a structural chromosomal abnormality is found. As can be seen from the karyotypes reported in Table 3 of our article[2-4] the karyotypes of those with an unbalanced structural chromosomal abnormality inherited from a carrier parent with the balanced structural abnormality are designated as either "mat" or "pat".

In future studies, we hope to further analyze the genotype and phenotype correlation of specific types of chromosome abnormalities, and add more clinical evidence to the existing database to benefit the clinicians more. Some of these have already been published.[1-4]

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References

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Tripterygium wilfordii Hook F is efficacious in the treatment of Henoch-Schönlein purpura nephritis in children

I read with interest the recently published article by Huang et al.[1] The article is very informative and has brought an utmost important insight on chronic glomerulonephritis in children. It is an interesting issue, because glomerulonephritis such as Schönlein-Henoch nephritis (HSPN) may lead to renal failure in children and adolescents. The well-presented clinical features and histopathological changes described in the article are valuable for pediatricians in diagnosing HSPN in the high-risk population.

Huang et al.[1] reported nine HSPN patients with the severest histopathological changes. They were classified as the International Study of Kidney Disease in Children (ISKDC) grade VI, and all had moderate to heavy proteinuria; all the patients in that series recovered well after treatment. Their treatment protocol is an imperative hint for managing HSPN patients. We found that 7/9 patients were given oral tripterygium glycosides; and the authors especially stressed in the methods section that tripterygium glycosides was only used in China. As they stated that tripterygium glycosides has been widely used in China as an effective immunosuppressant. It has been used for the treatment of glomerulonephritis for more than 30 years with dramatic antiproteinuric effects.[5-8] Disappointingly, they did not provide more information on tripterygium glycosides use for treatment of glomerulonephritis in the discussion section.

To our knowledge, tripterygium glycosides is the major active component of tripterygium wilfordii Hook F, which was firstly used in the nephritis treatment in 1977 by Li et al.[2] Tripterygium glycosides has been used in more than 100 000 patients in his institute.[6] It has been proven with multi-immunosuppress efficacy but with less side-effects than other immunosuppressant agents in animal and cell researches. Randomized-controlled studies have been carried out in adults. Due to the ethical issues, no clinical trials have been carried out in children; however, a nearly forty-year clinical experience in China has shown that this agent is safe, economical and efficacious for treating nephritis diseases in children. Therefore, we think that the author should introduce more information in the discussion section; the experience of treating severe HSPN patients will be helpful for pediatricians and nephrologists worldwide.

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4 Chen ZH, Qin WS, Zeng CH, Zheng CX, Hong YM, Lu YZ, et al. Triptolide reduces proteinuria in experimental membranous
The current retrospective study was aimed to define the clinical manifestations, pathological features, and prognosis of children with grade VI HSPN, our results also showed that tripterygium glycosides (T glycosides) alone or in combination with glucocorticoid had nephroprotective effects on grade VI HSPN in children.¹

T glycosides (leigongteng multi-glycosides tablets) used in this study is the debarked root preparation of Tripterygium wilfordii Hook F (TWHF), which is known as leigongteng or thunder god vine in traditional Chinese medicine. Since the 1960s, as an

Table. Summary of 15 trials on T glycosides administered in the treatment of HSPN in children

<table>
<thead>
<tr>
<th>Studies</th>
<th>No. of Age (y)</th>
<th>Sex m/f</th>
<th>Pathol grade</th>
<th>Intervention</th>
<th>Dosage</th>
<th>Control group</th>
<th>Background therapy</th>
<th>Intervetion</th>
<th>Dosage</th>
<th>Control group</th>
<th>Background therapy</th>
<th>Adverse effects</th>
<th>Follow-up dur (mon)</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zhao et al[9]</td>
<td>80 2-14</td>
<td>44/36</td>
<td>Unknow</td>
<td>T glycosides tab 1 mg/kg/d max &lt;60 mg/d</td>
<td>3-6</td>
<td>Usual care</td>
<td>Prednisone 1.5-2 mg/kg/d</td>
<td>Unknow</td>
<td>15</td>
<td>T glycosides combined with prednisone was superior to prednisone alone</td>
<td>T glycosides was superior to prednisone</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Xu et al[10]</td>
<td>75 2-16</td>
<td>45/30</td>
<td>Unknow</td>
<td>T glycosides tab 1 mg/kg/d max &lt;90 mg/d</td>
<td>3</td>
<td>Usual care</td>
<td>Prednisone 1 mg/kg/d</td>
<td>No</td>
<td>Unknow</td>
<td>T glycosides was superior to prednisone</td>
<td>Digestive, Hepatotoxity, Leukopenia,</td>
<td>12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wang et al[11]</td>
<td>59 5-14</td>
<td>42/17</td>
<td>Unknow</td>
<td>T glycosides tab 1 mg/kg/d max &lt;60 mg/d</td>
<td>3</td>
<td>Usual care</td>
<td>Prednisone 1-2 mg/kg/d</td>
<td>No</td>
<td>Unknow</td>
<td>T glycosides was superior to prednisone</td>
<td>T glycosides was superior to prednisone</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sheng et al[12]</td>
<td>172 2-18</td>
<td>98/74</td>
<td>I-III grade ≤25%</td>
<td>T glycosides tab 1.5 mg/kg/d max &lt;90 mg/d</td>
<td>3</td>
<td>Usual care</td>
<td>Prednisone 1 mg/kg/d</td>
<td>No</td>
<td>Unobvious</td>
<td>T glycosides was superior to prednisone</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wang et al[13]</td>
<td>104 3-12</td>
<td>56/48</td>
<td>Unknow</td>
<td>T glycosides tab 1 mg/kg/d max &lt;60 mg/d</td>
<td>3-6</td>
<td>Usual care</td>
<td>Prednisone 1.5-2 mg/kg/d</td>
<td>Digestive, Hepatotoxity, Leukopenia,</td>
<td>24</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hu et al[14]</td>
<td>60 3.5-14.6</td>
<td>37/23</td>
<td>I-III grade ≤25%</td>
<td>T glycosides tab 1-1.5 mg/kg/d max &lt;90 mg/d</td>
<td>3</td>
<td>Usual care</td>
<td>Captopril 1 mg/kg/d</td>
<td>Hepatotoxity, Leukopenia,</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peng et al[15]</td>
<td>46 3-12</td>
<td>48/16</td>
<td>Unknow</td>
<td>T glycosides tab 1 mg/kg/d max &lt;60 mg/d</td>
<td>6-9</td>
<td>Usual care</td>
<td>Prednisone 1.5-2 mg/kg/d</td>
<td>9</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Zheng et al[16]</td>
<td>66 3-18</td>
<td>34/32</td>
<td>Unknow</td>
<td>T glycosides tab 1 mg/kg/d max &lt;60 mg/d</td>
<td>3-6</td>
<td>Usual care</td>
<td>General therapy</td>
<td>Unknow</td>
<td>2</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liao et al[17]</td>
<td>40 3-17</td>
<td>8-17</td>
<td>Unknow</td>
<td>T glycosides tab 1 mg/kg/d</td>
<td>6</td>
<td>Leflunamide</td>
<td>Prednisone 1 mg/kg/d</td>
<td>Unknow</td>
<td>6</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zhou et al[18]</td>
<td>29 3.5-13.5</td>
<td>16/13</td>
<td>Unknow</td>
<td>T glycosides tab 1.5 mg/kg/d</td>
<td>6-9</td>
<td>Usual care</td>
<td>Prednisone 1-2 mg/kg/d</td>
<td>Unknow</td>
<td>12</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ma et al[19]</td>
<td>38 5-14</td>
<td>18/20</td>
<td>Unknow</td>
<td>T glycosides tab 1 mg/kg/d</td>
<td>6-9</td>
<td>Usual care</td>
<td>Prednisone 1.5-2 mg/kg/d</td>
<td>Not obvious</td>
<td>9</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zhang et al[20]</td>
<td>53 2.5-13</td>
<td>29/24</td>
<td>Unknow</td>
<td>T glycosides tab 1 mg/kg/d</td>
<td>3</td>
<td>Usual care</td>
<td>Prednisone 1.5-2 mg/kg/d</td>
<td>Unknow</td>
<td>3</td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>Zhang et al[21]</td>
<td>50 3-16</td>
<td>33/17</td>
<td>Unknow</td>
<td>T glycosides tab 1-1.5 mg/kg/d</td>
<td>3</td>
<td>Usual care</td>
<td>Prednisone 1-1.5 mg/kg/d</td>
<td>Unknow</td>
<td>12</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wang[22]</td>
<td>43 3-14</td>
<td>39/51</td>
<td>Unknow</td>
<td>T glycosides tab 1.5 mg/kg/d</td>
<td>3</td>
<td>Prednisone 1.5 mg/kg/d</td>
<td>Unknow</td>
<td>18-72</td>
<td></td>
<td></td>
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</tbody>
</table>

The study from Ding et al[13] was a randomized multi-center, and other studies were randomized single center studies. All references were written in Chinese. Pts: patients; y: year; m/f: male/female; Pathol: pathology; mon: month; dur: duration; tab: tablets; HSPN: Schönlein-Henoch nephritis; NS: nephrotic syndrome; Dur: duration.

do: 10.1007/s12519-016-0032-z
Triptolide is well known as a principal ingredient of TWHF preparations and displays potent biological activities. Initially, triptolide was shown to specifically target some transcription factors. Recently, several triptolide-binding proteins, including xeroderma pigmentosum B (XPB), polycystin-2 (pc-2), and dCTP pyrophosphatase 1 (DCTPP1), have been identified to update the mechanisms of triptolide action. XPB is a subunit of the general transcription factor TF II H that is essential for RNA polymerase II to recognize promoters and nucleotide excision repair in response to DNA damage. Triptolide can bind covalently to human XPB and inhibit RNA polymerase II-mediated transcription and probably interfere with repairing DNA damage. RPBI is the largest RNA polymerase II subunit, and critical for mRNA transcription. RPBI level can be lowered by triptolide. Therefore, at present, triptolide has been identified as a global transcription inhibitor (Fig.).

In our study, histopathological features of grade VI HSPN showed diffuse glomerular mesangial and endocapillary proliferation with double contour of the capillary walls and mesangial cell interposition. The therapeutic effects of T glycosides with/without glucocorticoid on children with grade VI HSPN may be related partially to the global transcription inhibition by triptolide.

In addition to its transcription inhibition function, triptolide also showed the transcription-independent actions through binding to PC-2, DCTPP1 and the other proteins, and enhanced the mRNA or protein levels of several molecules, including p53, nerve growth factor (NGF), etc. Therefore, the action mechanism of triptolide and other components isolated from TWHF should be investigated in depth in order to provide more evidence for the future therapeutic choice.

Systemic toxicities of TWHF preparations are extensively involved in multiple tissues and organs, including the digestive tract, bone marrow, heart, urogenital system and skin. Those toxicities are dose-dependent and could be monitored by dosage adjustments. TWHF preparations may cause ovarian...
injury resulting in menstruation, which is reversible if the agent is withdrawn in time.\textsuperscript{14} TWHF preparations have also been reported to cause reversible infertility in male patients in numerous studies. However, one animal study showed that the long-term (82 days) administration of triptolide induced deleterious effects on spermatogenesis and irreversible infertility even after cessation of the treatment.\textsuperscript{135} Therefore, the reproductive toxicity of TWHF preparations is difficult to monitor in clinical treatment especially in children. Indeed, the potential systemic and reproductive toxicity limits the clinical application of TWHF preparations in children. We try to reduce the side effects by shortening treatment duration, closer clinical observation and laboratory examination in patients treated with HSPN in our department.

In future, continuous efforts should be made to clarify the molecular targets of TWHF components, produce new derivatives to reduce toxicity, and design high-quality trials to confirm the balance between benefits and adverse effects in children and adults.

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