Clinical Observations

The Short-term Therapeutic Effects of TCM for IgA Nephropathy In Children

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Objective: To evaluate the short-term therapeutic effects of TCM for IgA nephropathy in children.

Methods: Sixty-two children with primary IgA nephropathy diagnosed for the first time by renal biopsy in the authors’ hospital were randomly divided into a group of 34 cases treated with both TCM and Western medicine and a group of 28 cases treated with Western medicine for six months. The improvements in urinary protein and red blood cell (RBC) were observed and the scores for TCM symptoms and signs were evaluated after 3 months and 6 months of treatment.

Results: There was no significant difference in the total effective rate between the two groups ($\chi^2=4.743, P>0.05$ after treatment for 3 months; and $\chi^2=1.953, P>0.05$ after treatment for 6 months). However, the cure plus marked effect rate in the group treated with both TCM and Western medicine was higher than that in the group treated with Western medicine (71.9% vs 45.5%, $P<0.05$ after treatment for 3 months). At the end of treatment, significant difference were found in the effective rate (9.3% vs 10.5%, $\chi^2=9.653, P<0.01$) and in the total score (0.81±1.18 vs 3.42±2.52, $t=4.19, P<0.001$) between the two groups.

Conclusion: Treatment with both TCM and Western medicine can effectively improve the TCM symptoms and signs in child patients with IgA nephropathy, and alleviate hematuria and albuminuria.

Keywords: IgA nephropathy; children; treatment with both TCM and Western medicine

IgA nephropathy, one of the common primary glomerulopathies leading to chronic renal failure, can develop into terminal nephropathy in 20%–40% of the adult patients with illness course for 20 years, and into chronic renal failure in 5%, over 6% and 10%–30% of the child patients with illness course for 5, 10 and 15–20 years respectively.1,2 It can be seen that the survival rate of kidney will gradually decline with the extension of illness course.

At present, due to lack of specific treatment, IgA nephropathy can only be treated according to the symptoms in Western medicine. Mainly attributing the disease to imbalance between yin and yang of the body and invasion of the body by exopathogen, TCM has accumulated certain experience in treating the adult patients with IgA nephropathy. TCM treatment can not only improve the symptoms but also obtain the effect of treating both superficiality and origin through regulating the balance between yin and yang of the body. Because children with delicate internal organs are more easily invaded by exopathogen, child patients have different characteristics from adult patients in TCM treatment. At present, there are few systematic researches for TCM treatment of IgA nephropathy in children. In the present study, the authors have observed the short-term therapeutic effects of TCM for IgA nephropathy in children in an attempt to look for more effective treatment so as to improve their prognosis when they grow up.

METHODS

General Data
Sixty-two child patients with IgA nephropathy diagnosed in the authors’ hospital from February 2008 to July 2010 were divided into two groups by random sampling. Among the 34 cases in the group treated with both TCM and Western medicine, there were 23 males and 11 females, aged 5–14 with illness course from 2 weeks to 4 years. Of them, 23 cases (67.6%) had macroscopic hematuria, 2 cases (5.9%) were transient renal insufficiency, and 3 cases (8.8%) nephropathy expression; 2 cases (5.9%) were grade I, 18 cases (52.9%) grade II, and 14 cases (41.2%) grade III in Lee’s grading of renal pathology. Among 28 cases in the group treated with Western medicine, there were 17 males and 11 females aged 6–13 with illness course from 2 weeks to 2 years, 16 cases (57.1%) had macroscopic hematuria, 2 cases (7.1%) transient renal insufficiency, and 3 cases (10.7%) nephropathy expression; 2 cases (7.1%) were grade I, 14 cases (50.0%) grade II, 11 cases (39.3%) grade III and 1 case (3.6%) grade IV in Lee’s grading of renal pathology. There was no obvious difference in the baseline of the clinical manifestations. The present research was approved by members of the committee in charge of ethics in the authors’ hospital. Guardians of the child patients signed a letter of consent on knowing the facts.

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This research is supported by the Capital Medical Development Fund (Traditional Chinese Medicine Category) (No.SF-20071107)
Diagnosis Standard in Western Medicine
Renal biopsy specimen shows immunocomplex sediment, mainly IgA, in the mesangium area. 3

Inclusive Standard
Child patients, aged 3-18, with primary IgA nephropathy and normal renal function, have been treated with hormone or immunosuppressant for less than 4 weeks. They take part in the research with the consent of their parents.

Exclusive Standard
Child patients with secondary IgA nephropathy, such as nephritis related to hepatitis B virus and allergic purpura nephritis; blood creatinine >1.0 mg/dL and obviously abnormal functions of other important internal organs have been treated with hormone or immunosuppressant for more than 4 weeks. Their parents don’t agree to let them take part in the research.

In the group treated with Western medicine, the patients were given dipyridamole, captopril, common three-wingnut, prednisone or cyclophosphamide according to illness condition. In the group treated with both TCM and Western medicine, the patients were given Chinese drugs on the basis of Western medical treatment. According to the clinical features of child patients and the experience of the authors hospital in diagnosis and treatment, IgA nephropathy is mainly divided into 4 types. 1) Pathogenic heat in the exterior: The symptoms may include rhinorrhea, nasal obstruction, fever, oliguria, edema, dark urine, red tongue tip, thin and white fur, floating and rapid pulse. It should be treated by inducing diaphoresis to eliminate pathogenic heat and removing heat from blood. Prescriptions: fresh Lu Gen (Rhizoma Phragmitis) 15–30 g, fresh Mao Gen (Radix Rubi Parvifolii) 15–30 g, Jin Yin Hua (Flos Lonicerae) 9 g, Lian Qiao (Fructus Forsythiae) 9 g, Ju Hua (Flos Chrysanthemi) 6–9 g, Chi Xiao Dou (Semen Phaseoli) 12–15 g, Sheng Di (Radix Rehmanniae) 9 g, Zhu Ye (Lophatherum) 4–6 g, Qian Cao (Radix Rubiae) 9 g and Ban Lan Gen (Radix Isatidis) 9 g. 2) Accumulation of damp-heat in the body: The symptoms may be hematuria, scanty dark urine, poor appetite, retention of feces, low fever, red tongue, white or greasy fur, slippery and rapid pulse. The disease is mainly treated in principle with strengthening the spleen, removing blood stasis and stopping bleeding. Prescription: Huang Qi (Radix Astragali seu Hedysari) 6–9 g, Sheng Di (Radix Rehmanniae) 9 g, Shu Di (Radix Rehmanniae Praeparata) 9 g, Shan Yu Rou (Fructus Corni) 9 g, raw Shan Yao (Rhizoma Dioscoreae) 15 g, Qian Shi (Semen Euryales) 9 g, Shi Wei (Folium Pyrrosiae) 9–12 g, Ku Shen (Radix Sophorae Flavescentis) 6 g, Ze Xie (Rhizoma Alismatis) 9 g, Dan Pi (Cortex Moutan Radicis) 9 g, Chi Xiao Dou (Semen Phaseoli) 12 g, charred Ce Bai (Bacumen Biotae) 9 g, Jian Qu (Massa Medicata Fermentata Fujianensis) 9 g, Yun Ling (Poria) 9 g and fresh Lu Gen (Rhizoma Phragmitis) 30 g. 3) Retention of blood stasis in the body: The symptoms of hematuria, dark tongue with ecchymosis, taut and thready pulse. The disease is mainly treated in principle with soothing the liver, strengthening the spleen, removing blood stasis and stopping bleeding. Main drugs are Jian Qu (Massa Medicata Fermentata Fujianensis) 9 g, raw Shan Yao (Rhizoma Dioscoreae) 12 g, Sha Ren (Fructus Amomi) 4 g, Mu Xiang (Radix Paeoniae Rubra) 9 g, Bai Shao (Radix Paeoniae Alba) 9 g, Dan Shen (Radix Salviae Miltiorrhizae) 9 g, Chi Shao (Radix Paeoniae Rubra) 9 g, Shu Di (Radix Rehmanniae Praeparata) 9 g, Sheng Di (Radix Rehmanniae) 9 g, raw Shan Yao (Rhizoma Dioscoreae) 15 g, Shang Shen (Radix Angelicae Sinensis) 9 g, Qian Shi (Semen Euryales) 1 g, Shi Wei (Folium Pyrrosiae) 9–12 g and fresh Mao Gen (Radix Rubi Parvifolii) 0.5–1 g (to be taken after being infused in boiling decoction). One dose is decocted twice and the decoction is orally taken in two times.

Course of Treatment
The patients were treated for 6 months (3 months as one course of treatment).

Evaluation of the Therapeutic Effect in Western Medicine
In reference to the principles instructing clinicia treatment of chronic nephritis with new Chinese drugs (stipulated by the Ministry of Health of the People’s Republic of China in 2002), clinical cure means that protein turns negative in routine urine examination or normal in quantity of 24 h urinary protein, RBC count normal in routine urine examination or in urinary sediment. Marked effect means that urinary protein is reduced by “++” in routine urine examination or the quantity of 24 h urinary protein decreased by >40%, and RBC lowered by ≥3/HP or “++”. Improvement means that urinary protein is reduced by “+” in routine urine examination or the quantity of 24 h urinary protein decreased by ≥40%, and RBC lowered by <3/HP or “+”. Failure means that the above-mentioned indexes are unimproved or aggravated.

Evaluation of the TCM Symptoms
In reference to the principles instructing clinical treatment of chronic nephritis with new Chinese drugs, according to the children’s features and through
pre-scoring in some child patients, 10 symptoms were selected for evaluation, such as common cold, hypodynamia, hyperhidrosis, red and dry throat, dark yellow urine, stomach distension, poor appetite, lumbago, edema and sallow complexion. Each symptom was given 0–3 according to the actual conditions. The improvement of TCM symptoms was evaluated by two physicians who not the doctors were giving the prescription.

Clinical cure means that the symptoms disappear, or the total score for symptoms is reduced by ≥95%. Marked effect means that the symptoms are alleviated by two grades from the severe to mild, or the total score for the symptoms is reduced by 70%-94%. Improvement means that the symptoms are alleviated by one grade from the severe to moderate or from the moderate to mild or the total score for the symptoms is reduced by 30%-69%. Failure means that the symptoms remain unchanged, or the total score for symptoms is reduced by <30%. The nimodiping method was adopted with formula: the total score before treatment – the total score after treatment/the total score before treatment × 100%.

Evaluation of Safety
Blood pressure, blood routine, functions of the liver and kidney, and blood coagulation were monitored in the course of treatment.

Statistical Process
The SPSS11.0 statistical software was used. χ² test was used for enumeration data and t test for measurement data. All the data were expressed as mean ± standard deviation ( X ± s), and with an obvious difference P<0.05.

RESULTS
Fifty-four of the 62 child patients completed the follow-up visit and treatment. Among the 8 cases who withdrew from the treatment, 2 cases in the group treated with both TCM and Western medicine received only one month of treatment, and 6 cases in the group treated with Western medicine did not revisit on time or paid no revisit at all.

Comparison of the Effects in Western Medicine
After 3 and 6 months of treatment, the cure and marked effect rates in the group treated with both TCM and Western medicine were higher than those in the group treated with Western medicine, but with no significant difference in the total effective rate between the two groups (Table 1 and Table 2). However, after 3 months of treatment, the cure plus marked effect was 71.9% in the former and 45.5% in the latter, with an obvious difference between the two groups (χ²=3.82, P<0.05).

Comparison of the Effects in TCM
There was significant difference in the baseline level of total score for TCM symptoms between the group both TCM and Western medicine evaluated in 27 cases and the group of Western medicine evaluated in 19 cases (9.41±4.79 vs. 9.05±2.86, P>0.05). At the end of treatment, there was an obvious difference (χ²=9.653, P<0.01) in the curative effects for TCM symptoms between the two groups (Table 3), with a significant difference (t=4.19, P<0.001) in the total score for TCM symptoms (Table 4).

Table 1. Therapeutic effects after 3 months of treatment for IgA nephropathy in children (Cases (%))

<table>
<thead>
<tr>
<th>Group</th>
<th>Cases</th>
<th>Cure</th>
<th>Marked effect</th>
<th>Improvement</th>
<th>Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>TCM and Western medicine group</td>
<td>32</td>
<td>2 (6.3)</td>
<td>21 (65.6)</td>
<td>7 (21.9)</td>
<td>2 (6.3)</td>
</tr>
<tr>
<td>Western medicine group</td>
<td>22</td>
<td>0 (0.0)</td>
<td>10 (45.5)</td>
<td>10 (45.5)</td>
<td>2 (9.1)</td>
</tr>
</tbody>
</table>

Table 2. Curative effects after 6 months of treatment for IgA nephropathy in children (Cases (%))

<table>
<thead>
<tr>
<th>Group</th>
<th>Cases</th>
<th>Cure</th>
<th>Marked effect</th>
<th>Improvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>TCM and Western medicine group</td>
<td>30</td>
<td>10 (33.3%)</td>
<td>18 (60.0%)</td>
<td>2 (6.7%)</td>
</tr>
<tr>
<td>Western medicine group</td>
<td>22</td>
<td>5 (22.7%)</td>
<td>13 (59.1%)</td>
<td>4 (18.2%)</td>
</tr>
</tbody>
</table>

Table 3. Therapeutic effects for TCM symptoms for IgA nephropathy in children (Cases (%))

<table>
<thead>
<tr>
<th>Group</th>
<th>Cases</th>
<th>Cure</th>
<th>Marked effect</th>
<th>Improvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>TCM and Western medicine group</td>
<td>27</td>
<td>16 (59.3%)</td>
<td>8 (29.6%)</td>
<td>3 (11.1%)</td>
</tr>
<tr>
<td>Western medicine group</td>
<td>19</td>
<td>2 (10.5%)</td>
<td>7 (36.8%)</td>
<td>8 (42.1%)</td>
</tr>
</tbody>
</table>

Table 4. Scores on TCM symptoms before and after treatment for IgA nephropathy in children ( X ± s)

<table>
<thead>
<tr>
<th>Group</th>
<th>Common cold</th>
<th>Hyperhidrosis</th>
<th>Hypodynamia</th>
<th>Red dry throat</th>
<th>Sallow complexion</th>
<th>Total score</th>
</tr>
</thead>
<tbody>
<tr>
<td>TCM and Western medicine group</td>
<td>1.70±0.78</td>
<td>1.11±0.80</td>
<td>1.48±0.70</td>
<td>1.07±0.68</td>
<td>0.70±0.72</td>
<td>9.41±4.79</td>
</tr>
<tr>
<td>Western medicine group</td>
<td>0.22±0.42</td>
<td>0.07±0.27</td>
<td>0.30±0.47</td>
<td>0.04±0.19</td>
<td>0.04±0.19</td>
<td>0.81±1.18</td>
</tr>
<tr>
<td>TCM and Western medicine group</td>
<td>1.26±0.93</td>
<td>1.15±0.37</td>
<td>1.42±0.61</td>
<td>1.52±0.51</td>
<td>0.63±0.59</td>
<td>9.05±2.86</td>
</tr>
<tr>
<td>Western medicine group</td>
<td>0.79±0.71**</td>
<td>0.47±0.51</td>
<td>0.84±0.50</td>
<td>0.52±0.51</td>
<td>0.37±0.49*</td>
<td>3.42±2.52**</td>
</tr>
</tbody>
</table>

Notes: *P<0.05 as compared with the datum in group A after 6 months of treatment; **P<0.01 as compared with the datum in group A after 6 months of treatment.
Side-effects
During the course of treatment, the blood routine, functions of the liver and kidney, and blood coagulation were dynamically monitored. A mild rise of glutamic-pyruvic transaminase was found in one case of the group treated with both TCM and Western medicine; but it returned to normal after one week of liver-protecting treatment, and the child patient did not stop the above treatment.

DISCUSSION
IgA nephropathy is a common disease leading to chronic renal failure. However, the pathogenesis has not been clearly known yet, and the specific treatment is not available. Treatment with both TCM and Western medicine may better improve hematuria and albuminuria, reduce relapse and renal damage, and alleviate the toxic side-effects of Western medicine. In recent years, rich clinical experience has been accumulated for treating adult IgA nephropathy. TCM treatment of IgA nephropathy can effectively reduce the excretion of urinary RBC and urinary protein, stabilize the renal function, retard the progress of nephropathy, improve renal pathological structure, obviously inhibit the multiplication of mesangium cell and matrix, alleviate glomerular sclerosis and saccule adhesion, reduce or eliminate sedimentary immunocomplex, regulate the inflammatory factor, and alleviate the damage to glomerulus and interstitial cells of the renal tubules by inflammatory reaction, thus improving the function of interstitial cells of the renal tubules.11-13

In the present study, the therapeutic effects of TCM for IgA nephropathy in children were evaluated. The results show that both the treatment with TCM and Western medicine and the treatment with Western medicine can improve the clinical symptoms and reduce the urinary protein and urinary RBC. But the cure and marked effect rates in the group of TCM and Western medicine were higher than those in the group of Western medicine (Table 1 and Table 2). Suggesting that TCM plus Western medicine may better and rapidly improve the clinical symptoms and reduce the urinary RBC and urinary protein.

As expected, the TCM symptoms were obviously improved in the group treated with both TCM and Western medicine. After treatment, there was significant difference in the total score between the two groups, indicating TCM plus Western medicine indicating that can more effectively improve the TCM symptoms, strengthen the body constitution, and balance the level of related T cell factor.19 Therefore, treatment with both TCM and Western medicine can be adopted as an ideal therapy for IgA nephropathy in children.

REFERENCES
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(Received December 22, 2010)