Effect of Zhuang medicine medicated thread moxibustion on protomics in serum of postherpetic neuralgia patient with *Herpes zoster*

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Abstract: The aim of this study was to observe the effect of Zhuang medicine medicated thread moxibustion on protomics in serum of postherpetic neuralgia patient with herpes zoster and discuss the action mechanism of Zhuang medicine medicated thread moxibustion in treating postherpetic neuralgia (PHN). Methods: patients were divided into three groups in clinic, namely the pre-treatment group (n=20), post-treatment group (n=20) and healthy group (n=20), patients meeting corresponding conditions were recruited in the voluntary principle to accept PHN pain evaluation and protomics tests respectively. Results: compared with the pre-treatment group, visual analogue scale (VAS) in post-treatment group obviously reduced, protomics indexes like MFG-ES, Lymphotoxin beta/TNFSF3, IL-19, Neuritin, NCAM-1/CD56 and PECAM-1/CD31 obviously changed. Conclusions: the Zhuang medicine medicated thread moxibustion can treat the postherpetic neuralgia patient with herpes zoster, its internal mechanism is to possibly change the protomics indexes like MFG-ES, Lymphotoxin beta/TNFSF3, IL-19, Neuritin, NCAM-1/CD56 and PECAM-1/CD31.

Keywords: Zhuang medicine medicated thread moxibustion, postherpetic neuralgia, protomics.

INTRODUCTION

The postherpetic neuralgia (PHN) is a kind of severe and refractory chronic nerve pain syndrome left after healing of herpes zoster, it can severely affect patients' work and life. As reported by literature, 9% ~ 34% patient with herpes zoster will suffer from PHN (Li *et al.*, 2012), and its incidence is positively correlated with age. It was reported by Wang Guolin (2003) that PHN commonly attacks the middle-aged and elderly people, the incidence for patients aged 50~59, 60~69 and 70~79 is 49%, 65% and 74% respectively. Currently, many methods can treat PHN, but no method can cure it. Therefore, treatment of PHN is a problem to be solved in medical circle. In clinic, it was found Zhuang medicine medicated thread moxibustion had better curative effect in treating PHN, with cure rate as high as 85% (Li *et al.* 2012), but its action mechanism hasn't been fully known. This paper studied the effect of Zhuang medicine medicated thread moxibustion on protomics in serum of postherpetic neuralgia patient with *Herpes zoster*, to discuss the action mechanism of Zhuang medicine medicated thread moxibustion in treating PHN and provide scientific basis for curing PHN.

Zhuang medicine medicated thread moxibustion method can directly acupuncture some acupoints or parts of patients' body surface through medicated thread, the warm and curative acupoint stimulation goes into the body through meridians, to adjust and balance Qi and blood, make parts of human body recovered to normal and three "Qi" reset and synchronous, so as to boost disease outcome and recover human energy. The modern clinical research has found that Zhuang medicine medicated thread moxibustion can cure PHN, with higher cure rate. Zhuang medicine medicated thread moxibustion can not only enhance function of T cell immunity and erythrocyte (Lu *et al.,* 2001), but also enhance immune function of erythrocyte, hemoglobin, hemogram and cells (Wei *et al.,* 1998). PHN is mainly caused by weakened immunity and weakened self-healing of neuritis, which macroscopically interpret the reasons of Zhuang medicine medicated thread moxibustion in treating PHN. But its internal mechanism, especially the effect on protomics is not fully known. The study was approved by the Medical Ethics Committee of the Guangxi University of Traditional Chinese Medicine, China. All patients provided written informed consent.

MATERIALS AND METHODS

Data

Diagnosis criteria. PHN was diagnosed as per standards stipulated by The American Academy of neurology. PHN refers to the continued and long-term pain for above 3 months after herpes zoster is cured clinically (Dubinsky *et al.,* 2014).

Inclusion criteria. Cases meeting PHN diagnosis standards; cases who voluntarily accepted testing and signed the informed consent; cased not participating in other clinical trials. Patients with severe diseases in heart, lungs, kidney and other organs were excluded.

Grouping. Patients were divided into three groups in clinic, namely pre-treatment group, post-treatment group

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and healthy group. As to pre-treatment group, 20 PHN patients meeting inclusive criteria were selected from Zhuang medicine clinic of our hospital; as to post-treatment group, 20 patients had accepted Zhuang medicine medicated thread moxibustion; as to healthy group, 20 healthy volunteers were recruited in voluntary principle.

Methods

Treatment methods and course: Zhuang medicine medicated thread moxibustion: the medicated threads were supplied by Zhuang Medicine College, Guangxi University of Chinese Medicine. Moxibustion acupoints: Kuihua acupoint (dependent on skin damage form and size, a set of acupoints surrounding and at middle point of damaged skin were selected, with the shape of sunflower), Meihua acupoint (by nerve plexus direction, a set of acupoints surrounding and at middle point of local lump or skin damage were selected, with the shape of plum blossom), Zusanli, Sanyinjiao, Taichong. Moxibustion methods: each acupoint was acupunctured within one second for each time. Each acupoint was acupunctured once every one day. Course: 10 days for each course, continuing three courses.

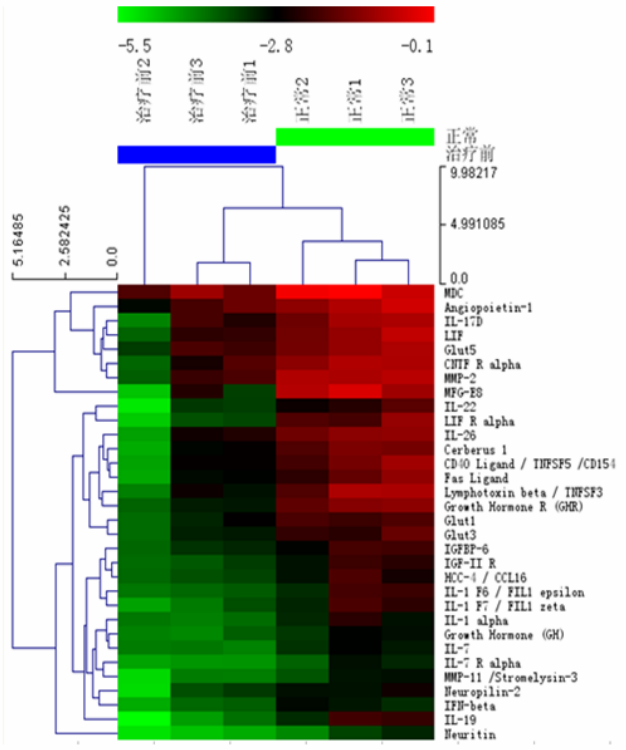

Fig. 1: Differences of indexes between postherpetic neuralgia patients with herpes zoster and healthy persons before treatment

Indexes detection and methods

PHN pain evaluation. Visual analogue scale (VAS) method formulated by Chinese Association for the Study of Pain was used to score the pre-treatment group, post-treatment group and healthy group. A ruler of 10cm was used (0 ~ 10 scores, each 1cm means 1 score) to indicate 10-grade pains, grade 0 means no pain, grade 10 means intolerable pain, respectively indicating best and poorest. For all patients, highest pain score was given, namely three grade: mild (0 ~ 4 scores), moderate (5 ~ 7 scores) and severe (8 ~ 10 scores).

Protomics tests. Nearly 500 protein markers were selected for detection; the biochip technology was adopted to perform corresponding inspection on three groups of serums. For the late-phase data analysis, the project group invited KangChen Bio-tech Inc. (protomics test unit) to assist analysis and processing.

STATISTICAL ANALYSIS

The data were all expressed in mean value ± standard deviation, PEMS3.1 statistical software was used for statistical analysis, chi-square inspection was used for comparison of counting data (rate), t test was used for comparison of measurement data before and after treatment, one-way analysis of variance was used for comparison of multiple groups of measurement data. $P<0.05$ was considered statistically significant.

RESULTS

Comparison of VAS Scores Before and After Treatment

Comparisons about pain scores for three groups before and after treatment were shown in table 1. Compared to the pre-treatment group, VAS score for post-treatment group significantly reduced, the difference had statistical significance ($P<0.05$). Results indicated that Zhuang medicine medicated thread moxibustion could obviously alleviate pain and provide better life quality for patients.

Comparison about detection results of protomics indexes in serum

It used the standard value of protein on chip (up or down 2.0 times, Pass Volcano Plot) for hierarchical clustering. Concrete test: similar samples or proteins were clustered for uniform protomics analysis.

(1) Differences of indexes between postherpetic neuralgia patient with herpes zoster and healthy person before treatment: Differences of indexes between postherpetic neuralgia patient with herpes zoster and healthy person before treatment were as shown in fig. 1. The fig. indicated that differences existed in MDC, Angiopoietin-1, IL-17D, LIF, Glut5, CNIF R alpha, MMP-2, MFG-E8, IL-26, Cerberus1, CD40 Ligand/TNFSFS/CD154, Fas Ligand, Lyaphotoxin, beta/TNFSF3, Gronth Mormone R (GHR), Glut1, Glut3, IGFBP-6, IGF-II R, HCC-4/CCL16, IL-1 F6/FIL1 epsilon, IL-1 F7/FIL1 zeta, IL-1 alpha,

Gronth Hormone(GH), IL-7, IL-7R alpha, MMP-11/ Stromelysin-3, Neuropilin-2, IFN-beta, IL-19 and Neuritin. The test results showed theses protomics indexes were the main causes for herpes zoster and postherpetic neuralgia (PHN).

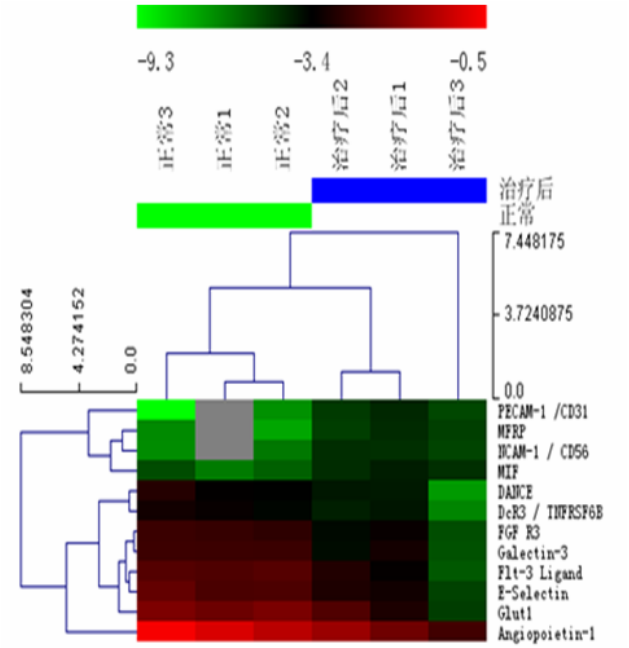

Fig. 2: Differences of indexes between postherpetic neuralgia patient with herpes zoster after treatment and none-neuralgia patients after healing of herpes zoster

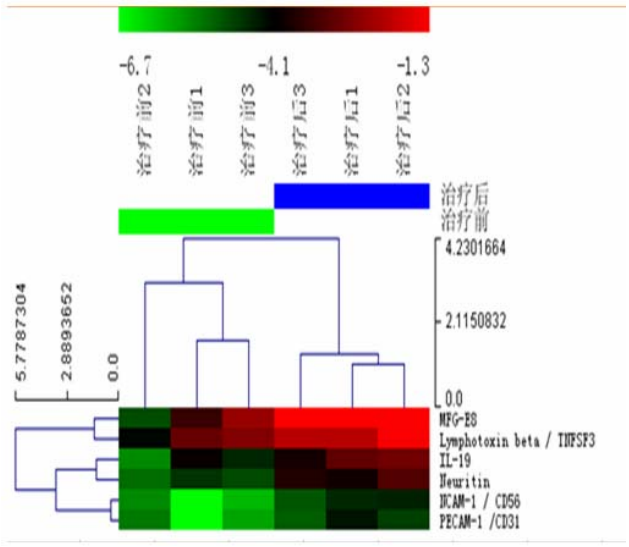

Fig. 3: Differences of indexes for postherpetic neuralgia patient with herpes zoster before and after treating with Zhuang medicine medicated thread moxibustion

(2) Differences of indexes between postherpetic neuralgia patient with herpes zoster after treatment and none-neuralgia patients after healing of herpes zoster Differences of indexes between postherpetic neuralgia patient with herpes zoster after treatment and none-neuralgia patients after healing of herpes zoster were as shown in fig. 2. The fig. indicated there were differences in PECAM-1/CD31, MFRP, NCAN1/CD56, MIF, DAJICE, DcR3/TNFRSF6B, FGF R3, Galectin-3, Galectin-3, Flt-3 Ligand, E-Selectin, Glut1 and Angiopoietin-1. The test results showed that these protomics indexes were the main causes for herpes zoster progressed into PHN.

(3) Differences of indexes for postherpetic neuralgia patient with herpes zoster before and after treating with Zhuang medicine medicated thread moxibustion Differences of indexes for postherpetic neuralgia patient with herpes zoster before and after treating with Zhuang medicine medicated thread moxibustion were as shown in fig. 3. The fig. indicated that difference sexisted in MFG-ES, Lymphotoxin beta/TNFSF3, IL-19, Neuritin, NCAM-1/CD56 and PECAM-1/CD31. The test results showed that protomics indexes were principal for Zhuang medicine medicated thread moxibustion in treating postherpetic neuralgia.

DISCUSSION

PHN, as a common skin disease, is a kind of neuropathic pain mainly caused by nerve injury or function disorders. PHN mainly attacks middle-aged and elderly people, the patients often suffer from neuralgia, invasion of the virus into corresponding cranial nerve will influence eyesight and result in facial paralysis and hearing disorder. Besides the pain, it can induce disorders of cardiovascular system, respiratory system, digestive system. The disease development and relapse trouble the patients' physiology and psychology, seriously affecting their work, study and daily life, even affecting their life quality. So, PHN treatment is a problem in the current medial circle.

Zhuang medicine medicated thread moxibustion method can directly acupuncture some acupoints or parts of patients' body surface through medicated thread, the warm and curative acupoint stimulation goes into the body through meridians, to adjust and balance Qi and blood, make parts of human body recovered to normal and three "Qi" reset and synchronous, so as to boost disease outcome and recover human energy. The modern clinical research has found that Zhuang medicine medicated thread moxibustion can cure PHN, with higher cure rate. Zhuang medicine medicated thread moxibustion can not only enhance function of T cell immunity and erythrocyte (Lu *et al.,* 2001), but also enhance immune function of erythrocyte, hemoglobin, hemogram and cells (Wei *et al.,* 1998). PHN is mainly caused by weakened immunity and weakened self-healing of neuritis, which macroscopically interpret the reasons of Zhuang medicine medicated thread moxibustion in treating PHN. But its internal mechanism, especially the effect on protomics is not fully known.

Table 1: Comparison about pain scores for three groups before and after treatment (n=20, $\bar{x}$ ±S)

Groups	n	VAS
Pre-treatment group	20	7.78±2.23
Post-treatment group	20	4.78±2.65*
Healthy group	20	—

Note: compared to pre-treatment group, *P<0.05

The clinical studies have shown that Zhuang medicine medicated thread moxibustion can better alleviate the pain of PHN patients. In this study, compared to the pre-treatment group, VAS scores for post-treatment group significantly reduced, differences were of statistical significance. The test results showed that Zhuang medicine medicated thread moxibustion could alleviate pain of PHN patients and could cure PHN, which was in coincidence with literature reports (Gazewood *et al.,* 2003). DeLea JA et al. found that pain caused by PHN was possibly related to inflammatory edema, nerve fiber demyelination change, hyperplasia and denaturation and immune system activation left after acute attack of varicella-zoster virus infection, and also possibly related to neurons inflammatory injury lesions progress. PECAM-1/CD31, MFRP, NCAN1/CD56, MIF, DAJICE, DcR3/TNFRSF6B, FGF R3, Galectin-3, Galectin-3, Flt-3 Ligand, E-Selectin, Glut1 and Angiopoietin-1 were the signature molecules on the cellular and humoral immune system, they participated in the inflammatory edema, nerve fiber demyelination change, hyperplasia and denaturation, immune system activation and neurons inflammatory injury lesions progress. In this study, comparison about protomics indexes of post-treatment postherpetic neuralgia patient with herpes zoster and none-neuralgia patients after healing of herpes zoster indicated that there were differences in PECAM-1/CD31, MFRP, NCAN1/CD56, MIF, DAJICE, DcR3/TNFRSF6B, FGF R3, Galectin-3, Galectin-3, Flt-3 Ligand, E-Selectin, Glut1 and Angiopoietin-1. The test results indicated that the differences of protomics indexes were major causes for progress of herpes zoster into PHN.

CONCLUSION

Currently, the mechanism of Zhuang medicine medicated thread moxibustion in treating PHN is under discussion and not fully known. Chen Pan et al. found that the mechanism of Zhuang medicine medicated thread moxibustion in treating PHN was possibly related to regulation of JNK expression and suppression of inflammatory response. Li Jingjing *et al.* found that the mechanism of Zhuang medicine medicated thread moxibustion in treating PHN was to alleviate pain by stimulating secretion of anti-inflammatory factor IL-10 and reducing hyperalgesia at nerve injury part, while not suppressing secretion of pro-inflammatory cytokineIL-1β. In this study, the comparison about protomics indexes of postherpetic neuralgia patient with herpes zoster before and after treatment indicated that there was differences in MFG-ES, Lymphotoxin beta/TNFSF3, IL-19, Neuritin, NCAM-1/CD56 and PECAM-1/CD31. The test results showed that the changes of protomics indexes like MFG-ES, Lymphotoxin beta/TNFSF3, IL-19, Neuritin, NCAM-1/CD56 and PECAM-1/CD31 were principal for Zhuang medicine medicated thread moxibustion in treating PHN.

In conclusion, Zhuang medicine medicated thread moxibustion can treat PHN, and its internal mechanism is to change the protomics indexes like MFG-ES, Lymphotoxin beta/TNFSF3, IL-19, Neuritin, NCAM-1/CD56 and PECAM-1/CD31.

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