

# Mechanism of Huanglian Detoxification Soup Relieving Postherpetic Neuralgia by Enhancing IL-2 Levels in Rats

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**Abstract** [Objectives] To explore the mechanism of Huanglian detoxification soup improving pain behavior by affecting serum IL-2 levels in postherpetic neuralgia (post herpes neuralgia, PHN) model rats. [Methods] 20 PHN rats were randomly divided into model group (PHN group) and detoxification decoction group ( $n = 10$ ). In the group, 10% Huanglian detoxification soup (0.4 mL/0.1 kg) was given once in the morning and evening for 14 d. The PHN group was filled with an equal volume of 0.9% sodium chloride solution. Tail vein serum inflammatory factor interleukin-2 (IL-2), IL- $\beta$  and IL-6 levels were measured using ELISA kits at 7 and 21 d. [Results] IL-2 increased at 14 and 21 d in IL group, while IL- $\beta$  and IL-6 decreased compared with the PHN group ( $P < 0.05$ ). [Conclusions] Huanglian detoxification soup may raise IL-2 levels after VZV infection to promote the differentiation of cells of the immune system, so as to relieve the pain caused by IL- $\beta$  and IL-6 inflammatory factors.

**Key words** Huanglian detoxification soup, Postherpetic neuralgia, Serum inflammatory factor

## 1 Introduction

Herpes zoster (HZ) is an acute skin and nerve injury disease caused by varicella-zoster virus (VZV) infection, with skin blisters and severe pain as the main features<sup>[1]</sup>. The pathological basis of neuralgia may be related to the production of a large number of inflammatory mediators after VZV infection, such as the inflammatory factors interleukin-2 (IL-2), IL- $\beta$  and IL-6. In this paper, on the basis of preparing PHN model rats, the rats in the detoxification decoction group were treated with Huanglian detoxification soup, and the effect on serum inflammatory factors in PHN model rats was observed to discuss the possible mechanism.

## 2 Materials and methods

**2.1 Experimental animals** 20 SPF SD rats (male or female) were 56 days old, with body mass of 230–240 g.

**2.2 Reagents and equipment** IL-2, IL- $\beta$  and IL-6 ELISA kits (Lot; E-EL-M0044c, E-EL-M0107c) were purchased from Corre Biotechnology Co., Ltd. Huanglian detoxification soup is mainly composed of 9 g of huanglian and gardenia, and 6 g of bicalensis and Phellohelchinensis, issued by the pain department of the hospital and fried in the pharmacy.

**2.3 Methods** Method of establishing rat PHN model: at first,

rats were inoculated with VZV virus inoculation solution<sup>[2]</sup>. Groups: PHN group and coptis detoxification decoction group ( $n = 10$ ). The treatments are as follows: in the group, 10% Huanglian detoxification soup was given at 0.4 mL/0.1 kg on the 7 d after inoculation, once in the morning and evening for 14 d (*i. e.*, 14 and 21 d of all the observation time points), and the PHN group was filled with 0.9% sodium chloride solution. ELISA detection of serum inflammatory factors: 0.1 mL of tail vein blood was taken on the 7 and 21 d of rats, and the levels of IL-2, IL- $\beta$  and IL-6 were detected by double antibody sandwich.

**2.4 Statistical analysis** One-way homogeneity of variance analysis was firstly carried out by SPSS 21.0 software. Experimental data were expressed as mean  $\pm$  standard deviation ( $\bar{x} \pm s$ ); intra-group and between-group comparisons were performed by pairwise comparisons with *LSD*, Dunnett C test and Games-Howell test, and  $P < 0.05$  was considered as statistically significant difference.

## 3 Results and analysis

**3.1 Serum inflammatory test factors** Seen from Table 1, in Huanglian detoxification soup group, IL-2 was significantly higher than PNH group at 21 d, while IL- $\beta$  and IL-6 were lower than PNH group, and the difference was significant ( $P < 0.05$ ).

**Table 1** Comparison of groups in IL-2, IL- $\beta$ , and IL-6 levels ( $n = 10$ ,  $\bar{x} \pm s$ )

Group	IL-2//pg/mL		IL- $\beta$ //pg/mL		IL-6//pg/mL	
	7 d	21 d	7 d	21 d	7 d	21 d
PNH	27.39 $\pm$ 1.12	29.45 $\pm$ 1.07	32.91 $\pm$ 1.51	33.82 $\pm$ 1.37	12.04 $\pm$ 1.14	11.56 $\pm$ 0.74
Huanglian detoxification soup	28.52 $\pm$ 1.54	35.14 $\pm$ 0.89 <sup>a</sup>	32.54 $\pm$ 1.01	4.73 $\pm$ 0.11 <sup>a</sup>	12.62 $\pm$ 1.07	6.56 $\pm$ 0.32 <sup>a</sup>

**NOTE** Compared with the PNH group, <sup>a</sup> $P < 0.05$ .

## 4 Discussion

HZ is also known as snake plate sores, snake string sores, waist

fire Dan, and waist dragon<sup>[3]</sup>. The ant nerve pain (PHN) after healing of HZ is one of the most common complications of HZ<sup>[4]</sup>. Because VZV is neurotropic and dermatotropic, when the autoimmune function of the body is reduced, VZV invades the posterior root ganglion of the spinal cord nerve and causes inflammation in

the ganglion of the infection site, and necrosis in severe cases. Due to the massive release of inflammatory factors such as IL- $\beta$  and IL-6 in the endings, the formation of scar and adhesion in some nerve fibers, hypersensitization to pain, and more sensitive to nociceptive stimulation. Burning pain occurs under the persistent stimulation of inflammatory factors, thus producing transient or persistent pain<sup>[5]</sup>. As a T-cell growth factor, IL-2 can stimulate T cells to enter the cell division cycle, promote the expression of IL-2R by B cells and enhance NK cell activity in a short time, stimulate macrophages and increase their phagocytosis capacity<sup>[6]</sup>. IL-6 and IL- $\beta$  are regarded as biological markers of osteoarthralgia and neuralgia in the mechanism of pain development<sup>[7]</sup>. Clinical data also confirmed that the evolution of PHN and the incidence of PHN were positively correlated with serum IL-6 and IL- $\beta$  levels, and it was speculated that high levels of IL-6 and IL- $\beta$  may be one of the factors causing neurological damage after VZV infection<sup>[8]</sup>. VZV infection will cause the body's immune system dysfunction. The immunocompetent IL-2 synthesis is reduced in a short term, and the inflammatory mediators IL- $\beta$  and IL-6 are released in large quantities. This also agreed in this experiment. For instance, IL-2 decreased at 7 d in the PNH group, and IL- $\beta$  and IL-6 were higher than those in the blank control group. Inhibition of inflammatory mediators IL- $\beta$  and IL-6 synthesis can reduce nerve excitability and sensitivity to inflammatory response.

"Huanglian detoxification soup" from the "elbow backup", has the effect of fire detoxification, and can treat three coke fire poison heat sheng certificate. Previous studies have shown that Huanglian detoxification soup has anti-bacterial, fungal and viral infection effects<sup>[9]</sup>. It has obvious effects in improving PHN symptoms, relieving pain and preventing posterior neuralgia<sup>[10]</sup>. According to traditional Chinese medicine, PNH patients have the spleen through dampness and heat, the liver through fire, and when the exogenous hot evil leads to fire, dampness and heat accumulate steaming, soaking the skin, veins and hair as herpes<sup>[11]</sup>. In this experiment, the rats were vaccinated with VZV. Fire poison hot, full of three coke, so appropriate "fire detoxification". Fang Zhongjun medicine "Huanglian" clear diarrhea heart fire, minister medicine "Scutellaria baicalensis" clear diarrhea on the fire of coke, and then with "yellow cypress" clear diarrhea under the fire of coke. And "gardenia" through three coke, heat down, so that evil heat from childhood. For use, "collect the company of great cold, Qin, cypress, zhi in one side, bitter cold straight fold, fire evil to heat and poison, play heat and detoxification, fire and cool blood, dampness and pain relief, herpes self-healing, avoid left"<sup>[12]</sup>.

To sum up, Huanglian detoxification soup with "the effect of

reducing fire and detoxification" can improve the level of IL-2 after VZV infection to promote the differentiation of immune system cells, stimulate macrophages, improve its phagocytic ability to remove VZV, at the same time reduce the inflammatory mediators IL-1  $\beta$ , IL-6 levels, to reduce the inflammation site nerve excitability, and relieve inflammatory mediators stimulus caused by pain.

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