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Study on effect of Traditional Chinese Medicine Jianpi Chushi decoction and ointment on chronic eczema

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ABSTRACT

Objective: To study the effects of Traditional Chinese Medicine Jianpi Chushi decoction and ointment on chronic eczema.**Methods:** DNCB acetone solution was used to sensitize the skin of back and ears of 36 rats in order to establish chronic eczema model. A total of 36 rats were divided into four groups of 9 randomly including oral medicine group, external inunction group, combination therapy group, and model control group respectively. Besides, the blank group of 4 healthy rats were set. The oral medicine group was given Traditional Chinese Medicine Jianpi Chushi decoction [*Poria cocos*, Chinese yam, *Cortex dictamni*, *Zaocys dhumnade*, *Rhizoma atractylodis*, *Pericarpium citri reticulatae*, *Scutellaria baicalensis*, Radix Sophorae Flavescentis, Raw Radix Paeoniae Alba, Licorice roots (Northwest Origin)] by gastric infusion (1.6 g/mL·5 mL/d); the external inunction group was given Qingpeng ointment on the skin, the combination therapy group was given Jianpi Chushi decoction by gastric infusion and Qingpeng ointment combination therapy. The model control group was given normal saline (NS) of the same volume by gastric infusion and vaseline on skin. Continuous administration 15 d and stopped for 3 d. The thickness difference and weight difference of left and right ear of every group were measured and the degree of ear swelling were evaluated. The CD4+ and CD8+ content and the IL-2, IL-4 level of serum were detected, and the inflammatory cells counts of back skin were recorded.**Results:** After treatment, the degree of ear swelling of oral medicine group, external inunction group and combination therapy group significant decreased compared with model control group ($P < 0.05$). The CD4+, CD8+ cell content and IL-2 level of oral medicine group, external inunction group, combination therapy group and model control group significant decreased compared with blank group, and IL-2 level and the inflammatory cells count increased. After 15 d of treatment, the CD4+, CD8+ cell content and IL-2 level of serum of oral medicine group, external inunction group and combination therapy group raised and the IL-4 level and the inflammatory cells count had significant decreased compared with model control group, and the effect of combination therapy group was more obvious ($P < 0.05$).**Conclusions:** Oral Jianpi Chushi decoction could treat chronic eczema effectively, and oral Chinese medicine combined with ointment could enhance and speed up the efficacy.

1. Introduction

Chronic eczema is a very common skin inflammation, classically appearing as persistent itching, rubedo, infiltration, thickening, roughness, etc. Upon the onset of the disease, the life

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quality of patients would be affected severely [1]. The pathogenesis of chronic eczema is complicated, mainly caused by metabolic abnormalities, endocrine dyscrasia, digestive system disease of the patients themselves, virus and bacteria in the external environment, and the stimulation of temperature & humidity and foreign body allergen, etc. [2–5], which resulted in treatment difficulties to some degrees. Some common drugs for external use always treated the symptoms, not the disease, causing the patients' condition repeatedly

manifesting. Many prescriptions in Traditional Chinese Medicine were chosen to treat eczema, the most common ones including Sanhuang anti-itching lotion, Xiaofeng powder, Chushi decoction, etc. [6–8], of which Jianpi Chushi decoction was applied most. At this stage, there were already many studies on the application of decoction to remove dampness in eczema treatment, but their specific mechanism of action has not been fully and systematically researched, in addition, further improvement should be made in the therapeutic effect. In this study, with the pointcut of combining the Traditional Chinese Medicine internally and externally, research on mechanism of action in eczema treatment by Traditional Chinese Medicine and different therapies have been made, providing new thoughts for the application guidance of Traditional Chinese Medicine in clinic eczema treatment.

2. Materials and methods

SD rats for the experiment were purchased from Laboratory Animal Centre (LASC) of Zhengzhou University, totally 40, half of which were male and half were female. All were about 4 weeks, weighing (212 ± 24) g. Prior to the experiment, rats were allowed to acclimate for 1 week in a laboratory featuring constant temperature, constant humidity and sterilization environment.

2, 4 dinitrochlorobenzene (DNCB) and barium sulfide were bought from Sigma; DNCB acetone solution with the percentage of acetone of 5% and 0.1% were prepared for standby application. CD4⁺, CD8 antibody, IL-2, INF- γ and IL-4 reagent were bought from BD company, America. Qingpeng Ointment (20 g) was bought from Tibet Qizheng Tibetan Medicine Ltd.; prescription of Jianpi Chushi decoction: 20 g of *Poria cocos*, Chinese yam and *Cortex dictamni*; 15 g of *Zaocys dhumnade*, *Rhizoma atractylodis* and *Pericarpium Citri Reticulatae*; 10 g of *Scutellaria baicalensis*, Radix Sophorae Flavescentis and raw Radix Paeoniae Alba; and 5 g of Licorice roots (Northwest origin); which were boiled for 30 min, filtrated and concentrated to drug juice with the concentration of 1.6 g/mL.

2.1. Group and therapy

Four rats were selected to blank group without any further processing. Other 36 rats were divided into four groups of 9 randomly, namely model control group, oral medicine group, external inunction group and combination therapy group. Rats of above 4 groups were depilated in same position on their back, for the size of 3 cm \times 2 cm, by barium sulfide. After 1 d, 5% DNCB 100 μ L was coated on the depilated skin of each rat for sensitization, once per day, continuing for 3 d; after one week, 0.1% DNCB 50 μ L were coated in the interior right ears to challenge and sensitize them, once every 3 d, totally for 5 times. After the last time for coating, skin tissue change of their right ears was observed. Any symptoms of red and swollen, exudation and incrustation indicated the successful establishment of eczema model.

Three days after the last challenge following the medication and treatment to each group: The oral medicine group was given 5 mL Traditional Chinese Medicine Jianpi Chushi decoction by gastric infusion, the external inunction group with Qingpeng ointment on the skin, the combination therapy group with Jianpi Chushi decoction by gastric infusion and Qingpeng ointment

combination therapy, and the model control group was given normal saline (NS) of the same volume by gastric infusion and vaseline on skin. All treatments were performed once per day, continuing for 15 d.

2.2. Processing experiment after the treatment

3 d of medication withdrawal after the end of the treatment, each rat were sacrificed by cervical dislocation. Ears of each rat were cut. Tissues (holes with the diameter of 0.8 mm) were punched at same positions on each ear by the puncher and weighed, thickness and weight difference between their left ears and right ears were calculated. Femoral artery blood was taken and the serum IL-2, IL-4 level were detected with the ELISA method in accordance with reagent specification; fcm flow cytometry was used to detect CD4⁺ and CD8⁺ cellular level; skin tissue of the back eczema model was taken to make paraffin section, with HE stain, and dermis inflammatory cell count was observed through microscope. All data was processed with SPSS 19.0 and expressed in the form of Mean \pm SD, variance analysis were conducted with *t* test between groups.

2.3. Ethical approval of the experiment

All experiments of this study were performed in accordance with animal healthcare and user manual of Laboratory Animal Centre (LASC) of Zhengzhou University, Henan province, and with the approval of local Ethics Committee, conforming to experimental animal care and application guidance of National Institutes of Health (NIH) (No. 85 publication-23, revised in 1985).

3. Results

Ear swelling of rats in each group was showed in following Table 1. Generally, degree of ear swelling was believed to reflect objectively the reaction degree of the inflammation. It was shown in Table 1 that, compared with model control group, the degree of ear swelling of oral medicine group, external inunction group and combination therapy group decreased significantly ($P < 0.05$); and compared with oral medicine group and external inunction group, the degree of ear swelling treated in combination therapy group was lower.

CD4⁺ and CD8⁺ cell and the interleukin 2 IL-2, IL-4 level of rats in each group were shown in Table 2. Compared with normal rats in blank group, CD4⁺, CD8⁺ cell content and serum IL-2 level of the ones in model control group decreased, while IL-4 level increased. After different therapies were performed to on each group, CD4⁺ content and serum IL-2 level raised gain, while IL-4 level decreased. In addition, compared with oral medicine group and external inunction group, the effect of combination therapy group was more obvious ($P < 0.05$).

Dermis inflammatory cell count of each eczema model group was showed in Table 1. It was indicated that, compared with blank group, inflammation cell count of each model control group differed significantly ($P < 0.01$); after treatment, compared with model control group, inflammation cell number of each group decreased significantly; in addition, compared with external inunction group and oral medicine group, the effect of combination therapy group was more obvious ($P < 0.05$).

Table 1Degree of ear swelling and inflammatory cell count of different rat eczema mode (Mean \pm SD).

Group	Thickness (μm)			Weight (μg)			Cell count (cell/ mm^2)
	Left ear	Right ear	Increase	Left ear	Right ear	Increase	
Blank	30.14 \pm 5.56	33.08 \pm 4.53	2.94 \pm 1.64	12.56 \pm 4.33	13.77 \pm 4.24	1.21 \pm 0.68	18.56 \pm 3.48
Model control	32.01 \pm 4.59	43.56 \pm 6.74	11.55 \pm 2.33	13.28 \pm 4.28	18.14 \pm 5.67	4.86 \pm 1.17	64.23 \pm 7.52
Oral medicine	32.23 \pm 5.23	38.53 \pm 5.25	6.30 \pm 1.64*	13.43 \pm 4.72	15.64 \pm 5.36	2.21 \pm 0.67*	36.56 \pm 5.27*
External inunction	31.56 \pm 6.46	38.39 \pm 5.64	6.83 \pm 1.24*	13.15 \pm 4.32	15.58 \pm 5.27	2.43 \pm 0.53*	40.21 \pm 6.24*
Combination therapy	30.67 \pm 5.73	35.85 \pm 6.23	5.18 \pm 1.53* Δ #	12.78 \pm 5.12	14.11 \pm 4.79	1.33 \pm 0.57* Δ #	30.24 \pm 4.56* Δ #

* $P < 0.05$ compared with blank group; # $P < 0.05$ compared with model control group; $\Delta P < 0.05$ compared with oral medicine group.**Table 2**T-cell subgroup and IL level of rats in each group (Mean \pm SD).

Group	CD4 ⁺ (%)	CD8 ⁺ (%)	IL-2 (ng/mL)	IL-4 (ng/mL)	IL2/IL4
Blank	50.31 \pm 5.67	15.25 \pm 3.04	3.68 \pm 1.34	0.42 \pm 0.16	8.762
Model control	25.74 \pm 6.75*	13.42 \pm 4.56*	2.94 \pm 0.87*	0.51 \pm 0.14*	5.765
Oral medicine	38.96 \pm 5.87*#	14.32 \pm 3.11*	3.48 \pm 0.77*#	0.46 \pm 0.16*#	7.733
External inunction	36.75 \pm 5.23*#	14.24 \pm 2.89*	3.39 \pm 0.96*#	0.45 \pm 0.13*#	7.370
Combination therapy	42.31 \pm 4.96* Δ #	15.01 \pm 3.14#	3.57 \pm 0.85 Δ #	0.43 \pm 0.12 Δ #	8.302

* $P < 0.05$ compared with blank group; # $P < 0.05$ compared with model control group; $\Delta P < 0.05$ compared with oral medicine group.

4. Discussion

Chronic eczema, a kind of skin inflammation reaction caused by human immunodeficiency with various pathogenesis, could not be well treated with ordinary antiphlogistine and medication. Therapy of Traditional Chinese Medicine, boasting the idea of symptomatic relieves & radical treatment and combination therapy of external symptom and internal disease, played an important role in eczema treatment. Jianpi Chushi decoction was derived from the *Formula Dictionary of Traditional Chinese Medicine* and was effective in treating chronic eczema caused by spleen vacuity with damp-heat [9,10]. Previous studies showed that the Traditional Chinese Medicine description could not only function in eczema treatment but also in regulating immunity and endocrine, therefore, it could also be used in Traditional Chinese Medicine treatment of gastritis, gastric ulcer, diabetes, rheumatoid arthritis, etc. [11-13]. However, as for its site of action was the whole body of the patient but not the lesion, it had shortcoming in longer treatment period. From this point, chronic eczema rat models were established and therapies integrating Traditional Chinese Medicine Jianpi Chushi decoction and external use ointment on chronic eczema were implemented in order to find more effective Traditional Chinese Medicine therapy for eczema treatment, and the mechanism of action of the Traditional Chinese Medicine therapy was studied through testing the immune adjustment.

Chronic eczema was a kind of inflammation reaction caused by stimulation, and the effective factor was the T-cell which had a role to play in immunity [14,15]. CD4⁺ and CD8⁺ belonged to two different T-cell subsets, and CD4⁺ fell into Th1 and Th2 auxiliary subsets, of which Th1 cell mainly secreted factors such as IL-1, IFN- γ , etc., primarily revolving in mediated cell immune response. All of them were important factors to regulate immune response [16]. Th2 usually secreted factors such as IL-4, IL-5, IL-6, IL-10, primarily revolving in mediated humoral immunity and functioning well in enhancing phagocytosis and cytotoxicity of neutrophil-mediated. Normally, above two T-cell and T auxiliary cell subsets were maintained in dynamic

equilibrium. While after the body was stimulated, with the appearance of allergen, the inflammation was out of balance, therefore leading to cytokine secretion disorder and vascular permeability change, and vasodilatation further resulting in skin red, swollen and lesion, namely eczema [17,18]. Therefore, CD4⁺ and CD8⁺ cell content reflected the degree of immune response inside the body, while IL-2, IL-3, and IL-2/IL-4 rate indicated the balanced secretion of cell factors. In this experiment, serum test results of model control group and blank group proved that: the decreasing of CD4⁺, CD8⁺ cell content implied immune abnormalities; the decreasing of IL-2 and the increasing of IL-4 showed the hypofunction of Th1 and hyperfunction of Th2, and the Th1/Th2 out of balance. However, comparing treatment group with model control group, it was indicated that T-cell subsets, CD4⁺, CD8⁺ cell content and serum IL-2 level immunologic process were dramatically improved by Jianpi Chushi decoction and Qingpeng ointment, while IL-4 level and the number of inflammatory cells decreased. Therefore, through improving the endocrine system of the body and regulating unbalanced immune system, motivating the rising of CD4⁺, CD8⁺ cell level, the normalization of Th1 and Th2, restoration of equilibrium for Th1/Th2, Jianpi Chushi decoction could restrain the development of eczema, which was essentially consistent with existing research conclusions [19]. Besides, Qingpeng ointment was effective in antiseptis and anti-inflammation and improving microcirculation, and accordingly functional well in restrain the increasing of partial inflammatory cells and bacterial infection from the external environment [20,21]. In conclusion, the therapeutic effect and speed would be significantly improved if Jianpi Chushi decoction was used combining with Qingpeng ointment.

To sum up, Jianpi Chushi decoction featured unique immunomodulatory effect in chronic eczema treatment, and its curative effect could be enhanced combining with Traditional Chinese Medicine ointment. In addition, its mechanism of action to chronic eczema was realized by regulating immunity of T lymphocyte participation. At the experimental design of this study, Jianpi Chushi decoction by gastric infusion and Qingpeng ointment combination therapy were conducted to chronic

eczema rat model, which enhanced therapeutic effect and effect speed. However, in practical clinic, it is needed to study that weather any mutual forbearance of above two therapies existed and weather by which adverse reaction would be caused.

Conflict of interest statement

We declare that we have no conflict of interest.

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