



## Short Communication

# Effect of Acupuncture and Moxibustion on Cellular Immune Indices and Th1/Th2 Cell Dysfunction in Chronic Urticaria

Xinyan Huang<sup>1</sup>, Songzhao Zhang<sup>2</sup>, Limei Zhang<sup>3</sup> and Maocan Tao<sup>4\*</sup><sup>1</sup>Department of Dermatology, The Second Affiliated Hospital Zhejiang University School of Medicine, Hangzhou 310003, Zhejiang Province, China<sup>2</sup>Department of Laboratory, The Second Affiliated Hospital Zhejiang University School of Medicine, Hangzhou 310003, Zhejiang Province, China<sup>3</sup>Department of Dermatology, The Third Clinical Medical College of Zhejiang University of Traditional Chinese Medicine, Hangzhou 310053, Zhejiang Province, China<sup>4</sup>Department of Dermatology, Zhejiang Provincial Hospital of Chinese Medicine, Hangzhou 310003, Zhejiang Province, China

## ABSTRACT

Studies have reported that Th1/Th2 cytokine imbalance plays a crucial part in the development of chronic urticaria (CU). The differentiation function of TH1 and TH2 cells is one of the important links in the body's immune regulation. The study evaluated the effect of acupuncture and moxibustion (AM) on cellular immune indices and Th1/Th2 cell dysfunction in CU patients. Seventy CU patients who received diagnosis and treatment admitted between January 2020 and April 2022 were carefully chosen and subsequently allocated into two distinct groups, control group (COG) and observation group (OBG). The patients in the COG were treated with loratadine, and the patients in the OBG were treated with loratadine combined with acupuncture. The treatment effects, quality of life scores, IgE levels, levels of TH1 cytokines, TH2 cytokines. After treatment, the DLQI (dermatology life quality index questionnaire) score and serum IgE level of the OBG were reduced than before treatment and the COG. Following the intervention, the concentrations of IL-2, IFN- $\gamma$ , and TNF- $\alpha$  in both groups exhibited a significant increase compared to their pre-treatment levels. Furthermore, the OBG demonstrated a reduced level of these cytokines compared to the COG. After treatment, the IL-6 and IL-8 in the two groups were increased while the IL-4 level was reduced compared to the respective control. Acupuncture and moxibustion balance the function of Th1/Th2 cells, enhance the clinical manifestations and overall well-being of the individual.

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## Authors' Contribution

XH and SZ: Conducted the experiments in this study. LZ and MT: Contributed to the design and interpretation of the current study and wrote the article. All authors read, revised, and approved the final manuscript.

## Key words

Acupuncture, Chronic urticaria, Clinical efficacy, Cellular immunity, Helper T lymphocytes

Chronic urticaria (CU) is a common skin disease, which refers to the repeated attacks more than six weeks of urticaria, with blood vessels, mucous membrane, skin inflammatory hyperemia and edema in the organization for the pathological characteristics, main performance for patients with sporadic skin urticaria or accompanied by clinical symptom such as erythema, itching, impact on patients' daily functioning and occupational performance

is substantial (Ayse-Ornek *et al.*, 2022). Currently, the clinical treatment with CU mainly using glucocorticoid, inhibit mast cell degranulation drugs, antihistamine drugs and western medicine is given priority to with symptomatic treatment, although can to a certain extent, the amelioration of the patients' clinical symptoms is achieved, albeit with the concomitant occurrence of more pronounced side effects upon prolonged administration, the dependence on drugs to patients is stronger, drug withdrawal is easy to relapse (Rodríguez-Garijo *et al.*, 2022). Therefore, it is a problem to find a safer treatment. With the deepening of the theoretical research of traditional Chinese medicine (TCM), TCM has demonstrated superior efficacy in the management of dermatological conditions. Acupuncture and moxibustion (AM), as a simple, cheap external treatment of TCM with little adverse reactions (Zhao and Ma, 2020). CU is mainly caused by the external attack

\* Corresponding author: zhangzhituo8114358@163.com  
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of wind evil and the discord between camp and guard, and AM “treating six points of wind” has the effect of evacuating wind evil and harmonizing camp and guard (Zhang *et al.*, 2019). Based on this, this research aimed to investigate the effectiveness of acupuncture in managing CU, as well as its impact on cellular immune indicators and the dysregulation of TH1/ TH2 (T helper type 1/ T helper type 2) cell function. Hence, the purpose of this study was to gain insights into the mechanisms by which AM could affect cellular immune indexes and Th1/Th2 cell dysfunction in CU patients.

### Materials and methods

Seventy patients diagnosed with CU, who received treatment at our hospital between January 2020 and April 2022 were randomly assigned to either the control group (COG) or the observation group (OBG), with 35 cases in each group. The CU patients aged 22-65 years old, and did not receive western medicine or traditional Chinese medicine treatment within 2 weeks before enrollment. The patients with other skin diseases, allergic to drugs and these with chronic hepatic, renal, and cardiac failure and acute urticaria were excluded from the study.

The COG were treated with loratadine, loratadine tablets (Sinophosphatid: H20070030, Xi'an Janssen Pharmaceutical Co., LTD) 10mg once a day for 8 weeks. The OBG was treated with loratadine with acupuncture. Acupuncture point were Fengchi, Fengmen, Fengfu, Bingfeng, Fengshi six points and the procedure was performed by experts.

The rate at which DLQI (Dermatology Life Quality Index questionnaire) scores were reduced was used to determine clinical efficacy (Fayaz *et al.*, 2021), recovery: DLQI score reduction rate  $\geq 90\%$ ; effective: 60%~89%; effective: 31%~59%; invalid 30% or less. Total effective rate (TER) = (cured + marked effect + effective) cases/total cases  $\times 100\%$ . The DLQI was employed for the assessment of patients quality of life, with scores ranging from 0 to 30.

Serum from fasting venous blood sample was used for determination of TheIL-2, IFN- $\gamma$ , TNF- $\alpha$ , IL-6, IL-8, and IL-4 by ELISA. Additionally, the levels of serum immunoglobulin E (IgE) were measured using a sandwich antibody ELISA.

The SPSS 20.0 was employed to conduct the analysis, specifically utilizing the chi-square test for count data, and was used for measurement data. The t-test was employed to conduct a comparison between two distinct groups. In comparison to the COG, statistical significance was observed ( $P < 0.05$ ).

### Results

From the 70 CU patients in the study, there were 17 males and 18 females, aged 22-65 years, with an average

age of  $42.62 \pm 4.56$  years, and the course of disease was 9-60 months, with an average course of  $16.62 \pm 4.52$  months in the COG. In the OBG, there were 16 males and 19 females, with an average age of  $42.23 \pm 5.24$  years (range, 22-64 years) and a disease duration of  $17.48 \pm 5.57$  months (range, 10-61 months).

Table I indicates descriptive data for the treatment effect for the OBG and COG after the treatment. The results show that the effective rate of OBG was increased compared with COG. The results for the comparison of quality of life score and IgE level after treatment in Table II show that DLQI score and serum IgE level in the OBG were reduced than those before treatment in the COG.

**Table I. Clinical efficacy of patients (%).**

|                | Control group<br>(n=35) | Observation<br>group (n=35) | $\chi^2$ | P     |
|----------------|-------------------------|-----------------------------|----------|-------|
| Recovery       | 7(20.00)                | 10(28.57)                   |          |       |
| Excellent      | 12(34.29)               | 14(40.00)                   |          |       |
| Effective      | 6(17.14)                | 8(22.86)                    |          |       |
| Invalid        | 10(28.57)               | 3(8.57)                     |          |       |
| Effective rate | 25(71.43)               | 32(91.43)                   | 4.629    | 0.031 |

TH1 cytokine levels after treatment showed that the IL-2, IFN- $\gamma$  and TNF- $\alpha$  were increased than before treatment. The OBG was reduced than the COG in the two cohorts. Furthermore, TH2 cytokine levels after treatment showed that the IL-6 and IL-8 in the two cohorts were increased than before treatment, while those in the OBG were reduced than the COG. The IL-4 in the OBG was reduced than that in the COG (Table II).

The results for the comparison of adverse reactions in Table III show that there was a lack of significant variation in the overall occurrence of adverse reactions observed between the two cohorts.

### Discussion

CU has the potential to manifest at any age and during any season, although it exhibits a higher propensity for occurrence during the springtime, and the study found that more than 40% of the patients with CU may suffer from skin disease more than half a year, half of the patients could get in 1 year of symptoms, however, in certain instances, the duration of symptoms may extend for a period of 10 years or more, significantly impacting the overall quality of life and professional productivity of individuals affected (Zhang *et al.*, 2022). Currently, western drugs such as glucocorticoids, anti-mast cell degranulation drugs and antihistamines are mainly used in the clinical treatment with CU. Loratadine is a second-generation antihistamine drug, which can inhibit histamine induced allergic symptoms

**Table II. Effects of acupuncture and moxibustion (AM) on quality scores and IgE, TH1 and TH2 (T helper type 1 and 2) cytokine levels in control and observation groups before (T0) and after (T1) treatment.**

|               | Control group (n=35) |              | Observation group (n=35) |             | t      | P     |
|---------------|----------------------|--------------|--------------------------|-------------|--------|-------|
|               | Time 0               | Time 1       | Time 0                   | Time 1      |        |       |
| DLQI (score)  | 13.02±6.01           | 8.32±3.00    | 14.41±5.86               | 4.56±1.64   | -9.845 | 0.000 |
| IgE (pg/mL)   | 114.89±27.14         | 47.11±9.29   | 115.05±27.22             | 34.32±8.03  | 14.835 | 0.000 |
| IL-2 (pg/mL)  | 43.21±7.25           | 30.37±5.42   | 42.56±8.23               | 23.42±4.37  | -5.906 | 0.000 |
| IFN-γ (pg/mL) | 14.53±3.24           | 26.13±8.73   | 14.30±3.12               | 20.52±6.82  | -2.996 | 0.004 |
| TNF-α (pg/mL) | 7.82±2.10            | 15.42±2.85   | 7.41±2.58                | 11.38±3.14  | -5.636 | 0.000 |
| IL-6 (pg/mL)  | 35.65±8.46           | 84.34±15.92  | 35.42±8.67               | 70.44±12.56 | -4.055 | 0.000 |
| IL-8 (pg/mL)  | 55.25±14.84          | 108.62±25.44 | 52.68±15.62              | 75.62±21.02 | -5.916 | 0.000 |
| IL-4 (pg/mL)  | 56.53±12.24          | 40.13±9.73   | 56.30±11.12              | 34.52±9.82  | -2.401 | 0.019 |

Time 0, before treatment; Time 1, after treatment

**Table III. Comparison of adverse reactions (%).**

|                                         | Control group (n=35) | Observation group (n=35) | $\chi^2$ | P     |
|-----------------------------------------|----------------------|--------------------------|----------|-------|
| Nausea and vomiting                     | 3(8.57)              | 0(0.00)                  |          |       |
| Acupuncture syncope                     | 0(0.00)              | 1(2.86)                  |          |       |
| Drowsiness                              | 3(8.57)              | 0(0.00)                  |          |       |
| Impairment of liver and kidney function | 0(0.00)              | 0(0.00)                  |          |       |
| Total incidence                         | 6(17.14)             | 1(2.86)                  | 2.540    | 0.111 |

by competitively inhibiting histamine H1 receptor (Chiang *et al.*, 2022). However, according to clinical studies, antihistamines can cause drug eruption, anaphylactic shock, acute severe drug-induced hepatitis, leukopenia, and various other adverse reactions have been reported (Shah *et al.*, 2022). Furthermore, CU is a persistent ailment necessitating prolonged pharmacological intervention, potentially leading to the development of drug resistance among afflicted individuals (Shi *et al.*, 2019a, b). The presence of adverse effects associated with long-term medication poses a significant burden on patients suffering from urticaria, impeding their ability to adhere to prescribed medication regimens. Consequently, suboptimal compliance negatively impacts the clinical effectiveness of pharmaceutical interventions (Xiao *et al.*, 2019). Considering the various problems of western medicine in the treatment of urticaria, the discovery of a safer and more efficacious treatment is of utmost importance and requires immediate attention. TCM has demonstrated positive therapeutic outcomes in the management of dermatological conditions. Acupuncture and moxibustion, as a simple, cheap and less adverse reaction external treatment of TCM, possesses distinct advantages in the clinical management of patients with urticarial (Xiao *et al.*, 2020).

The pathogenesis of CU has not been fully explained, but recent study has substantiated the close association

between the pathogenesis of the condition and IgE-mediated type I allergy (Orzan *et al.*, 2022). The IgE levels in individuals who are considered to be in a state of normal, optimal health are typically characterized by their low concentrations, which tend to experience an elevation solely in response to the presence of external allergens. Studies have found that most patients with CU do have a high serum IgE level, the alteration in IgE content serves as a biochemical indicator for assessing the state of urticarial (Kalmarzi *et al.*, 2022). In addition, studies have found that Th1/Th2 cytokine imbalance also plays a crucial part in the development of CU (Picado *et al.*, 2022). The differentiation function of TH1 cells and TH2 cells is one of the important links in the body's immune regulation. TH1 cells, characterized by their CD4<sup>+</sup> positive phenotype, primarily secrete cytokines such as TNF-α, IFN-γ, and IL-2, which aiding in the differentiation of cytotoxic T cells and facilitating the mediation of cellular immune responses (Yu *et al.*, 2020; Chen *et al.*, 2018). The secretion of IgE by B cells can be stimulated by IL-4, whereas the secretion of IgE can be inhibited by IFN-γ. Consequently, an imbalance between IFN-γ and IL-4 may serve as a significant factor contributing to aberrant IgE levels (Movahedi *et al.*, 2017). The results revealed that after treatment, the serum IgE level in the OBG was reduced than that before treatment and the COG. After treatment, the IL-2, IFN-γ and TNF-α were increased than before treatment, and the OBG was reduced than the COG. After treatment, the IL-6 and IL-8 were increased than before treatment, and the IL-4 in the OBG were reduced than before treatment, and the IL-4 in the OBG were increased than the COG. It is suggested that acupuncture in the treatment with CU can enhance the cellular immune function and balance the function of Th1/Th2 cells. According to modern pharmacological studies, acupuncture and moxibustion can reduce the symptoms of CU by regulating the plant nerves, so that immune cells do not secrete or secrete less slow-reactive substances, bradykinin and histamine (Qiu *et al.*, 2020).

### Conclusion

The utilization of AM in the management of CU demonstrates a favorable clinical outcome, which is beneficial to improve the cellular immune function of patients, balance Th1/Th2 cell function, and then enhance the clinical manifestations experienced by patients, thereby enhancing their overall quality of life, and the treatment effect is safe and effective.

### DECLARATIONS

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#### IRB approval

This study was approved by the Advanced Studies Research Board of Zhejiang Provincial Hospital of Chinese Medicine, Hangzhou 310003, China.

#### Ethical approval

The study was carried out in compliance with guidelines issued by Ethical Review Board Committee of Zhejiang Provincial Hospital of Chinese Medicine, China. The official letter would be available on fair request to corresponding author.

#### Statement of conflict of interest

The authors have declared no conflict of interest.

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