Influence of tacrolimus combined mometasone furoate on serum inflammatory factors and immune function in children with eczema

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ABSTRACT

Objective: To study the influence of tacrolimus combined mometasone furoate on serum inflammatory factors and immune function in children with eczema. Methods: A total of 122 children with eczema based on random data table method were divided into control group (n=58) and observation group (n=64). The control group were given 0.1% mometasone furoate ointment treatment and the observation group of patients were given 0.03% tacrolimus ointment treatment on the basis of the control group. After 3 weeks, the serum levels of inflammatory factors and index of immune function before and after treatment were compared. Results: Before the treatment, the levels of IL-2, IL-4, IL-5, INF-γ, CD3+, CD4+, CD8+, CD4+/CD8+ were similar in two groups, there was no statistically significant difference. Comparing the levels of inflammatory after treatment, IL-2, INF-γ levels of two groups were significantly higher than those of the same group before treatment, and IL-2, INF-γ levels of the observation group were significantly higher than those of the control group. After treatment, IL-4 IL-5 levels of the two groups were significantly declined and IL-4 IL-5 levels of the observation group were significantly lower than those of the control group. Immune function indicators level detection indicated that the levels of CD3+, CD4+, CD8+, CD4+/CD8+ of control group before and after treatment had no significant change. After treatment, the levels of CD3+, CD4+ and CD4+/CD8+ of observation group were significantly increased and were significantly higher than those of the control group, whereas the levels of CD8+ were significantly reduced and significantly lower than those of the control group. Conclusions: Tacrolimus combined mometasone furoate is an effective therapy to adjust the serum levels of inflammatory cytokines and improve immune function of children eczema. Indeed, it has a certain clinical value.

1. Introduction

Children eczema is a common inflammatory skin disease clinically. Its clinical symptoms are more characterized by erythema, skin lesions, erosion and accompanied by severe itching and it is easy to repeat, prolonged, and seriously threatens the quality of children’s life. The disease causes more complex, and its pathogenesis is still unclear, but the study suggests that the occurrence and T cell-mediated immune imbalance[1-2]. Tacrolimus as a new drug was used for anti-inflammatory and clinical treatment of autoimmune repellency reaction[3,4]. Furoic acid mo betamethasone is one of the effective drug treatment of infant skin disease, which belongs to medium-effect corticosteroid drugs[5]. This study was to explore the effective of inflammatory factors and immune function of children with eczema by treating with tacrolimus combined moetasone furoate.

2. Materials and methods

2.1. Clinical data

A total of 122 children with eczema were admitted into the objects of this study in our hospital dermatological department from September 2015 to April 2015. The eczema degree of all
children met the related diagnosis standard[6], and according to the standard[7] of Rajka and Langeland, the eczema degree of these children belongs to moderate eczema. Ruled out: (1) the skin damaged area exists serious infections; (2) with blood coagulation dysfunction, chronic infectious diseases and autoimmune diseases; (3) taken within a week of glucocorticoid (a hormone steroid) or other immunosuppressive drugs treatment; (4) participate in other research and treatment at the same time; (5) those who are allergy to the drug used in the study; (6) those who have poorer compliance, fail to complete the treatment in strict accordance with the doctor's advice, and drop off halfway; (7) those who are admitted the hospital with incomplete clinical data. Based on random data table method, the 122 patients were divided into control group and observation group. The control group included 58 cases of children with 35 male children and 23 female patients, whose ages were range from 2 to 12 years old; For the observation group, there were 64 cases of children, including 39 male children and 25 female children, whose ages were range from 2 to 13 years old. The information of the gender structure and age of two groups' children is relatively close, without big difference (P>0.05). Besides, this study was in accord with the permit standard of hospital ethics committee, the study process conformed to regulations, and all the children and their families have been informed to receive the treatment contently and voluntarily.

### 2.2. Therapeutic method

Two groups of patients were given by conventional treatment methods, such as anti-inflammatory, anti-itching and other conventional methods at first. Then, based on the conventional treatment method, the control group of patients were given by 0.1% furoic acid mo betamethasone ointment namely Eloson (produced by Shanghai Schering Pharmaceutical Co., Ltd., Approval No. H19991418). And then spread an adequate amount of the ointment on their affected area in the morning with twice a day for 3 weeks. While the observation group of children were given by 0.03% tacrolimus ointment namely Protopic (produced by Astellas Pharmaceutical (China) Co. Ltd., Approval No. J20140147). And spread the tacrolimus ointment on their affected area on the morning with once a day. At the same time, also spread 0.1% furoic acid mo betamethasone ointment on their affected area once a day for 3 weeks. It didn’t stop the treatment until their lesions were dissipated. Outside the dose of medication every time by using fingertips unit (FTU), namely 1 FTU is equivalent to 0.5 g ointment, one hand area equivalent to adults (both the front and back of the card).

### 2.3. Observation index

Before treatment and 3 weeks after treatment, patients’ peripheral venous blood of an empty stomach was extracted to detect the serum levels of inflammatory factors and related parameters of immune function. Inflammatory cytokines included interleukin 2 (IL-2), interleukin 4 (IL-4) and interleukin-5 (IL-5) and interferon gamma (INF-γ). Detection method was ELISA method, and enzyme-linked kits was bought from Shanghai Biological Technology Co., Ltd. Use BD both FACS Canto II flow cytometry instrument to detect T lymphocyte subsets (CD3*, CD4*, CD8*, CD4*/CD8*) level, and specific steps were in strict accordance with the operating instructions.

### 2.4. Statistical analysis

Research data processing and analysis used SPSS 17.0 statistical software, and the level of inflammatory factors and indexes of immune function accord with normal distribution; representation method was terms of mean ± standard deviation (Mean ± SD); comparison was by t test. Statistics P<0.05 was the standard of statistical significance in differences.

### 3. Results

#### 3.1. Serum inflammatory factors

Inflammatory factor of two groups before treatment: comparing the levels of IL-2, IL-4, IL-5 and INF-γ, there were no significant difference (P > 0.05). After treatment, the levels of IL-2 and the INF-γ were respectively (41.85 ± 5.07) ng/L and (39.86 ± 8.23) ng/L in observation group, while these levels in the same group were significantly higher than those before treatment (P<0.05) and were significantly higher than those of the control group after treatment; the difference was statistically significant (P<0.05); After treatment, the levels of IL-4 and IL-5 in the control group were (36.73 ± 7.27) ng/L and (54.22 ± 4.94) ng/L respectively, while the levels of IL-4 and IL-5 in observation group were (30.76 ± 6.86) ng/L and (38.14 ± 4.81) ng/L respectively. Compared with those before treatment in the same group, they were significantly lower (P<0.05), and the levels in the observation group were significantly lower than those of the control group (P<0.05), shown in Table 1.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Treatment time</th>
<th>IL-2 (ng/L)</th>
<th>IL-4 (ng/L)</th>
<th>IL-5 (ng/L)</th>
<th>INF-γ (ng/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>58</td>
<td>Pre treatment</td>
<td>25.47±5.61</td>
<td>44.89±8.12</td>
<td>74.59±7.83</td>
<td>23.52±5.69</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Post treatment</td>
<td>32.64±3.82</td>
<td>36.73±7.27</td>
<td>54.22±4.94</td>
<td>34.55±7.98</td>
</tr>
<tr>
<td>Observation group</td>
<td>64</td>
<td>Pre treatment</td>
<td>25.60±4.96</td>
<td>44.57±8.23</td>
<td>75.02±8.13</td>
<td>23.47±5.72</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Post treatment</td>
<td>41.85±5.07</td>
<td>30.76±6.86</td>
<td>38.14±4.81</td>
<td>39.86±8.23</td>
</tr>
</tbody>
</table>

Note: # showed compared with before treatment in the group, P<0.05; \* showed horizontal comparison in two groups after treatment, P<0.05.
Table 2.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Treatment time</th>
<th>CD3⁺(%)</th>
<th>CD4⁺(%)</th>
<th>CD8⁺(%)</th>
<th>CD3⁺/CD8⁺</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>58</td>
<td>Pre treatment</td>
<td>56.23±5.29</td>
<td>31.56±3.83</td>
<td>32.98±4.46</td>
<td>1.03±0.21</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Post treatment</td>
<td>58.24±6.32</td>
<td>33.16±4.97</td>
<td>30.76±5.81</td>
<td>1.10±0.39</td>
</tr>
<tr>
<td>Observation group</td>
<td>64</td>
<td>Pre treatment</td>
<td>55.72±5.27</td>
<td>31.64±3.65</td>
<td>32.84±5.31</td>
<td>1.03±0.34</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Post treatment</td>
<td>62.26±4.49</td>
<td>37.18±4.05</td>
<td>24.17±3.19</td>
<td>1.35±0.42</td>
</tr>
</tbody>
</table>

Note:** showed compared with before treatment in the group, *P*<0.05; # showed horizontal comparison in the two groups after treatment, *P*<0.05.

3.2 Comparing the levels of immune function indexes before and after treatment

Before the treatment, two groups of CD3⁺, CD4⁺, CD8⁺, CD4⁺/CD8⁺ levels are relatively similar, the difference is not significant (*P*>0.05). Compared with before treatment in the same group, the levels of CD3⁺, CD4⁺ and CD4⁺/CD8⁺ have different degrees of reduction and CD8⁺ levels were increased slightly in control group after treatment. The difference is not significant (*P*>0.05). The levels of CD3⁺, CD4⁺ and CD4⁺/CD8⁺ in observation group after treatment were (62.26±4.49)%, (37.18±4.05)% and (1.35±0.42), which were significantly higher than those before the same group and control group after treatment; the difference was statistically significant (*P*<0.05). The CD8⁺ level of observation group after treatment was (24.17±3.19)%, which is significantly reduced comparing with the same group before the treatment (*P*<0.05), and significantly lower than the control group (30.76±5.81)%. It has significant difference (*P*<0.05), shown in Table 2.

4. Discussion

Children eczema is an inflammatory skin disease caused by the external factors and internal factors. Its pathogenesis is more complex, with itching, exudative, recurrent and pleomorphic clinical manifestations[8]. The disease can occur in any season, any age and any place. since children skin development is not yet perfect and cuticular corneous layer is very thin and their immune resistance ability is weak, therefore, it is easy to produce allergic reaction[9]. The main purpose of clinical treatment is to control the clinical symptoms, reduce recurrence and improve patient quality of life, and local treatment is the main treatment means[10]. Topical corticosteroids inhibitor drugs are the main drugs in the clinical treatment of eczema, but they can cause skin atrophy, angiotelectasis and secondary infection of adverse drug reactions happened if long-term use[11,12]. So it is key to screening safe and effective treatment drugs.

Moetasone furoate belongs to synthetic glucocorticoid betamethasone. Because of its distinctive molecular structure and formula, it has strong skin penetration, and therefore it has strong anti-inflammatory effects, work fast, relieving itching and good anti seepage effect. Its clinical curative effect is equal to the powerful effect of glucocorticoid hormone drugs[13]. In addition, the percutaneous absorption rate is low and its effect of hypothalamic-pituitary-adrenal axis is equal to the inefficiency of glucocorticoid hormone drugs, thus it has less adverse reaction and high security features[14]. Moetasone furoate is considered to be conventional topical drug for the treatment of eczema in children. Related research pointed out that the curative effect of treating children eczema can amount to 78.5% with less adverse reaction and no systemic adverse reactions happen[15]. Tacrolimus is extracted from Streptomyces cultures of large ring lactone class antibiotic and it was the first successful production of topical immune modulators. Its mechanism is mainly by inhibiting calcineurin activity of T cell to inhibit T cell activation and cytokine in immune cells transcription and synthesis, meanwhile inhibits skin mast cells, eosinophils, such as the release of inflammatory medium[16,17]. In addition, tacrolimus has no effect of inhibiting the synthesis of collagen. So although use for a long time, there will be no skin atrophy, the hypothalamus - pituitary - adrenal axis inhibition series of adverse reactions occur and will not increase the risk of infection[18].

So far, the occurrence of children eczema mechanism is still unclear, but the study suggests that it has relationship more closely with the occurrence and the imbalance of Th1 and Th2 cells activity and immunity dysfunction[19]. TNF-α, IL-2 and INF-γ are secreted by Th1 cytokine, so they can be referred to as Th1 cytokines. They can mediate cellular immunity and inhibit the synthesis of IgG and Th2 type cytokines[20]. IL-4, IL-5 belongs to the Th2 type cytokines and they can mediate humoral immunity. The levels of IL-4 and IL-5 Th2 type cytokines are abnormally raised in the phase of skin lesions of patients with eczema. IL-4 can induce the synthesis of IgG and inhibit Th1 cells to secrete INF-γ and reduce the Th1 cytokine levels at the same time, thus aggravating Th1/Th2 ratio imbalance[21,12]. This study found that both kinds of solution treatment can effectively increase the level of IL-2 and INF-γ, lower levels of IL-4 and IL-5, and the regulating role of type Th1 and Th2 cytokines better after treatment with tacrolimus. The results further confirmed that moetasone furoate has strong anti-inflammatory effects, and on the basis of this combined with tacrolimus, so the effective of improve inflammatory factor levels is more. The reason may be related to s the adjustment role of Th1/Th2 imbalance state caused by tacrolimus.

T cell-mediated cellular immunity plays an important role in occurrence and development of eczema. CD4⁺ T cells is mainly mediated by T lymphocytes and mononuclear phagocytes infiltration series exudative inflammatory reactions, CD8⁺ T cells can directly inhibit cellular immune response when it reaches higher levels[23].
This study found that there is no obvious improvement of the level of T lymphocyte in children with eczema before and after treatment with moetasone furoate, which reveal that moetasone furoate is useless to immune function. Compared with before treatment, the levels of CD3+, CD4+, CD8+, CD4+/CD8+ were significantly improved after treatment with tacrolimus, which explain tacrolimus considerably the curative effect of treating children eczema may be related to its effect on the regulation of cellular immunity. The results revealed that tacrolimus plays an important role for children with eczema in regulating immune function state.

To sum up, both moetasone furoate and tacrolimus are have strong anti-inflammatory effects in the treatment of childhood eczema. Because of the effect of superimposition can further adjust the serum anti-inflammatory effects in the treatment of childhood eczema. To sum up, both moetasone furoate and tacrolimus are have strong anti-inflammatory effects in the treatment of childhood eczema.

References


