Clinical Observations

Multi-central Clinical Research into Treating 80 Cases of Chronic Thrombocytopenia with Qi-supplementing and Yin-nourishing Therapy and Western Medicine

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Objective: To probe the effects of qi-supplementing and yin-nourishing therapy (blood-increasing decoction and blood-generating powder) on chronic thrombocytopenia.

Methods: Two hundred patients with chronic thrombocytopenia were randomly divided into control (n=100) and test groups (n=100) with Amino-polypeptide as a basic treatment for both. Test group patients consumed a blood-increasing decoction and blood-generating powder for 1–3 months. Improvements in platelet counts and TCM syndrome were observed.

Results: One hundred and sixty-four (80 in the test group and 84 in the control group) of 189 total participants were treated for 3 months. The total effective rate in improving TCM syndrome was 95.00% in the test group and 79.76% in the control group (P<0.05). There was significant difference (P<0.05) in the accumulated score of TCM syndrome between the two groups treated at different time points. The total effective rate of platelet counts was 86.25% in the test group and 59.52% in the control group (P<0.05). There was a significant difference in platelet counts before and after treatment in the two groups (P<0.05). There was no significant difference in platelet count between the two groups treated for 1–2 months; however, a significant difference was found between the two groups after treatment for 3 months (P<0.05).

Conclusions: After a 3-month treatment of chronic thrombocytopenia patients with qi-supplementing and yin-nourishing therapy, TCM syndrome was improved and platelet counts increased with no obvious side effects, and the quality of life of the participants was enhanced with noticeable long-term curative effects.

Keywords: supplementing qi and nourishing yin; chronic thrombocytopenia; platelet count; accumulated score of TCM syndrome

Chronic thrombocytopenia is caused by a decreased quantity or reduced function of blood platelets, leading to bleeding. TCM attributes the disease over 12 months to purpura. Engaging in clinical research into the disease for more than 30 years, our hospital has found that most patients with lingering illness have a deficiency or failure of qi to control blood and bleeding. Therefore, starting from “qi and yin”, we use qi-supplementing and yin-nourishing therapy to treat the disease with good curative effects. Our research is reported as follows.

METHODS

Diagnostic Standards

Diagnostic standards of thrombocytopenia in Western medicine: According to the standard referenced in Zhang and Shen: 1) decreased platelet counts in many tests; 2) in chronic thrombocytopenia with platelet counts \( \leq 80 \times 10^9/L \), no obvious bleeding tendency, only scattered bleeding in the skin and mucosa and no bleeding in the internal organs; and 3) increased, normal or slightly decreased megalolocaryocytes in bone marrow tests.

Diagnostic standards of thrombocytopenia in TCM: According to the standard referenced in Zheng: 2) 1) main symptoms are lassitude, dizziness, palpitation, shortness of breath, hot sensation in the palms and soles, dry mouth and vexation; 2) secondary symptoms are pale or red ecchymosis, poor appetite, dizziness, tinnitus, tidal fever, night sweats, red cheeks, pale tongue, decreased or thin white body hair and a thready pulse. The disease can be diagnosed according to all the main symptoms and 2 or more of the secondary symptoms in combination with tongue and pulse condition.

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Inclusive Standards
1) Patients conform to both the diagnostic standard in Western medicine and TCM. 2) Patients are 12–80 years old. 3) Patients voluntarily attend the test and sign an agreement to state understanding of the facts of the clinical research.

Standard for Withdrawal
Participants who know the facts and conform to the standard but have not completed the treatment course or cannot continue the test due to serious complications.

General Data
Patients from the First Hospital Affiliated to Zhejiang TCM University (Zhejiang TCM hospital), Zhejiang TCM Academy (Zhejiang Provincial Tongde Hospital), Hospital Affiliated to Nanjing TCM University, Jinhua Municipal TCM Hospital and Lishui Municipal People’s Hospital were randomly divided into groups by computer and clinically observed for 3 months using a single-blind method.

Among 189 participants (11 participants not conforming to the study guidelines were withdrawn from 200 in the total sample) were 95 cases, 33 males and 62 females, aged 12–77, with an average age of 39 and an illness course from 13 months to 25 years (48.3±54.7 months on average) in the test group; and 94 cases, 29 males and 65 females, aged 13–77, with an average age of 41 and an illness course from 14 months to 26 years (43.1±56.9 months on average) in the control group. There were no statistically significant differences in data between the 2 groups. Among the 189 participants, 182 cases were treated for 1 month, 176 cases for 2 months and 164 cases, 80 cases in the test group and 84 cases in the control group, for 3 months.

Therapy
In the control group, patients orally consumed Amino-polypeptide Tablets (0.2 g/tablet), 1 g a time, 3 times daily. Amino-polypeptide, produced by Wenzhou biochemical pharmaceutical factory, is the main ingredient extracted from the nails of pig feet.

In the test group, in addition to the Amino-polypeptide Tablets, patients orally consumed a blood-increasing decoction consisting of 30g Huang Qin (Radix astragaliseu hedysarii), 15g Bie Jia (Carapax trionycis), 20g Tai Zi Shen (Radix pseudostellariae), 30g Hai Luo (Rapanae thornianae), 9g Zi Cao (Radix arnebiae seu lithospermi), 9g Qian Cao (Radix rubiae) and 15g Gan Lu Gen (Rhizoma phragmitis), one dose a day in the morning and evening. Participants also consumed blood-generating powder (bone powder produced by our hospital, 4.5 g per pack) 1 pack at a time, 2 times daily. Because orally taking small dosages of hormones (prednisone <20mg a day) cannot be immediately stopped or reduced, patients should maintain and gradually reduce the dosage according to recovery of the condition until eventually the hormone treatment can be stopped.

Observed Index and Method
Platelet counts (× 10^9/L).

Clinical symptoms and signs: Is ecchymosis in the skin and mucosa improved? Are there new bleeding points?

TCM symptoms: Are dizziness, lassitude, vexation and night sweats improved or alleviated?

Laboratory index: Is the megalocaryocyte count changed in routine examination of the bone marrow?

Safety indexes: Function of the liver and the kidneys, electrocardiogram, and routine urine and stool examination.

Standard for Curative Effect
Main index for evaluating curative effect: According to the standard by Zhang and Shen,1 an obvious effect means that platelet counts are >100 × 10^9/L and bleeding has stopped for over 3 months. Effectiveness means that platelet counts are >50 × 10^9/L or increased by 30 × 10^9/L as compared with before treatment and bleeding has stopped for more than 2 months. Improvement means that platelet counts increase and bleeding is improved for more than 2 weeks. Ineffectiveness means that platelet counts and bleeding are not improved. The total effective rate comprises the obvious effect, effectiveness and improvement.

Evaluating curative effect on TCM syndromes: According to the standard by Zheng,2 cure means that TCM symptoms disappear after treatment, the score for syndromes is reduced and the index for curative effects is ≥95%. An obvious effect means that after treatment, TCM symptoms are remarkably alleviated, syndromes are reduced and the index for curative effects is ≥75% but <95%.

\[
\text{Score before treatment} - \text{Score after treatment} \\
\frac{\text{Index for curative effect on syndrome}}{\times 100\%} = \frac{\text{Score before treatment}}{\text{Score after treatment}}
\]

Effectiveness means that after treatment, TCM symptoms are alleviated, the score for syndromes is reduced and the index for curative effects is ≥30% but <75%. Ineffectiveness means that after treatment, TCM symptoms are not obviously alleviated and the index for curative effects is <30%. The total effective rate comprises the obvious effect, effectiveness and improvement.

Statistical Methods
SPSS 15.0 (SPSS Inc.) was used to carry out statistical analysis and \( \bar{X} \pm s \) used to express normally distributed
data and $t$-tests conducted for comparisons. Non-parametric tests were used for abnormally distributed data. $P<0.05$ was used to indicate statistical difference.

**Adverse Incidents and Their Management**

In clinical observation for 1–3 months, routine blood tests, hepatic and renal functions, electrocardiogram, and routine urine, stool and bone marrow examinations were performed regularly. Scores for TCM syndromes were evaluated monthly.

Patients could tolerate mild adverse reactions, which did not influence treatment and recovery and needed no special management. Because it is difficult for patients to tolerate moderate adverse reactions, which directly influence recovery, it was necessary for patients to stop taking the drug or to be specially treated when such reactions became apparent. Because severe adverse reactions can jeopardize life or disable patients, it was necessary for patients to immediately stop taking the drug or to be emergetly treated when such reactions became apparent.

**RESULTS**

**Comparison of the Total Curative Effects on TCM Syndromes between the 2 Groups**

As shown in Table 1, the total effective rate in the test group was superior to that in the control group ($P<0.05$).

<table>
<thead>
<tr>
<th>Group</th>
<th>Cases</th>
<th>Cure</th>
<th>Obvious effect</th>
<th>Effectiveness</th>
<th>Ineffectiveness</th>
<th>Total effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test group</td>
<td>80</td>
<td>18 (22.50)</td>
<td>22 (27.50)</td>
<td>36 (45.00)</td>
<td>4 (5.00)</td>
<td>76 (95.00)</td>
</tr>
<tr>
<td>Control group</td>
<td>84</td>
<td>17 (20.24)</td>
<td>8 (9.52)</td>
<td>42 (50.00)</td>
<td>17 (20.24)</td>
<td>67 (79.76)</td>
</tr>
</tbody>
</table>

**Comparison of the Accumulated Score for TCM Syndromes before and after Treatment in the Two Groups**

As shown in Table 2, there was a statistically significant difference ($P<0.05$) in the accumulated score for TCM syndromes before and after treatment in the two groups, and after treatment at different time points between the 2 groups.

**Comparison of the Total Curative Effects on Platelet Count between the Two Groups**

As shown in Table 3, the total effective rate in the test group was higher than that in the control group ($P<0.05$).

<table>
<thead>
<tr>
<th>Group</th>
<th>Cases</th>
<th>Cure</th>
<th>Obvious effect</th>
<th>Effectiveness</th>
<th>Ineffectiveness</th>
<th>Total effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test group</td>
<td>80</td>
<td>9 (11.25)</td>
<td>34 (42.50)</td>
<td>26 (32.50)</td>
<td>11 (13.75)</td>
<td>69 (86.25)</td>
</tr>
<tr>
<td>Control group</td>
<td>84</td>
<td>7 (8.33)</td>
<td>23 (27.38)</td>
<td>20 (23.81)</td>
<td>34 (40.48)</td>
<td>50 (59.52)</td>
</tr>
</tbody>
</table>

**Comparison of Platelet Count before and after Treatment in the Two Groups**

As shown in Table 4, there was a statistically significant difference ($P<0.05$) in platelet counts after treatment for 3 months and no significant difference after treatment for 1 or 2 months in the two groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>Cases</th>
<th>Before treatment</th>
<th>After 1-month treatment</th>
<th>After 2-month treatment</th>
<th>After 3-month treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test group</td>
<td>80</td>
<td>44.57±18.64</td>
<td>52.70±35.94</td>
<td>62.18±43.86</td>
<td>75.59±54.36</td>
</tr>
<tr>
<td>Control group</td>
<td>84</td>
<td>42.32±20.25</td>
<td>52.09±31.43</td>
<td>63.42±30.11</td>
<td>60.79±32.37</td>
</tr>
</tbody>
</table>

Notes: *$P<0.05$ as compared with the value before treatment in the same group; †$P<0.05$ as compared with the value after treatment for same time in the control group.

**Adverse Reactions**

No effect of the test drug was found on indexes of hepatic and renal function, electrocardiogram, or routine urine and stool tests in the follow-up visit. However, during the research, after taking the test drug, 2 patients had loose stool and 3 patients had a mild reaction in the...
gastrointestinal tract. The 5 patients with no special treatment continued taking the drug for 2-3 days and their symptoms were alleviated automatically.

**DISCUSSION**

Thrombocytopenia is mainly treated by clearing away heat from the blood, removing toxins, promoting blood circulation, and by supplementing *qi* and nourishing *yin*. Supplementing the bone marrow, replenishing the bone and generating blood can repair the damaged organs and improve symptoms.

Based on long-term research into thrombocytopenia, we have found that most patients with chronic thrombocytopenia display a deficiency of both *qi* and *yin*.

“*Qi* as the commander of blood” and “blood being the mother of *qi*” are the cause and result of each other. Only by treating the disease at the early stage with *qi*-supplementing and *yin*-nourishing drugs can the development of the illness be obstructed. Long-term thrombocytopenia mentioned by Cui Xujiang seemingly belongs to the category of “*yin*” and “deficiency”. It has been discovered in clinical research that a *qi*-supplementing and *yin*-nourishing method (blood-increasing decoction and blood-generating powder) can improve the TCM symptoms of chronic thrombocytopenia very well and reduce side-effects of immune inhibition. A 3-month treatment can enhance platelet counts, reduce bleeding risk and improve quality of life. We also have found that a good curative effect is achieved without hormone treatment, a poor curative effect is achieved with hormone treatment, and that no curative effect is achieved with repeated use of hormone treatment.

“Blood-generating powder”, a proven recipe developed by famous veteran TCM physicians in our hospital, has been used for many years to treat all kinds of thrombocytopenia and some kinds of leucopenia caused by long-term contact with radioactivity, with a good curative effect achieved and some research accumulated. A blood-increasing decoction, consisting of Huang Qi (*Radix astragali seu hedysari*), Bie Jia (*Carapax trionycis*), Tai Zi Shen (*Radix pseudostellariae*), Hai Luo (*Rapanae thornianae*), Zi Cao (*Radix arnebiae seu lithospermii*), Qian Cao (*Radix rubiae*) and Gan Lu Gen (*Rhizoma phragmitis*), can supplement *qi* and nourish *yin*. Modern pharmacological research shows that most drugs in the recipe have good effects on regulating immunity and stopping bleeding. Huang Qi, sweet in taste and slightly warm in nature, with its therapeutic action related to channels of the spleen and lung, has the effect of supplementing *qi*, consolidating superficial resistance, astringing sweats, discharging toxins, generating tissue, causing diuresis and subduing swelling. Jiao Zhonghua has achieved a good curative effect of *Zi Cao* in a purpura-eliminating decoction. Zhang Haowen and others indicate that Huang Qi has the effect of supplementing *qi* and generating blood. Danggui Buxue Tang, an ancient recipe, can treat poor *qi*, blood deficiency and other deficiency syndromes. Modern pharmacological research indicates that Huang Qi has an obvious effect on regulating immunity and promoting the maturity of megalocaryocytes. *Zi Cao* has the effect of clearing away heat from the blood, promoting blood circulation, removing toxins and promoting eruption. Li Hong has used *Zi Cao* to treat colpporrhagia after miscarriage with an obvious effect, indicating that *Zi Cao* can reduce the amount of bleeding and shorten bleeding time. Research shows that *Zi Cao* can inhibit damage to the vascular endothelium caused by immune compounds. Qian Cao has the effect of clearing away heat from the blood, stopping bleeding, promoting blood circulation and removing blood stasis. Song Shanjun and others have discovered through in vitro experiments that *Qian Cao* can promote the generation of thromboplastin, thrombase and fibrin, and that its coagulation effects may be related to the effect of anti-heparin. Tai Zi Shen can nourish the spleen and lungs, supplement *qi* and generate body fluids. Modern pharmacological research proves that it can strengthen immunity. Animal experiments have shown that a 75% alcoholic extract of Tai Zi Shen can inhibit a reduction in the weight of the thymus gland and the spleen caused by cyclophosphamide and increase levels of expression of DNA and RNA in the thymus gland as well as DNA in the spleen.

In the current research, 2 patients had loose stool and 3 patients had a mild reaction in the gastrointestinal tract. These 5 patients were not specially treated and their symptoms resolved automatically. The reaction is related to the medicinal nature of Bie Jia, which is slightly cold in nature and salty in taste, with a therapeutic action related to the channels of the liver and kidneys, nourishing *yin*, checking the exuberance of *yang*, and softening and resolving hard mass. Some patients with a cold syndrome of the stomach who cannot tolerate the cold nature of Bie Jia have a mild reaction of the gastrointestinal tract and loose stool. Modern pharmacological research proves that the bioactive substance extracted from Bie Jia has the effect of inhibiting tumor growth and radiation damage as well as enhancing immune function. Research by Wang Huiming and others has shown that a polysaccharide of Bie Jia can enhance nonspecific immune function in immunosuppressant mice with a dose-dependent effect.

Thrombocytopenia patients have a disorder of humoral immunity and an abnormality of cytoimmunity. Disorders of the immunoregulation mechanisms of T-cells play a very important role in the occurrence of the disease. Professor Ma Rou has pointed out that scholars have attached importance to the effects of abnormally oligocloned T- and B-lymphocytes on destroying platelets in the occurrence of the disease. Our clinical research finds that there is an obvious difference in the expression of a subgroup of T-lymphocytes in peripheral blood before and after treatment of thrombocytopenia with blood-increasing and blood-generating therapy; a marked increase in the expression of CD3+ and CD4+, a
remarkable decrease in the expression of CD4+ and a noticeable increase in the ratio of CD4+ to CD8+ after treatment, indicating that the recipe does have the effect of regulating the expression of a subgroup of T-lymphocytes in the peripheral blood of thrombocytopenia patients.22

Despite our significant results, limitations of the current study include the different compliance rates of participants and a single index for evaluating curative effects. Therefore, in our future research, we will consider using additional laboratory indexes such as the level of expression of human leukocyte antigen DR (HLADR) and a specific antibody of platelets (PBlgG). The HLADR locus as a marker of the activation of T-cells.23 Yang Xiaohong and others24 have found that a CD4+/HLADR+ subgroup of T-cells are significantly increased in patients with refractory ITP, indicating that HLADR is related to prognosis of ITP. Song Qiang25 and others have found that the level of expression of HLADR in ITP patients is much higher than that in the control group, indicating that abnormal activation of T-cells and HLADR is related to the occurrence of ITP. We also have discovered that qi-supplementing and yin-nourishing therapy can improve some symptoms of chronic thrombocytopenia patients with a deficiency of both qi and yin. However, some patients mainly have a yin deficiency while others mainly have a qi deficiency. Therefore, we will regulate drugs appropriately so as to observe the difference in the curative effects and the direct clinical use of drugs in a better way.

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