Effects of Jiangtang Fanglong Wan on hearing in an animal model of diabetes

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Abstract

Objective To study effects of Jiangtang Fanglong Wan (glucose-lowering and deafness-preventing capsule) on hearing in an animal model of diabetes.

Methods Wistar rats were used to create a diabetes model by intraperitoneal injection of streptozotocin (STZ, 55 mg/kg). Forty rats were randomly selected to receive Jiangtang Fanglong Wan (10 g/kg/day) through intragastric gavage (treatment group) or normal saline (control group). Auditory brainstem responses (ABRs) were recorded at Months 1, 2 and 3. Results ABR latencies and wave intervals were similar between the two groups at Month 1 (P > 0.05). ABR latencies and wave intervals were shorter in the treatment group than those of the control group at Months 2 and 3 (P < 0.05 and P < 0.01, respectively). Conclusion Our results suggest that Jiangtang Fanglong Wan may have a beneficial effect in preventing and treating hearing impairment associated with diabetes.

Keyword deafness; diabetic; Jiangtang Fanglong capsule; Wistar rats

Introduction

Diabetes may lead to sensorineural deafness, through mechanisms that are yet to be defined. In our practice, Jiangtang Fanglong Wan has been used in patient with diabetes and hearing loss, with some benefits. The current study is aimed at understanding its effects in an animal model of streptozotocin (STZ) induced diabetes.

Materials and methods

Animals Healthy adult male Wister rats (200–250g, n=40) with no noise exposure history were provided by the Experiment Animal Center, Hebei Medical Uoniversity.

Drugs Major ingredients of the Jiangtang Fanglong Wan (developed by the authors) were root kudzu vine, red sage root, rhizome of sichuan lovage, fox glove, Chinese wam, indianbread, alismatis rhizome, dogwood fruit, magnetite, etc. The ingredients were purchased from Le Ren Tang, Shijiazhuang, Hebei, China, and are certified as geo-authentic Chinese medicinal materials.

Animal model

The diabetic animal model was replicated as reported by Wang Shi-Li, et al. The rats were fasted 12 hours and given intraperitoneal injection of streptozotocin (Sigma) diluted in 0.1 mg/L natrium citricum buffer (pH 4.2) at 55 mg/kg. The levels of blood glucose and urine glucose were measured after one week of streptozotocin treatment. Blood glucose >14.2 mmols/L and urine glucose > (+++) represented successful diabetes modeling. After two months of streptozotocin treatment, auditory brainstem response (ABR) recording was conducted in all rats. Elevated ABR thresholds (≥ 40 dB nHL) were considered representing diabetes-related hearing loss and an indication of appropriate time for drug testing.

ABR tests were conducted at Months 1, 2 and 3 following Jiangtang Fanglong Wan treatment.

ABR testing

Rats were anesthetized with intraperitoneal pentobarbital sodium (45 mg/kg) before testing. A Traveler Express E ABR device was used for ABR recording. Recording electrode was placed at the vertex (center point between the two pinna), reference electrode was placed at the ipsilateral pinna, and ground electrode was placed at the contralateral pinna. Sound stimulation was delivered through a TDH–39P head phone placed at 2 cm from the external auditory meatus at 60 dB nHL. The bandpass filter was set at 100–3000 Hz. Testing was performed in a sound-proof room. ABR threshold (wave
Results
ABR latencies and interwave intervals were not significantly different between the two groups after the first month, but were noticeably shorter for the treatment group than those for the control group \((P < 0.05)\) after the second month. After the third month, latencies and inter-wave intervals of all waves in the treatment group were further shorter than those of the control group \((P < 0.01)\), although the increments between the first, second and third months was not statistically significant (Table 1).

Discussion
Auditory damage associated with diabetes has been reported in China and abroad. 3, 4 Modern medicine theorizes that the mechanism of deafness in diabetes is due to vascular lesions, particularly those involving small vessels, such as those in the cochlear stria vascularis, basilar membrane, modiolus, spiral ligament, endolymphatic sac and acoustic nerve. Artery lumen endothelial proliferation (endotheliosis), lipidosis and decreased lumen size are most frequently seen. Blood vessel wall thickening and lumen stenosis affect local blood supply, and local microcirculatory obstruction and chronic hypoxia lead to acoustic hypoesthesia. Currently the exact pathogenesis has not been fully clarified. From the holism in traditional Chinese medicine, all diseases are manifestation of a systemic disorder involving certain tissues and organs. The traditional Chinese medicine theories claim that the “kidney” works with the ear. On the principle of adopting modern medicine technologies as the “means” under the guidance of traditional Chinese medicine fundamentals as the “core” to deepen the understanding of a particular disease, 5 we decided to study effects of Jiangtang Fanglong Wan on diabetes-associated hearing impairment in an animal model.

STZ induces the diabetes mellitus by selectively damaging pancreatic islet B cells. This animal model has been used to study mechanisms by which diabetes mellitus causes damage to important parenchymatous viscera, such as heart, brain and kidney. Successful modeling rates of 94% or 95% have been reported when STZ is given at 55 mg/kg or 60 mg/kg for two months with acoustic hypoesthesia in all rats, but the mortality rate is extremely high in rats receiving STZ at 60 mg/kg. So we decided to give STZ at 55 mg/kg via intraperitoneal injection in our modeling.

Jiangtang Fanglong capsule was made up of root kudzu vine, red sage root, rhizome of sichuan lovage, fox glove, chinese wam, indiangrass, alismatis rhizome, dogwood fruit, magnetite, etc. In Chinese medicine theories, rhizome of sichuan lovage runs through the twelve “Regular Meridians”, red sage root promotes blood circulation to dispel “blood stasis”, root kudzu vine raises the lucid “Yang” and guides medicine, fox glove gently enriches the blood and nourishes the kidney while replenishing the essence, Chinese wam invigorates the spleen and stomach and helps digestion, indiangrass damps the spleen, alismatis rhizome

<table>
<thead>
<tr>
<th>Group</th>
<th>Time (month)</th>
<th>Latency (ms)</th>
<th>Inter-wave interval (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Wave I</td>
<td>Wave II</td>
</tr>
<tr>
<td>Control</td>
<td>1</td>
<td>1.13 ± 0.08</td>
<td>2.53 ± 0.10</td>
</tr>
<tr>
<td>((n=20))</td>
<td>2</td>
<td>1.23 ± 0.13</td>
<td>2.62 ± 0.15</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>1.27 ± 0.28</td>
<td>2.82 ± 0.21</td>
</tr>
<tr>
<td>Treatment</td>
<td>1</td>
<td>1.15 ± 0.09</td>
<td>2.54 ± 0.11</td>
</tr>
<tr>
<td>((n=20))</td>
<td>2</td>
<td>1.12 ± 0.12*</td>
<td>2.53 ± 0.14</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>1.13 ± 0.19*</td>
<td>2.57 ± 0.17*</td>
</tr>
</tbody>
</table>

Note: *\(P < 0.05\), compared with the control group; # \(P < 0.01\)
promoting kidney clearance dogwood fruit nourishes the liver and kidney, and heavy magnetite (Main ingredient: FeO4) can replenish kidney Yin deficiency. Jiangtang Fanglong Wan therefore may play an important role of invigorating the kidney Yin and promoting blood circulation by removing blood stasis. We have seen that diabetic patients with deafness show various degrees of kidney–deficiency symptoms, who benefit from tonifying kidney and activating blood circulation. 6-8 ABRs are used routinely as a measure of hearing. Using electronic and computer technologies, ABR testing records responses to sound stimulation from various structures of the auditory system. In this study, Jiangtang Fanglong Wan helped maintain ABR threshold, wave latencies and intervals, indicating its potential in reducing auditory damage in this rat animal model of STZ induced diabetes and deafness. The results provide us with a novel idea and method to use traditional Chinese medicine to prevent and treat deafness associated with diabetes mellitus.

References


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