Features analysis on Traditional Chinese Medicine syndromes in patients with diabetic peripheral neuropathy

Mingdi Li, Hao Su, Yuyan Xiang, Jingyi Zhang, Jingjie Zhao, Lan Lin

OBJECTIVE: To study the features of the distribution and differentiation of Traditional Chinese Medicine (TCM) syndromes in patients with diabetic peripheral neuropathy (DPN).

METHODS: We collected clinical data on illness course, age, fasting blood glucose, saccharogenic hemoglobin, TCM syndromes, tongue, and pulse of 238 DPN patients. Differentiated main syndromes (Yin deficiency and exuberant heat, invasion of spleen by damp-heat, deficiency of both Qi and Yins, and deficiency of both Yin and Yang) and accompanying syndromes (blood stasis and phlegm-dampness) of diabetes were also recorded. The features of DPN syndromes were then analyzed.

RESULTS: Among the four main syndromes of diabetes, deficiency of both Yin and Yang was the most common in the 238 DPN patients, of which 89%-96% had blood stasis.

CONCLUSION: The method of differentiating syndromes of diabetes can be applied to DPN patients. Deficiency of both Yin and Yang, often accompanied by blood stasis, is commonly seen.

© 2013 JTCM. All rights reserved.

Key words: Diabetic neuropathies; Syndrome differentiation classification; Symptom complex; Blood stasis

INTRODUCTION

Diabetic peripheral neuropathy (DPN), one of the most common chronic complications of diabetes, causes significant disability and mortality of diabetic patients. Over 50% of diabetics suffer from DPN. With longer illness courses of diabetes, incidence has risen up to more than 90%. Traditional Chinese Medicine (TCM) has some merit for treating DPN. Although syndrome differentiation and type classification of DPN is still being studied, standardizing the differentiation of syndromes of diabetes is being discussed. Therefore, based on the universally acknowledged standards for differentiating diabetic syndromes, we analyzed the features of syndrome distribution of 238 DPN patients and explored the laws on differentiating DPN syndromes to provide evidence for TCM treatment of DPN.

METHODS

Diagnostic standards

The diagnostic standard in Western Medicine for diagnosing diabetes was issued by WHO in 1999. The standard for diagnosing DPN was created in reference to China guide for preventing and treating diabetes B
published in 2010 and the DPN-diagnosing standard stipulated at the US ADA and Society of Neurology conferences held in San Antonio in 1988. Diabetics with at least one of the following items were diagnosed as suffering from DPN. (a) Patients have one of the following symptoms: numbness, sensitivity, pricking pain, burning, crawling, or coldness in lower limbs or feet. (b) According to neuro-electro-physiological examination, patients have one of the two following conditions: abnormal motor nerve conductive velocity (MNCV) or abnormal sensitive nerve conductive velocity (SNCV). (c) Patients have abnormal results in the quantitative sensitive nerve examination. In reference to TCM standards for differentiating syndromes from Diabetes in the Principle Instructing Regulations of TCM in 1997 and in accordance with clinical experience, we have defined the standard for diagnosing the main accompanying syndromes of DPN as follows: (a) The syndrome of blood stasis has the symptoms of: dim complexion, dark purple lips, squamous and dry skin, chest pain, dry mouth, lack of thirst, numbness or pain in the limbs, cold limbs, dark tongue, ecchymosis in the tongue, purple vein under the tongue, and a thready and rapid pulse. (b) The syndrome of phlegm-dampness has the symptoms of: puffy body, fatigue, lethargy, heavy limbs, abdominal fullness, dizziness, mucous stool, enlarged tongue with greasy fur, and a slippery pulse.

Inclusion standards
Patients conformed to the diagnostic standards in Western Medicine and in TCM regardless of their illness course, age, and sex.

Exclusion standards
(a) Patients with injury of the spinal cord, spinal deformity, or cerebrovascular diseases. (b) DPN patients with hereditary, toxic, immune, traumatic, or nervous diseases.

General data
Among the 238 DPN inpatients in the Endocrine Department of Guang’anmen Hospital affiliated to the China Academy of Chinese Medical Sciences from January to June 2012 there were 126 males and 112 females aged 30-80 years, (59±11) years on average, with a diabetic illness course of 0.01-32 years, (11±7) years on average.

Methods for collecting cases
In our retrospective research into cases, we designed a unified case-observing table and collected and recorded the clinical data of age, illness course, fasting blood glucose, saccharogenic hemoglobin, TCM syndromes, tongue condition, and pulse condition of the 238 DPN patients. We then classified and recorded cases according to the standards for diagnosing diabetes, the TCM standards for differentiating syndromes, main accompanying syndromes (blood stasis, phlegm-dampness), and main accompanying syndromes (blood stasis, phlegm-dampness). Specially assigned researchers carried out data arrangement and statistical analysis.

Statistical methods
SPSS 16.0 software (SPSS Inc, Chicago, IL, USA) was used to process data. Measurement data are expressed in the form of means ± standard deviation and compared by the t-test. Differences were considered statistically significant when *p* < 0.05.
with mean value±standard deviation ( $\bar{x}$ ±s). Analysis of variance for single factors was used to compare average values among groups. The LSD method was used for comparison between two groups. Chi-squared test was used for enumeration data. $P<$0.05 was considered to be statistically significant.

RESULTS

Distribution of 238 DPN patients in diabetic syndromes
Among the 25 cases of Yin deficiency and exuberant heat there were 19 males and 6 females. Among the 13 patients with invasion of spleen by damp-heat there were six males and seven females. Among the 87 patients with deficiency of both Qi and Yin there were 48 males and 39 females. Among the 113 patients with deficiency of both Yin and Yang there were 53 males and 60 females. There was no statistical difference ($P>$0.05) in sex among groups.

Comparison of blood stasis with phlegm-dampness in patients with various syndromes
Table 1 shows that the incidence of blood stasis was significantly higher than that of phlegm-dampness ($P<$0.05).

Comparison of age in patients with different syndromes
As shown in Table 2, there was a statistical difference ($P<$0.05) between Yin deficiency and exuberant heat with deficiency of both Yin and Yang. There was a statistical difference ($P<$0.01) between Yin deficiency and exuberant heat with deficiency of both Qi and Yin. There was no statistical difference ($P>$0.05) between the rest of the syndromes. There was a statistical difference ($P<$0.05) between fasting blood glucose among syndromes.

Comparison of saccharogenic hemoglobin HbA1c of patients with different syndromes
Table 3 shows that there was a statistical difference ($P<$0.05) between deficiency of both Qi and Yin with deficiency of both Yin and Yang and with invasion of spleen by damp-heat. There was no statistical difference ($P>$0.05) between the rest of the syndromes. However, the clinical significance of these statistical differences has not yet been defined.

Notes: TCM: Traditional Chinese Medicine. As compared with the data of deficiency of both Qi and Yin, *$P<$0.05; as compared with the data of deficiency of both Yin and Yang, †$P<$0.01.

Table 1 Comparison of blood stasis with phlegm-dampness in patients with various syndromes (%)

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>$n$</th>
<th>Case of blood stasis</th>
<th>Case of phlegm-dampness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yin deficiency and exuberant heat</td>
<td>25</td>
<td>24 (96.00)</td>
<td>0 (0.00)</td>
</tr>
<tr>
<td>Invasion of spleen by damp-heat</td>
<td>13</td>
<td>12 (92.31)</td>
<td>3 (23.07)</td>
</tr>
<tr>
<td>Deficiency of both Qi and Yin</td>
<td>87</td>
<td>81 (93.10)</td>
<td>8 (9.19)</td>
</tr>
<tr>
<td>Deficiency of both Yin and Yang</td>
<td>113</td>
<td>101 (89.38)</td>
<td>20 (17.70)</td>
</tr>
<tr>
<td>Total</td>
<td>238</td>
<td>218 (91.60)</td>
<td>31 (13.03)</td>
</tr>
</tbody>
</table>

Table 2 Comparison of age, illness course, and FBG of DPN patients with different syndromes ( $\bar{x}$ ±s)

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>$n$</th>
<th>Age (years)</th>
<th>Illness course (years)</th>
<th>FBG (mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yin deficiency and exuberant heat</td>
<td>25</td>
<td>53.08±10.42</td>
<td>7.92±5.45</td>
<td>9.81±2.76</td>
</tr>
<tr>
<td>Invasion of spleen by damp-heat</td>
<td>13</td>
<td>58.08±9.86</td>
<td>6.39±4.89</td>
<td>8.65±2.57</td>
</tr>
<tr>
<td>Deficiency of both Qi and Yin</td>
<td>87</td>
<td>59.20±12.10</td>
<td>9.62±6.63</td>
<td>9.59±3.76</td>
</tr>
<tr>
<td>Deficiency of both Yin and Yang</td>
<td>113</td>
<td>60.56±11.00</td>
<td>12.36±6.87</td>
<td>8.97±2.93</td>
</tr>
</tbody>
</table>

Notes: FBG: fasting blood glucose; DPN: diabetic peripheral neuropathy. As compared with the data of Yin deficiency and exuberant heat, *$P<$0.05; as compared with the data of deficiency of both Yin and Yang, †$P<$0.01.

Table 3 Relations of TCM syndromes to HbA1c (% $\bar{x}$ ±s)

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>$n$</th>
<th>HbA1c</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yin deficiency and exuberant heat</td>
<td>21</td>
<td>8.63±2.22</td>
</tr>
<tr>
<td>Invasion of spleen by damp-heat</td>
<td>13</td>
<td>6.61±3.13</td>
</tr>
<tr>
<td>Deficiency of both Qi and Yin</td>
<td>87</td>
<td>8.22±3.99</td>
</tr>
<tr>
<td>Deficiency of both Yin and Yang</td>
<td>113</td>
<td>8.50±2.48</td>
</tr>
</tbody>
</table>

Notes: TCM: Traditional Chinese Medicine. As compared with the data of deficiency of both Qi and Yin, *$P<$0.05.
DISCUSSION

At present, there are several viewpoints on differentiating TCM syndromes of DPN: Lin et al. divided DPN into five syndromes: (a) deficiency of both Qi and blood, and blockage of channels and collaterals; (b) Yin deficiency of both liver and kidney, and feebleness of tendons and bones; (c) stagnation of the liver-Qi, and obstruction of blood vessels by blood stasis; (d) Yang deficiency of both spleen and kidney, and stagnation of both phlegm and blood stasis; and (e) Yang deficiency and cold accumulation, and obstruction of blood vessels by blood stasis. Li et al. divided DPN into four syndromes: (a) deficiency of both Qi and Yin; (b) Yang deficiency of both liver and kidney; (c) Yang deficiency of both spleen and kidney; and (d) deficiency of both essence and marrow. Liang et al. divided DPN into four syndromes: (a) blood stasis due to deficiency of kidney Yin; (b) blood stasis due to deficiency of kidney Yang; (c) Yin deficiency of both liver and kidney, and up-stirring of liver; and (d) deficiency of both spleen and kidney, and stagnation of both phlegm and blood stasis. In the TCM Guide for Preventing and Treating Diabetic Peripheral Neuropathy issued by the China Association of TCM in 2011, DPN is divided into four syndromes: (a) blood stasis due to Qi deficiency; (b) blood stasis due to Yin deficiency; (c) blockage of collaterals by phlegm stagnancy; and (d) deficiency of both liver and kidney. The above-mentioned syndromes are differentiated in accordance with the eight principal syndromes, with internal organs, or with a combination of both. No consensus has yet been reached on these syndrome-differentiating methods.

There are many articles on clinical research into differentiating syndromes of DPN. For example, Gao et al.11 Sun et al.,10 and Lin et al.14 use a single TCM syndrome as a standard. Other researchers create their own standard,15 or use the TCM Guide for Preventing and Treating Diabetic Peripheral Neuropathy issued by the China Association of TCM as the standard.16,17 Diabetes is the precursor to DPN, a common micro-vascular complication of diabetes. Therefore, TCM syndromes of DPN should be mainly differentiated according to the TCM syndromes of diabetes. Researchers have reached a consensus on the standards for differentiating syndromes of diabetes by using the Principle for Directing Clinical Research into Treatment of Diabetes with New Chinese Drugs published in 2002. Therefore, this publication can be used to study the features of DPN syndromes and the standards for classifying its types.

In the Principle for Instructing Research Into Treatment of Diabetes with New Chinese Drugs issued in 2002, the syndromes of diabetes are divided into Yin deficiency and exuberant heat, invasion of spleen by damp-heat, deficiency of both Qi and Yin, deficiency of both Yin and Yang, blood stasis and water stagnation, and blockage of blood vessels by blood stasis. In Lin Lan’s research into "differentiating 3 diabetic syndromes", diabetes is divided into three types of Yin deficiency and exuberant heat, deficiency of both Qi and Yin, and deficiency of both Yin and Yang, corresponding to early stage, moderate stage, and late stage of diabetes. Overweight patients with type 2 diabetes have abdominal obesity, heavy body, thick greasy fur on the tongue, and a slippery rapid or slippery slow pulse. TCM considers such diabetics as having damp-heat syndrome commonly seen in clinical practice. To include this patient population, invasion of spleen by damp-heat was added to the Principle for Instructing Research into Treatment of Diabetes with New Chinese Drugs. However, blockage of blood vessels by blood stasis should belong to an accompanying syndrome of diabetes and should not be listed as a main syndrome. Therefore, blood stasis and phlegm-dampness are regarded as the main accompanying syndromes of DPN in this research.

Through the statistical distribution of 238 DPN patients in the four main syndromes and the three accompanying syndromes, we have provided evidence for comprehensively recognizing TCM syndromes of DPN. We found that the 238 DPN patients can be classified according to the differentiation of diabetic syndromes, among which, the deficiency of both Yin and Yang is most commonly seen, accounting for about 47% of DPN patients, followed by deficiency of both Qi and Yin. However, DPN is not the same as diabetes. In addition to suffering from diabetes, DPN patients have other symptoms. Therefore, it is not sufficient to research DPN only by means of TCM methods to differentiate syndromes of diabetes. Consideration should be given to other relevant factors. Because stress is part of deficiency syndromes of internal organs in the above-mentioned four syndromes of diabetes, little consideration is given to accompanying syndromes evolving from deficiency syndromes to excess syndromes. Therefore, in this research, blood stasis and phlegm-dampness, two accompanying syndromes belonging to excess syndrome, are added to the four TCM syndromes of diabetes to recognize the special factors of DPN syndromes.

We found that 89%-96% of DPN patients have blood stasis and 9%-23% have phlegm-dampness in addition to the four main syndromes. Therefore, regardless of DPN syndromes, blood stasis is a main accompanying syndrome. Deficiency of both Yin and Yang accompanied by blood stasis is the syndrome type most commonly seen in DPN patients.

In addition, the age and illness course of DPN patients can influence their syndrome type. With increasing age, the percentage of patients with deficiency of both Yin and Yang and deficiency of both Qi and Yin gradually rises. Judging from the illness course, deficiency of both Yin and Yang is often seen in patients living with diabetes for more than 12 years. Yin deficiency and exuberant heat and invasion of spleen by damp-heat are
mainly seen in the early stages of DPN. DPN syndrome types are not influenced by fasting blood glucose and are not influenced by saccharogenic hemoglobin.

REFERENCES


