < 0.01 (compared to control); <sup>b</sup><i>P</i> < 0.05 (compared to control); <sup>c</sup><i>P</i> < 0.01 (compared to group 3); <sup>d</sup><i>P</i> < 0.05 (compared to group 3)
vant. Increase of GSH can be due to either enhanced GSH synthesis and/or diminished GSH utilization. Taurine being an antioxidant would have caused diminished consumption of GSH and the mechanism of this effect is to be explored. Another possibility is that taurine might increase the activity of GSH reductase and this needs to be verified. It is concluded that taurine abates atherogenesis possibly due to it’s hypocholesterolemic and antioxidant property.

References