Rapid Communication

Morphological Changes of the Aorta in Monosodium Glutamate-induced Obese Rats*


Introduction

The administration of monosodium-L-glutamate (MSG) to mice in the neonatal period induces destructive lesions in the arcuata and ventromedial nuclei of the hypothalamus and results in a syndrome of obesity, stunting, hypogonadism and hypopituitarism1). With regard to the autonomic nervous system, MSG rats are thought to be comparable to spontaneously hypertensive rats (SHR), because the sympathetic nervous system of MSG-treated rats is presumed to be suppressed2). This model has been used in endocrinological, neurochemical, behavioral, and lipid metabolical research. Little is known, however, about the morphological changes of the arteries in this model.

The purpose of this study is to evaluate morphological changes of the aorta of MSG rats by morphometrical analysis.

Materials and Methods

Wistar rats were injected subcutaneously with MSG at a dosage of 3 mg/g body weight for 6 days following birth. Thirty-seven male MSG rats were used in this study. Thirty-one controls were randomly selected from male Wistar rats of identical ages. Blood pressure was measured by an indirect tail-cuff method. The Lee-index was calculated as \(3 \sqrt{\text{body weight (g)/nasal-anal length (cm)}}\). The animals were killed at the ages of 6, 11, 22, and 56 weeks by decapitation. For morphological studies, the descending thoracic aorta was excised and cross-sectioned into five consecutive segments each for light and electron microscopy. The segments which contained branching sites were avoided for morphometrical analysis. The values used in this study were the averages of up to five segments in each animal. Histological sections, 3 μm thick, were stained with elastica van Gieson’s, hematoxylin-eosin, and Azan-Mallory’s. The wall thickness, outer diameter, cross sectional area, and media/radius ratio were analyzed morphometrically by using Leitz AMS Image Analysis System. Total length of the internal and the external elastic membranes were traced and then each element could be calculated for a hypothetical state, where the internal elastic membrane was perfectly circular. For electron microscopic examination, aortas from 56-week-old rats were used in this study. Up to 5 epoxy resin blocks for each animal were cut and observed in order to determine the incidence of intimal thickening and the volume percent of extracellular matrix in the media including ground substance, collagen and elastin. The incidence of intimal thickening was estimated from thick sectionings with toluidine blue staining. The volume percent of medial extracellular matrix was calculated as the summation of extracellular matrix area/total area of scanned media by using the same image analyser. About seven micrograph for each EM block were taken.

* This paper was presented at the winter meeting of Japan Atherosclerosis Society in February 1987

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Received: April 14, 1987
Accepted: May 29, 1987
Table 1

<table>
<thead>
<tr>
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<th>6 w</th>
<th>11 w</th>
<th>22 w</th>
<th>56 w</th>
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<tbody>
<tr>
<td>Wistar (n)</td>
<td>10</td>
<td></td>
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<td></td>
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<tr>
<td>wall thickness (μm)</td>
<td>85.7 ± 9.5</td>
<td>82.3 ± 6.9</td>
<td>98.7 ± 4.8</td>
<td>105.0 ± 8.1</td>
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<td>outer diameter (μm)</td>
<td>1,579 ± 93</td>
<td>1,724 ± 86</td>
<td>1,935 ± 87</td>
<td>2,002 ± 72</td>
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<tr>
<td>X-sectional area (mm²)</td>
<td>1.56 ± 0.18</td>
<td>1.91 ± 0.22</td>
<td>2.41 ± 0.22</td>
<td>2.52 ± 0.19</td>
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<tr>
<td>media/radius ratio (10⁻²)</td>
<td>10.7 ± 0.8</td>
<td>9.6 ± 1.0</td>
<td>10.1 ± 0.6</td>
<td>10.5 ± 0.8</td>
</tr>
<tr>
<td>MSG (n)</td>
<td>10</td>
<td>6</td>
<td>10</td>
<td>11</td>
</tr>
<tr>
<td>wall thickness (μm)</td>
<td>74.0 ± 7.3**</td>
<td>74.0 ± 6.8**</td>
<td>92.2 ± 6.1**</td>
<td>94.8 ± 9.0**</td>
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<tr>
<td>outer diameter (μm)</td>
<td>1,390 ± 90**</td>
<td>1,599 ± 114**</td>
<td>1,681 ± 90**</td>
<td>1,888 ± 169*</td>
</tr>
<tr>
<td>X-sectional area (mm²)</td>
<td>1.21 ± 0.15**</td>
<td>1.65 ± 0.24**</td>
<td>1.78 ± 0.20**</td>
<td>2.26 ± 0.41**</td>
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<tr>
<td>media/radius ratio (10⁻²)</td>
<td>10.8 ± 0.9</td>
<td>9.5 ± 0.6</td>
<td>10.8 ± 0.7**</td>
<td>10.0 ± 1.1</td>
</tr>
</tbody>
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Data: mean ± SD, *p < 0.01, **p < 0.001

Results

Growth and Blood Pressure:

The MSG rats exhibited obesity and shorter body length from the age of 6 weeks old. On laparotomy, intraabdominal fat was more conspicuous in MSG rats compared to Wistar rats.

Blood pressure in the MSG rats was negatively correlated to the Lee-index (r = -0.68, p < 0.02), indicating that typical obese MSG rats have a much lower blood pressure. From the age of 6 weeks old, MSG rats showed an average 11 to 26 mmHg lower systolic blood pressure than Wistar rats throughout life.

Light Microscopy:

The results of light microscopic morphometrical analysis are shown in Table 1. The values of wall thickness, outer diameter, and cross-sectional area were significantly smaller in MSG rats than in Wistar rats at all ages. The media/radius ratio showed no specific tendency.

Electron Microscopy:

Edematous intimal thickening was often encountered in 56-week-old Wistar rats, while MSG rats displayed almost intact intima. The edematous intimal lesion, regarded as a normal aging process, was composed of amorphous and granular ground substance, collagen, and elastic fibers. The incidence of intimal thickening is listed in Table 2. Wistar rats showed higher incidence of intimal thickening than MSG rats, but statistically there was no significant difference between them. The volume percent of extracellular matrix is shown in Table 3. Stereological analysis was performed on a total of 343 electron micrographs. Wistar rats had a significantly higher value than MSG rats.

Discussion

It is generally accepted that obesity is one of the risk factors for atherosclerosis. However, morphological evidence concerning the relationship between obesity and atherosclerosis has been rarely reported. Previous reports described a negative correlation between obesity and atherosclerosis. Warnes et al. examined extremely obese patients who died prematurely, and concluded that they did not have more coronary atherosclerosis than might be expected at their ages. Divitiis et al. studied the changes of cardiac function in 10 relatively young volunteers who had varying degrees of obesity and were free from pathologic conditions such as arterial hypertension, diabetes, and respiratory disease. They indicated that systemic vascular resistance was normal to low and correlated negatively with body weight. A hemodynamic study showed that simple obesity without hypertension conducts reduction of vascular resistance. The present study revealed that MSG rats...
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have a less atherosclerotic aorta, which is consistent with previously described studies.

Elevated blood pressure and frequent aortic intimal lesions are features of the aging process in SHR9). It is well known that the activity of the sympathetic nervous system in SHR is increased10). On the contrary, MSG rats showed lowered blood pressure and less frequent intimal thickening of the aorta. In this model the sympathetic nervous system activity is presumed to be decreased. Yoshi-
da et al.5) demonstrated a low norepinephrine turnover in interscapular brown adipose tissue of MSG-treated mice. Kabuto, one of our co-authors, noticed a low concentration of urine catecholamine in MSG rats (unpublished data), indicating a decrease in sympathetic nerve activity in these rats.

There are two possible interpretations for the low occupancy rate of extracellular matrix in the media of 56-week-old MSG rats. One is a low activity of protein synthesis in the medial smooth muscle cells and the other is a retardation of the aging process in this model.

Acknowledgement

The authors thank Mr. B. Burke-Gaffny for his editorial assistance, and Miss K. Nagaishi for her skillful typing.

References

2) Yoshida, T., Nishioka, H., Nakamura, Y., Kana-

Summary

The purpose of this study is to evaluate the morphological changes of the aorta in monosodium-1-glutamate (MSG)-treated rats by light and electron microscopy. Thirty seven male MSG rats and thirty one male Wistar rats were used. The animals were sacrificed at the ages of 6, 11, 22, and 56 weeks. The blood pressure of the MSG rats was negatively correlated to the Lee index, and they showed an average 11 to 26 mmHg lower systolic blood pressure than the Wistar rats. Wall thickness, outer diameter, and cross-sectional area were significantly smaller in MSG rats than in Wistar rats at all ages. However, there was no specific trend in media/radius ratio. The incidence of edematous intimal thickening and the volume percent of medial extracellular matrix were much lower in MSG rats. It is concluded that MSG obese rats have lower blood pressure and less atherosclerotic aorta than Wistar rats.

Key words: Monosodium glutamate, Obesity, Aorta, Rat.