Serum TGF–β1, MMP–9 and TIMP–1 change in patients with pustules psoriasis after treatment of Huayinjiedu decoction

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1. Introduction

Pustular psoriasis is severe type of psoriasis. It is lasting and recurring. Acitretin is an effective oral drug for treating psoriasis erythroderma and pustular psoriasis. However, it is of side-effect and recurring. Huayinjiedu decoction is effective proved recipe by Ouyang. In this study, we aim to study the effect of Huayinjiedu decoction on transforming growth factor β1 (TGF–β1), matrix metalloprotease (MMP)-9 and tissue inhibitor of metalloproteinase-1 (TIMP-1), and to explore the mechanism of Huayinjiedu decoction.

2. Materials and methods

2.1. Clinical information

A total of 60 cases with pustular psoriasis visited from February 2011 to November 2013 were selected. All cases accorded to diagnosis standard of pustular psoriasis both in Western medicine and tradition Chinese medicine. They aged 21-71 years old, and had no drug treatment in 3 months before visiting. All cases were randomly divided into control group and observation group. Patients with other skin diseases, with severe viscera diseases, with glucocorticoid treatment in 1 month before, with external use of glucocorticoid in large area 1 week before treatment, pregnant patients and lactating patients were excluded. There were 30 cases in observation group, including 13 females and 17 males, aged 22-67 years old, with PASI score as (37.27±6.19), average age as (37.71±12.8) years old, and average disease course as (8.64±5.43) years old. There were 30 cases in control group, including 14...
females and 16 males, aged 20-69 years old, with PASI score as (38.83±7.86), average age as (36.48±12.34) years old, and average disease course as (8.51±7.89) years old. No function injury of heat, lung or kidney, or no dyslipidemia were found in all subjects. There was no significant difference in gender, age, disease course, disease situation, PASI score etc (P>0.05), and were comparable. Another health volunteers were selected as normal control group, including 12 females and 18 males, with average age as (31.9±13.16) years old. There was no significant difference in gender and age among three groups (P>0.05), and were also comparable. All patients signed informed consent before trial.

2.2. Treatment method

Patients in observation group were treated with Huayinjiedu decoction (including rehmannia rhizome, radix paeonia, Salvia miltiorrhiza, lithospermum, la lang grass rhizome, honeysuckle flower, air potato, sarsaparilla, glabrous greenbrier rhizome, etc), once per day, po, for twice. Patients in control group were treated by acitretin, po., 10 mg every time, twice per day. Besides, all patients were treated by external use of self-prepared cod liver oil ointment. The treatment course was 4 weeks, and all patients were treated for 2 courses. The psoriasis affected area and psoriasis area and severity index (PASI) were used to assess the efficacy\[3\] before treatment and 4, 8 weeks after treatment. The trial was terminated if the disease situation was aggravated and severe side effect occurred. Routine examination of blood and urine, test of liver and kidney function were performed before and after treatment. And the side effect was also observed.

2.3. Detection method

Five mL venous blood was extracted from elbow vein before treatment and 4, 8 weeks after treatment, and centrifugated at 2 000 rp/min for 15 min. The upper serum was obtained and restored at -20 °C. TGF-β1, MMP-9 and TIMP-1 were determined by ELISA assay. The kit was provided by Boster BioTech Limited Company of Wuhan.

2.4. Statistical analysis

All data were expressed as mean±SD, and analyzed by t test and χ². The correlation analysis was performed by Spearman correlation analysis. It was considered as significant difference when P<0.05.

3. Results

3.1. PASI score

There was significant difference in PASI score before and after treatment in observation group and control group (P<0.01). The difference was also significant between 8 weeks and 4 weeks after treatment (P<0.01) (Table 1).

3.2. Indexes result

Compared with normal control group, TGF-β1, MMP-9 and TIMP-1 levels were significantly increased in observation group and control group before treatment and 4 weeks after treatment (P<0.01). Eight weeks after treatment, the differences in these indexes were significant between observation group and control group (P<0.01) (Table 2).

Table 1

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Before treatment</th>
<th>4 weeks after treatment</th>
<th>8 weeks after treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>30</td>
<td>37.27±6.19</td>
<td>19.46±1.52*</td>
<td>6.51±2.71#</td>
</tr>
<tr>
<td>Control</td>
<td>30</td>
<td>38.83±7.86</td>
<td>17.72±1.69*</td>
<td>11.24±7.35*#</td>
</tr>
</tbody>
</table>

*Compared with before treatment, P<0.01; #Compared with 4 weeks after treatment, P<0.01.

Table 2

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Before treatment</th>
<th>4 w</th>
<th>8 w</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal control</td>
<td>30</td>
<td>TGF-β1</td>
<td>152.14±37.21</td>
<td>154.85±38.97*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>MMP-9</td>
<td>49.37±6.34</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>TIMP-1</td>
<td>69.31±22.59</td>
<td></td>
</tr>
<tr>
<td>Observation</td>
<td>30</td>
<td>TGF-β1</td>
<td>498.32±96.35</td>
<td>287.65±45.64*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>MMP-9</td>
<td>93.46±39.38</td>
<td>65.43±7.15*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TIMP-1</td>
<td>197.53±61.28</td>
<td>145.29±23.56*</td>
</tr>
<tr>
<td>Control</td>
<td>30</td>
<td>TGF-β1</td>
<td>501.43±98.71</td>
<td>311.21±62.43*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>MMP-9</td>
<td>89.51±18.27</td>
<td>67.24±48.45*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TIMP-1</td>
<td>201.49±62.57</td>
<td>153.75±42.71*</td>
</tr>
</tbody>
</table>

*Compared with normal control group, P<0.01; #Compared with before treatment, P<0.01; ﹟Compared with control group, P<0.01.

3.3. Correlation analysis

Spearman correlation analysis showed that there were positive correlation among TGF-β1, MMP-9 and TIMP-1 (P<0.05), and they were also positively correlated with PASI (P<0.05).

3.4. Side effect

There were 5 cases with increased triacylglycerol in control group, which was decreased to normal level after treatment. All patients had dry mouth and lip and desquamation to varying degree. All patients had normal level of blood sugar and lipid.

4. Discussion

Psoriasis is a common chronic recurring skin disease. The main skin lesion is red maculopapule or plaque with clear boundary and with coverage by silver scale\[4\]. In serious cases, it can be developed into erythroda psoriaticum with extensive pustule, leading to crippled joint. Pustular psoriasis is one special type and is characterized by red maculopapule or plaque with clear boundary and with coverage by silver scale of skin lesion. The corelation analysis was performed by Spearman correlation analysis. It was considered as significant difference when P<0.05.

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tumor metastasis. It plays different roles in occurrence and
development of different lesions in different organs. Therefore,
TGF-β1 level can be used as an indicator in diagnosis and
monitoring of diseases, and even as a treatment target. Yang et
al detected TGF-β1 level in patients with psoriasis arthritis and
patients with psoriasis vulgaris. The result shows that the difference
in TGF-β1 is significant. So they propose that dynamic monitoring
of TGF-β1 is necessary for treatment of psoriasis arthritis.

MMP and TIMP are two important enzyme systems in extracellular
matrix synthesis and metabolic balance, and they participate in
various physiological processes related with proteolysis and
remodeling of extracellular matrix. MMP can degrade extracellular
matrix, play a part in neovascularization, regulate cell adhesion, and
activate potential protein. TIMP can inhibit activity of MMP, and
promote cell proliferation[8,9]. By in situ hybridization, it is found
MMP-12 mRNA and MMP-9 mRNA expression in macrophage
invading into epidermal and inflammatory cell infiltrating in dermis[10].

In skin lesion, capillaries of dermal papilla are dilated and tortuous,
with high permeability and increased vessels. It is thought that
this change always occurs in postcapillary venule, and the earliest
tissue pathological changes are vascularization and distribution
change. Vascularization is the result of interaction of various factors
and multi-step coordinated development, in which endothelial cell
proliferation, infiltration, and basement membrane degradation are
most important steps. It is reported that TGF-β has significant
inhibition effect on epithelial cell, and has significant stimulation
effect on epithelial cell. MMP-9 is imperative for angiogenesis [13]. TIMP-1 is an active and
inhibitor is effective in treatment of psoriasis arthritis.

We find that Huayinjiedu decoction plays a role in treatment of
pustules psoriasis via regulating immunoregulation, cell proliferation and
angiogenesis, and it can also be used in treatment of other types of psoriasis.

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