Effect of hyperbaric oxygen combined with \(\alpha\)-lipoic acid on neurological function and serum indexes of patients with diabetic peripheral neuropathy

Yu Li\(^1\)*, Ling Qi\(^2\), Jun Li\(^3\)

\(\dagger\)Department of Endocrinology, the Sixth Affiliated Hospital of Xinjiang Medical University, Urumqi, Xinjiang, 830002, China

\(\ddagger\)Hyperbaric Oxygen Therapy Room, the Sixth Affiliated Hospital of Xinjiang Medical University, Urumqi, Xinjiang, 830002, China

\(\|^\)Department of Endocrinology, the First Affiliated Hospital of the Medical College, Shihezi University, Shihezi, Xinjiang, 832008, China

\*Corresponding author: Yu Li, Department of Endocrinology, the Sixth Affiliated Hospital of Xinjiang Medical University, No. 39, Wuxing South Road, Urumqi, Xinjiang, 830002, China.

Foundation project: Technology Xinjiang Project of the Corps (No: 2014AB049).

Tel: 2652985; 18999253257

ARTICLE INFO

Article history:
Received
Received in revised form
Accepted
Available online

Keywords:
Diabetic peripheral neuropathy
Hyperbaric oxygen
\(\alpha\)-lipoic acid
Neurological function

ABSTRACT

Objective: To analyze the effect of hyperbaric oxygen combined with \(\alpha\)-lipoic acid on neurological function and serum indexes of patients with diabetic peripheral neuropathy.

Methods: A total of 118 diabetic peripheral neuropathy patients who received treatment in our hospital were selected as research subjects, and according to the different clinical treatment they received, all included patients were divided into observation group 59 cases and control group 59 cases. Control group received conventional clinical treatment, and observation group received additional hyperbaric oxygen combined with \(\alpha\)-lipoic acid treatment. Differences in nerve conduction velocity, gastrocnemius nerve threshold, illness-related factors, oxidative stress indicator values, and so on were compared between two groups after treatment.

Results: MCV and SCV values of median nerve, ulnar nerve and tibial nerve of observation group after treatment were higher than those of control group \((P<0.05)\); gastrocnemius nerve threshold of observation group after treatment were significantly lower than those of control group \((P<0.05)\); serum CP and BDNF values of observation group after treatment were higher than those of control group while Cys-C, SDF-1 \(\alpha\), HMGB1 and MBP values were lower than those of control group \((P<0.05)\); serum MDA and NO values of observation group after treatment were lower than those of control group while SOD, CAT and GSH-Px values were higher than those of control group \((P<0.05)\).

Conclusions: Hyperbaric oxygen combined with \(\alpha\)-lipoic acid is a good method to optimize the neurological function and improve overall illness of patients with diabetic peripheral neuropathy, and is expected to become a new way of inhibiting disease progression and improving disease outcome.

1. Introduction

Diabetic peripheral neuropathy (DPN) is one of the most common complications of diabetes, which can lead to the limb dysfunction and lower quality of life. Current main treatment for DPN patients include decreasing blood sugar, reducing blood fat, controlling blood pressure, etc., but the effective treatment on recovering peripheral nerve function is little, and it has become a difficulty of clinical therapy\(^{[1,2]}\). \(\alpha\)-lipoic acid is a potent antioxidant with anti-inflammatory effect; hyperbaric oxygen has been recognized to have positive effect on the treatment of DPN, which can increase the oxygen supply and blood supply for peripheral nerve and promote the repair of damaged myelin and regeneration of neurons. In the research, the effect of hyperbaric oxygen combined with \(\alpha\)-lipoic acid on neurological function and serum indexes of patients with diabetic peripheral neuropathy was mainly analyzed, hereby reported as follows.
2. Materials and methods

2.1. Case information

A total of 118 DPN patients who received treatment in our hospital were selected as research subjects, and the time range of treatment was from May 2013 to June 2015. All patients met the diagnostic criteria for DPN established by WHO, and patients as well as their families learned about the research process and then signed informed consent forms.

According to the different clinical treatment they received, all included patients were divided into observation group 59 cases and control group 59 cases. Control group included 31 male cases and 28 female cases. They were 43-72 years old, with average age as (59.27±8.65) years. The course of diabetes was 5-11 years, with average as (7.92±1.05) years. BMI was (21-26) kg/m$^2$ and the average was (23.45±2.28) kg/m$^2$. Observation group included 32 male cases and 27 female cases. They were 41-70 years old, the average was (58.56±8.73) years. The course of diabetes was 4-12 years, the average was (7.85±1.17) years. BMI was (21-26) kg/m$^2$ and the average was (23.18±2.57) kg/m$^2$. Observation group included 32 male cases and 27 female cases. They were 41-70 years old, the average was (58.56±8.73) years. The course of diabetes was 4-12 years, the average was (7.85±1.17) years. BMI was (21-26) kg/m$^2$ and the average was (23.18±2.57) kg/m$^2$. Differences in gender, age, course of disease, body mass index and other baseline information were not significant between groups ($P>0.05$).

2.2. Clinical treatment plans

Control group received conventional clinical treatment for diabetic peripheral neuropathy, conventionally controlling blood glucose, blood fat and blood pressure, and improving blood circulation. Blood glucose was controlled in the level no more than 7.0 mmol/L, 2-hour postprandial blood glucose no more than 10.0 mmol/L, and blood fat as well as blood pressure levels being normal or close to normal.

Observation group received hyperbaric oxygen combined with α-lipoic acid treatment, which was as follows: GY3200 type hyperbaric oxygen chamber was used for patient’s treatment, pressure was elevated for 20 min at a constant speed to make chamber pressure rise to 0.22 MPa, patients wore mask to inhale pure oxygen for 60 min after the pressure was steady, stopped it for 10min to breathe in air in the chamber, chamber pressure was decompressed for 15 min at a constant speed to atmospheric pressure, and then patients got out of the chamber. Hyperbaric oxygen therapy was conducted 1 times a day, 10 days was for a course of treatment, interval between the two courses was 3-5 days, and a total of three courses were conducted. α-lipoic acid 0.45 g was diluted with 250 mL saline, wrapped with aluminum foil to avoid light, and intravenously dripped for 30 min with lightproof infusion set, 10 days was for a course of treatment, interval between two courses was 3-4 days, and a total of 3 courses were conducted. The rest of the treatment was the same as that of control group.

2.3. Nerve conduction velocity detection

Electromyography was used to test motor conduction velocity (MCV) and sensory nerve conduction velocity (SCV) in median nerve, ulnar nerve and tibial nerve. Test environment temperature was controlled at about 25.0 °C, the indexes were tested by the same name experienced inspector for 3 times and then the average was calculated.

2.4. Gastrocnemius nerve threshold detection

Motor nerve threshold: stimulation intensity was gradually increased to maximum stimulation intensity, then 30% electricity flow was increased, the stimulation point and intensity were kept unchanged after the biggest M wave was induced, stimulation intensity was gradually decreased to 500 μV/gain, and there was still no derivation of waveform. Current stimulation intensity at the minimum waveform was recorded.

Sensory nerve threshold: 18.3 mA and 0.1 ms wave width current was used to stimulate gastrocnemius and induce clear waveform, then the stimulation intensity was gradually decreased until there was still no waveform after stack after 20 times, and the current stimulation intensity was recorded when the minimum wave was induced.

2.5. Serum-related indexes

A total of 2 mL fasting peripheral venous blood was drawn from patients after treatment, let stand for 30 min at room temperature and then centrifuged to collect supernatant and preserved it in -20 °C refrigerator for use.

Enzyme-linked immunosorbent assay was used to detect C peptide (CP), cystatin C (Cys-C), stromal cell-derived factor-1ɑ (SDF-1ɑ), brain-derived neurotrophic factor (BDNF), high mobility group box B1 (HMGB1) and myelin basic protein (MBP).

Barbituric acid method was used to detect malondialdehyde (MDA), xanthine oxidase was used to detect superoxide dismutase (SOD), ammonium molybdate colorimetry was used to detect catalase (CAT), DTNB was used to detect glutathione peroxidase (GSH-Px) and chemiluminescence method was used to detect nitric oxide (NO).

2.6. Statistical methods

Data obtained in the research was analyzed by SPSS23.0 software, measurement data was in terms of mean±sd. Comparison between two groups was performed by t test, and $P<0.05$ was set as the standard of statistical significant differences.

3. Results

3.1. Nerve conduction velocity

The most intuitive performance in diabetic peripheral neuropathy patients is motor and sensory ability change of extremities and the change degree is highly consistent with the degree of neuropathy. Detection of peripheral neuropathy degree in included patients by electromyography showed that MCV and SCV values of median nerve, ulnar nerve and tibial nerve of observation group after treatment were higher than those of control group ($P<0.05$), shown in Table 1.

3.2. Gastrocnemius nerve threshold

Left gastrocnemius nerve threshold of observation group after treatment was (11.28±1.54) mA, and right gastrocnemius
nerve threshold was (11.56±1.41) mA; left gastrocnemius nerve threshold of control group after treatment was (13.17±1.43) mA, and right gastrocnemius nerve threshold was (13.42±1.38) mA. Gastrocnemius nerve threshold of observation group after treatment were significantly lower than those of control group (>0.05).

3.3. Serum illness-related factors

Results showed that serum CP and BDNF values of observation group after treatment were higher than those of control group while Cys-C, SDF-1α, HMGB1 and MBP values were lower than those of control group (>0.05), shown in Table 2.

3.4. Oxidative stress indicators

Detection of serum oxidative stress indicators by different methods showed that serum MDA and NO values of observation group after treatment were lower than those of control group while SOD, CAT and GSH-Px values were higher than those of control group (>0.05), shown in Table 3.

4. Discussion

DPN is the most common clinical diabetic chronic complication, and severe cases may lead to loss of limb function and significantly reduced quality of life in patients. The current treatment for DPN mostly focuses on the positive intervention of blood glucose, blood fat and blood pressure, and targeted therapy for peripheral neuropathy is needed, which is the root cause of the poor outcome of DPN patients[3-4]. α-lipoic acid is a powerful antioxidant that can increase blood flow in nerve-nutritional vessels, and play the role of repairing myelin, improving nerve conduction velocity and so on. Hyperbaric oxygen (HBO) is currently recognized method that can be used for the treatment of DPN, physical dissolved oxygen in the blood under HBO is more than a dozen times higher than oxygen inhalation at atmospheric pressure, does not require oxygen in the blood under HBO is more than a dozen times higher than oxygen inhalation at atmospheric pressure, does not require oxygen inhalation at atmospheric pressure, does not require

### Table 1

<table>
<thead>
<tr>
<th>Groups</th>
<th>Median nerve</th>
<th>MCV</th>
<th>Tibial nerve</th>
<th>SCV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>47.98±3.62</td>
<td>46.58±4.25</td>
<td>42.16±3.77</td>
<td>44.57±3.96</td>
</tr>
<tr>
<td>Control</td>
<td>42.01±3.99</td>
<td>41.19±4.03</td>
<td>38.24±3.58</td>
<td>40.19±4.32</td>
</tr>
<tr>
<td>t</td>
<td>5.374</td>
<td>6.192</td>
<td>5.893</td>
<td>6.092</td>
</tr>
<tr>
<td>P</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

### Table 2

<table>
<thead>
<tr>
<th>Groups</th>
<th>CP (μg/L)</th>
<th>Cys-C (mg/L)</th>
<th>SDF-1α (μg/L)</th>
<th>BDNF (ng/mL)</th>
<th>HMGB1 (ng/mL)</th>
<th>MBP (μg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>2.27±0.23</td>
<td>0.56±0.06</td>
<td>1.37±0.12</td>
<td>10.36±1.24</td>
<td>30.28±3.14</td>
<td>0.41±0.03</td>
</tr>
<tr>
<td>Control</td>
<td>1.72±0.15</td>
<td>0.72±0.07</td>
<td>2.18±0.23</td>
<td>6.29±0.58</td>
<td>49.76±5.58</td>
<td>0.68±0.07</td>
</tr>
<tr>
<td>t</td>
<td>6.384</td>
<td>5.271</td>
<td>5.983</td>
<td>7.392</td>
<td>8.394</td>
<td>5.271</td>
</tr>
<tr>
<td>P</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

### Table 3

<table>
<thead>
<tr>
<th>Groups</th>
<th>MDA (nmol/mL)</th>
<th>SOD (U/mL)</th>
<th>CAT (U/mL)</th>
<th>GSH-Px (U/mL)</th>
<th>NO (μmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>4.28±0.43</td>
<td>108.64±10.59</td>
<td>5.83±0.56</td>
<td>139.28±12.11</td>
<td>58.39±5.63</td>
</tr>
<tr>
<td>Control</td>
<td>7.15±0.75</td>
<td>99.75±9.47</td>
<td>5.07±0.51</td>
<td>127.55±12.05</td>
<td>70.56±6.87</td>
</tr>
<tr>
<td>t</td>
<td>6.932</td>
<td>7.283</td>
<td>5.384</td>
<td>6.182</td>
<td>7.394</td>
</tr>
<tr>
<td>P</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>
to insulin, and CP deficiency is one of the important causes of DPN. Recent study has found that CP has nerve protection and antiapoptotic effect, and helps to promote the C fiber regeneration and delay neuropathy. It is found that Cys-C levels increase in patients with diabetic microvascular lesion, and further research believes that Cys-C is also involved in the occurrence of DPN[8]. Cys-C degradation products can activate neutrophils and mediate inflammatory reaction, raise levels of C-reactive protein and lead to vascular endothelial dysfunction, which affects peripheral nerve blood supply and leads to the occurrence of lesions. Studies have shown that SDF-1 α level change plays a role in type 2 diabetes and its complications, SDF-1 α can promote nerve cell regeneration and inhibit inflammation, and it also has renal protection effect. There is a negative correlation between the incidence of complications and SDF-1 α level in patients with type 2 diabetes. BDNF is an endogenous regulator of the myelin formation in peripheral nervous system, and its combination with receptor P75 can promote myelination, and is one of the essential factors of formation and regeneration of damaged nerve myelin[9,10]. HMGB1 belongs to the proinflammatory factor, participates in a variety of diabetes complications, and can keep the body’s inflammation state and damage islet cells. MBP is a nerve myelin-specific lipoprotein that exists as nerve myelin nutrients. The presence of MBP helps maintain stable myelin structure and function in the central nervous system. Nerve ischemia hypoxia can lead to nerve tissue lesions, serum MBP level increases, and it is the specific index reflecting whether there is substantial damage in the nervous system[11,12]. Above research results showed that CP and BDNF values of observation group after treatment were higher while Cys-C, SDF-1 α, HMGB1 and MBP values, indicating that hyperbaric oxygen combined with α-lipoic acid therapy had active effect on optimizing DPN patients’ illness and reducing peripheral nerve damage. Study has suggested that oxidative stress reaction is throughout the occurrence and development process of type 2 diabetes, and is also an important factor of DPN. When the body is in a state of oxidative stress, the excessively produced active molecules not only directly damage DNA and protein, but can also cause structural and function disorders of neurons and vascular endothelial cells. Oxidative stress activates a variety of signal transduction molecules through the classic high blood glucose damage way, ultimately changing cell gene expression and causing neuron dysfunction and apoptosis[13]. MDA, SOD, CAT, GSH-Px and NO are the representative materials of oxidative stress. MDA and NO belong to oxidizing substances, and their levels can directly reflect the body’s oxidation ability and the nerve damage ability to patients with DPN. SOD, CAT and GSH-Px belong to antioxidants, and oxidation/antioxidation imbalance and decreased antioxidants in DPN patients is the direct cause of aggravated illness[14,15]. Above research results showed that serum MDA and NO values of observation group after treatment were lower while SOD, CAT and GSH-Px values were higher, indicating that hyperbaric oxygen combined with α-lipoic acid therapy could promote the recovery of oxidation/antioxidation balance in DPN patients and lay a foundation for the improvement of overall illness. To sum up, it is concluded as follows: hyperbaric oxygen combined with α-lipoic acid is a good method to optimize the neurological function and improve overall illness of patients with diabetic peripheral neuropathy, and it’s worth popularization and application in clinical practice in the future.

References


