Chen G, Xiang J, Ouyang LZ, *et al*. Effect of moxibustion stimulation on repair of injured gastric mucosa after common peroneal nerve transection. J Acupunct Tuina Sci, 2017, 15(3): 165-170
DOI: 10.1007/s11726-017-0995-x

Basic Study

Effect of moxibustion stimulation on repair of injured gastric mucosa after common peroneal nerve transection

艾灸刺激对腓总神经横断术后胃黏膜损伤修复的影响

Chen Guo (陈果), Xiang Juan (向娟), Ouyang Li-zhi (欧阳里知), Li Fei (李飞), Xiang Li-ting (向丽婷), Chen Ying (陈英), Yang Zhou (杨舟), Li Tie-lang (李铁浪), Peng Liang (彭亮)
School of Acupuncture, Moxibustion & Tuina, Hunan University of Chinese Medicine, Changsha 410208, China

Abstract

Objective: To investigate the protective effect of moxibustion in initiating the endogenous protection information on gastric mucosa, and its relationship with the pathway of common peroneal nerve.

Methods: Forty-eight Sprague-Dawley (SD) rats were randomly divided into a normal group (group A), a model group (group B), a moxibustion model group (group C) and a moxibustion model plus surgery group (group D), 12 in each group. Except for group A, rats in the other groups were treated with dehydrated ethanol and aspirin to prepare gastric mucosal damage model. The rats in group B were not treated with any interventions; rats in group C received moxibustion at Zusanli (ST 36), twice a day for continuous 3 d. The rats in group D were subjected to preparing the gastric mucosal damage model after the common peroneal nerve transection, followed by moxibustion at Zusanli (ST 36). After a 3-day intervention, UI (UI) in each group was observed, and the levels of gastric mucosa-related repair cytokines of tumor necrosis factor-α (TNF-α), interleukin-4 (IL-4) and heat shock protein 70 (HSP70) were detected.

Results: Compared with group A, the pathological changes and UI of group B were worse (P=0.000), but TNF-α in serum and tissue was changed significantly (P=0.000, P=0.002), IL-4 in serum and tissue was improved significantly (P=0.000, P=0.000). Compared with group B, TNF-α and IL-4 in group C and group D were significantly improved (TNF-α: P=0.003, P=0.016; IL-4: P=0.000, P=0.002). Compared with group C, the changes of UI in group B and group D were poor (both P=0.000); the levels of TNF-α and IL-4 in serum were significantly decreased (TNF-α: P=0.000, P=0.025; IL-4: P=0.000, P=0.034); and tissue HSP70 levels were decreased significantly (P=0.000, P=0.033).

Conclusion: Zusanli (ST 36) can transmit information through the pathway of common peroneal nerve, regulate the release of gastric mucosal protective factors, and up-regulate the expression of cytothesis-related proteins, so as to achieve the effect in repairing gastric mucosa.

Keywords: Moxibustion Therapy; Moxa Stick Moxibustion; Gastric Mucosal Damage; Point, Zusanli (ST 36); Rats

【摘要】目的：探讨艾灸启动内源性保护信息对胃黏膜的保护效应与腓总神经通路的关系。**方法：**将 48 只 Sprague-Dawley (SD)大鼠随机分为正常组(A 组)，模型组(B 组)，艾灸模型组(C 组)和艾灸模型手术组(D 组)，每组 12 只。除 A 组外，其余各组用无水乙醇、阿司匹林灌胃制备胃黏膜损伤模型。B 组不予治疗干预；C 组予艾灸足三里治疗，每日 2 次，连续治疗 3 d；D 组进行腓总神经切断术后制备胃黏膜损伤模型，予以艾灸足三里治疗。干预 3 d 后观察各组胃黏膜损伤指数(UI)，并进行胃黏膜相关修复细胞因子肿瘤坏死因子-α (TNF-α)、白介素-4 (IL-4)和热休克蛋白 70 (HSP70)检测。**结果：**与 A 组相比，B 组病理及 UI 改变较差(P＝0.000)；血清与组织中 TNF-α 改变明显(P＝0.000, P＝0.002)；血清与组织中 IL-4 改善明显(P＝0.000, P＝0.000)。与 B 组相比，C 组和 D 组 TNF-α 与 IL-4 改善明显 (TNF-α: P＝0.003, P＝0.016; IL-4: P＝0.000, P＝0.002)。与 C 组比较，B 组和 D 组 UI 改变效果较差(均 P＝0.000)；血清中 TNF-α 与 IL-4 下降明显(TNF-α: P＝0.000, P＝0.025; IL-4: P＝0.000, P＝0.034)；组织中 HSP70 值下降明显(P＝0.000, P＝0.033)。**结论：**足三里穴可通过腓总神经途径传递信息，调节胃黏膜保护因子的释放，并上调细胞修复相关蛋白表达，从而达到修复胃黏膜的效应。

【关键词】灸法；艾条灸；胃黏膜损伤；穴，足三里；大鼠

【中图分类号】R2-03　　**【文献标志码】**A

Author: Chen Guo, 2014 grade master degree candidate
Corresponding Author: Peng Liang, M.D., associate professor.
E-mail: match7@163.com

Gastric mucosal damage refers to gastric mucosal inflammation, bleeding and erosion caused by various physical and chemical factors, bacteria and other factors. It is manifested as gastric mucosal congestion, edema, erosion, shedding, necrosis, and ulceration[1]. At present, symptomatic treatment is usually applied in Western medicine. It is expensive with obvious side effects and brings a lot of inconvenience to the clinical diagnosis and treatment. Moxibustion is a part of traditional Chinese medicine therapy. It has obtained the clinician's favor due to the characteristics of simplicity, convenience, low price, and efficacy in the treatment of gastric mucosal damage[2], but the generalization of moxibustion therapy is restricted owing to the lack of experimental basis and clinical evidence for the treatment of acute alcohol gastric mucosal damage[3]. Therefore, it is necessary to explore the mechanism of moxibustion therapy.

The aim of this study was to discuss the effect of moxibustion at Zusanli (ST 36) on the transmission of common peroneal nerve pathway in alcohol-related gastric mucosal damage.

1 Materials and Methods

1.1 Experimental animals and grouping

Forty-eight Sprague-Dawley (SD) rats, 3-4 months old, weighing 200-240 g, half male and half female, were provided by the Hunan University of Traditional Chinese Medicine Experimental Animal Center, certificate number: SYXK (Hunan) 2013-0005. Disposal of animals during the experiment followed the stipulations of *Guiding Opinions on the Treatment of Experimental Animals* issued by the Ministry of Science and Technology in 2006. Rats were housed under the conditions of half day and night, comfortable humidity and temperature.

The forty-eight rats were divided into 4 groups according to the random number table method, including a normal group (group A), a model group (group B), a moxibustion model group (group C) and a moxibustion model plus surgery group (group D), 12 rats in each group.

1.2 Main reagents and instruments

Li Shi-zhen smokeless Qi moxa stick (4 mm in diameter, Qichun Shizhen Materia Medica Technology Co., Ltd., China); aspirin effervescent tablets (AstraZeneca Pharmaceutical Co., Ltd., China); physiological saline (Changsha Wei'er Biotechnology Co., Ltd., China); aspartic acid, penicillin injection (North China Pharmaceutical Co., Ltd., China); TGL-16 refrigerated centrifuge (Hunan Xiangyi Laboratory Instrument Development Co., Ltd., China); PW-812 automatic microplate reader washing machine (Jinan Gaokui Medical Equipment Co., Ltd., China); MB-530 enzyme league immune detector (Jinan Gaokui Medical Equipment Co., Ltd., China); THZ-C constant temperature oscillator (Taicang Qiangle Experimental Equipment Co., Ltd., China); TS-92 shaker (Haimen Kylin-Bell Lab Instruments Co., Ltd., China); E-201-C precision pH meter (Shanghai Leici Precision Science Instrument Co., Ltd., China); DY89-1 electric glass homogenizer (Ningbo Xinzhi Biotechnology Co., Ltd., China); homemade moxibustion frame, common chemistry reagents (Sinopharm Holdings Shanghai Biomedical Co., Ltd., China); Tris, APS, SDS, TEMED, Tween-20, ponceau, N, N'-methylene bisacrylamide and acrylamide (Sigma, USA); RIPA lysate (Applygen Technologies Inc., China); developer solution, fixative solution (Changsha Well-Biology., Co., Ltd., China); Super ECL Plus hypersensitive luminescent solution (Thermo, USA); proteinase inhibitors (Merck, Germany); HRP goat anti-mouse IgG (Proteintech, USA); ponceaux (Sigma, USA); methylene diacrylamide (Sigma, USA).

1.3 Modeling method

1.3.1 Common peroneal nerve transection modeling for rats in group D

Rats were fasted preoperatively for 24 h, and intraperitoneally anesthetized with 10% chloral hydrate at the concentration of 3.5 mL/(kg·bw), with the skin prepared. Dorsal skin of the thigh was opened by longitudinal incision. Biceps flexor cruris was separated with blunt instruments. The common peroneal nerve was separated with a glass needle and cut using ophthalmic scissors. The anatomical surface was treated with penicillin powder after the surgery. The incision was stitched by layers. Penicillin sodium 160 000 U/d was administrated by intramuscular injection for 3 d. The rats were housed separately in different cages and developed into alcohol-related gastric ulcer model after 3 d observations.

1.3.2 Gastric ulcer modeling

The rats were modeled according to the method in the literature with modifications[4], which had been tested in the pre-experiments. Rats received fasting for 24 h before administrated with 6 mL/(kg·bw) ethanol (rats in group A was administrated with saline). Aspirin effervescent tablets (Asp) were dissolved in physiological saline to prepare Asp suspension (20 mg/mL). Asp suspension was intragggastrically administrated at the concentration of 200 mg/(kg·bw) (group A was given saline) after 1 h of intragastric administration of ethanol. The rats were fasted for 12 h each time before intragastric administration; 3 d after a continuous administration of Asp, rats were treated with moxibustion at Zusanli (ST 36).

1.4 Group processing

Group A: No modeling, administrated with normal saline and subjected to binding, 30 min each time, twice a day for 3 d.

Group B: Received gastric ulcer modeling and subjected to binding, 30 min each time, twice a day for 3 d.

Group C: Received gastric ulcer modeling and moxibustion at Zusanli (ST 36). Zusanli (ST 36) locates at the posterior lateral side of the knee joint, about 5 mm below the capitulum fibulae[5]. After modeling, rats were stabled to the rat plate, with the skin prepared. Insulation stickers with 3 mm holes at the center were affixed on the acupoints to expose bilateral Zusanli (ST 36). The moxa stick was fixed on the self-made moxibustion frame to perform moxibustion about 5 mm away from the acupoints with local temperature around 42 ℃, 30 min each time, twice a day for 3 d.

Group D: Received gastric ulcer modeling after the common peroneal nerve transection, followed by the same moxibustion treatment as that in group C.

1.5 Detection indicators

1.5.1 Gastric mucosal ulcer index (UI)

UI: Separated the whole stomach after anesthesia. The Guth's method was used to score the rats with a ruler and a magnifying glass after rinse with ice saline[6]: ucer length ≤1 mm (including erosion point) is 1 point; ucer length >1 mm, but ≤2 mm was 2 points; ucer length >2 mm, but ≤3 mm was 3 points; ucer length >3 mm, but ≤4 mm was 4 points; ucer length >4 mm was 5 points. The original score was doubled when the ucer width >2 mm. UI was the total score of erosion around the gastric mucosa.

1.5.2 Enzyme-linked immunosorbent assay (ELISA) for detecting tumor necrosis factor-α (TNF-α) and interleukin-4 (IL-4) in gastric mucosa

TNF-α and IL-4 were detected in the homogenate of gastric mucosal tissue according to the instructions of TNF-α and IL-4 ELISA kit.

1.5.3 Western-blot for detecting heat shock protein 70 (HSP70)

The HSP70 was detected in homogenate of gastric mucosal tissue according to instructions of gastric mucosal tissue HSP70 Western-blot kit.

1.6 Statistical analysis

The SPSS 23.0 software was used for statistical analysis. All the measurement data were tested for normality. The data with normal distribution were expressed as mean ± standard deviation ($\bar{x}\pm s$). One-way ANOVA was used to compare the measurement data in multiple groups. Least significant difference (LSD) was used when the variance was homogeneous. Dunnett T3 method was used when the variance was not homogeneous. The rank sum test was used when the data were not in normal distribution. $P<0.05$ indicated a statistically significant difference.

2 Results

2.1 Effect of moxibustion at Zusanli (ST 36) on UI of common peroneal nerve transection rats with gastric ulcer

After the intervention, hematoxylin-eosin (HE) staining showed that the gastric mucosa of group A was rich in capillaries with complete epithelial structure and neatly arranged cells; gastric mucosa of Group B was damaged in the structure of all the layers with a large amount of gastric gland cell necrosis and cell arrangement disorder; gastric mucosal surface of group C partially fell off with significantly improved intracellular congestion; gastric mucosal ulcer of group D was more serious with improved intracellular congestion, but still had visible congestion (Figure 1).

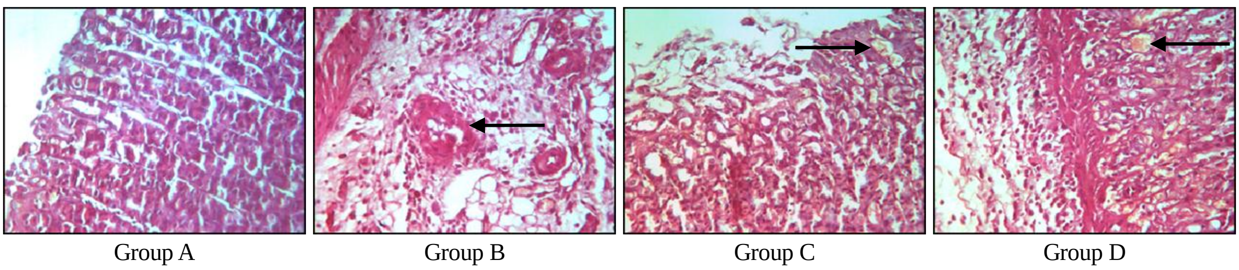

Figure 1. Morphology of gastric mucosa in rats (HE, ×400)

After the intervention, the gastric mucosal UI of group B, group C and group D increased significantly (all $P=0.000$) compared with group A; the UI in group C was higher than that in group B and group D ($P=0.001$, $P=0.014$). There was no statistical difference in UI between group D and group B ($P=0.380$). The above results suggested that moxibustion at Zusanli (ST 36) can effectively promote the repair of gastric mucosal damage, and the repair effect should be based on the complete pathway of common peroneal nerve (Table 1).

Table 1. Comparison of rat UI in each group ($\bar{X}$ ±s, point)

Group	*n*	UI
Group A	12	1.75±1.22
Group B	12	25.67±12.89$^{1)}$
Group C	12	15.08±4.12$^{1)2)}$
Group D	12	23.08±6.13$^{1)}$

Note: Compared with group A, 1) P<0.01; compared with group B, 2) P<0.01

2.2 Effect of moxibustion at Zusanli (ST 36) on initiation of endogenous protection information

2.2.1 Rat's serum TNF-α

After the intervention, compared with group A, the serum TNF-α levels in group B, group C and group D were significantly higher (P=0.000, P=0.042, P=0.000); compared with group B and group D, it was increased significantly in group C (P=0.000, P=0.025); there was no statistically significant difference between group D and group B (P=0.127), (Table 2).

2.2.2 TNF-α in rat's gastric mucosa

After the intervention, compared with group A, the increases of TNF-α in gastric mucosa of group C and group D were not obvious (P=0.880, P=0.438); compared with group B, the increases of TNF-α in gastric mucosa were obvious in group A, group C and group D (P=0.002, P=0.003, P=0.016); the increase was more significant in group C than in group B (P=0.003), and the difference was not statistically significant between group C and group D (P=0.532); the increase was higher in group D than in group B (P=0.016), (Table 2).

2.2.3 Rat's serum IL-4

After the intervention, serum IL-4 level in group A was significantly higher than that in group B, group C and group D (P=0.000, P=0.006, P=0.000); it was significantly higher in group C than that in group B and group D (P=0.000, P=0.034); the difference between group D and group B was not statistically significant (P=0.065), (Table 2).

2.2.4 IL-4 in rat's gastric mucosa

After intervention, the increase of IL-4 in gastric mucosa of group A was higher than that in group B, group C and group D (P=0.000, P=0.001, P=0.000); which were significantly higher in group C and group D than in group B (P=0.000, P=0.002); there was no significant difference between group C and group D (P=0.660), (Table 2).

The results suggested that moxibustion can regulate the levels of TNF-α and IL-4 in serum and gastric mucosa, so as to effectively promote the repair of gastric mucosal damage. The repair is partially based on the complete condition of the common peroneal nerve pathway.

Table 2. Comparing TNF-α and IL-4 levels in serum and gastric mucosa of rats in each group ($\bar{X}$ ±s, pg/mL)

Group	*n*	Serum		Gastric mucosal tissue	
		TNF-α	IL-4	TNF-α	IL-4
Group A	12	8.72±0.41	14.70±1.41	110.53±12.69	5.66±1.35
Group B	12	10.25±0.70$^{1)3)}$	12.81±0.07$^{1)3)}$	139.22±30.42$^{1)3)}$	3.66±0.17$^{1)3)}$
Group C	12	9.25±0.33$^{2)}$	13.92±0.18$^{1)}$	111.86±16.51	4.68±0.07$^{1)}$
Group D	12	9.84±1.11$^{1)4)}$	13.33±0.82$^{1)4)}$	117.43±12.29	4.55±0.85$^{1)}$

Note: Compared with group A, 1) P <0.01, 2) P <0.05; compared with group C, 3) P<0.01, 4) P<0.05

2.3 Effect of moxibustion at Zusanli (ST 36) on HSP70 in gastric mucosa

After the intervention, there was no significant difference in HSP70 between group B and group A (P=0.099); the increases of HSP70 in group C and group D were significantly higher than the increase in group A (P=0.000); the increase of HSP70 in group C was more significant than that in group B and group D (P=0.000, P=0.033); there was no statistically significant difference in the increase between group D and group B (P=0.051). The results above suggested that moxibustion can regulate the expression of HSP70 in gastric mucosa and promote the repair of gastric mucosal damage effectively. The repair effect is based on the complete condition of the common peroneal nerve pathway (Table 3 and Figure 2).

Table 3. Comparison of HSP70 in rat mucosal tissues in each group ($\bar{X}$ ±s)

Group	*n*	HSP70
Group A	12	58.63±1.00
Group B	12	61.48±5.47$^{2)}$
Group C	12	68.55±3.51$^{1)}$
Group D	12	64.86±5.52$^{1)3)}$

Note: Compared with group A, 1) P<0.01; compared with group C, 2) P<0.01, 3) P<0.05

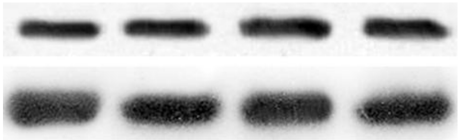

Figure 2. Expression of HSP70 in gastric mucosal tissues

3 Discussion

Repair of injured gastric mucosal depends on the body's multi-facet, multi-level complex defense and repair function, which synergistically forms a complex network system. Different factors in the gastric mucosal protection mechanisms are not isolated, but interact with each other. Various factors of the network regulate the expression of gastric mucosal repair factors via neural pathways, which is one of the major study direction in current gastric mucosal damage protection and repair mechanism[7].

Moxibustion therapy is an important part of traditional Chinese medicine, and also one of the oldest therapies. It has been used in clinic so far because of the characteristics of simplicity, convenience, low cost and efficacy. The core theory of the meridian system is that 'meridians are closely associated with internal organs'. The Meridian of Foot Yangming belongs to stomach and connects with spleen, and is an important link in the treatment of stomach disease by moxibustion. Zusanli (ST 36) is the lower He-Sea point of the stomach, and also the He-Sea point of the Stomach Meridian. Zusanli (ST 36) plays an important role in the information transmission in the repair of gastric mucosa by moxibustion according to the theory of 'meridians and viscera are related'.

According to modern medicine, there are lateral sural cutaneous nerve in the superficial layer of Zusanli (ST 36), and rami musculares nervi fibularis profundi in the deep layer of Zusanli (ST 36). Stimulation information at Zusanli (ST 36) can be transmitted from lateral sural cutaneous nerve and rami musculares nervi fibularis profundi, common peroneal nerve, sciatic nerve into the spinal cord, then into the central nervous system, to regulate the relevant factors and repair the gastric mucosa.

TNF-α, also known as cachectin, is a cytokine released by macrophages and monocytes due to the stimulation of proinflammatory cytokines. It is a proinflammatory protein, and can induce neutrophil migration and adhesion, and penetration of white blood cell out from the blood vessel wall, by up-regulating the expressions of adhesion molecules on the neutrophils and endothelial cells, consequently leading to gastric mucosal endothelial cell damage and reduced blood flow[6]. In addition, TNF-α can cause the production of oxygen free radicals and the lysis of lysosomes by affecting the phospholipid metabolism of the target cell membrane, resulting in cell death and tissue damage[8]. The induction of TNF-α on cell apoptosis has been recognized. It has become an important evaluation indicator of gastric mucosal cell apoptosis in many studies.

IL-4 is a cytokine found in 1982 with a variety of biological functions, mainly secreted by the activated T cells, monocytes, as well as mast cells and basophils[9]. IL-4 plays an important role in the regulation of T and B lymphocyte differentiation and activation, and promotion of immune responses characterized by Th2 cells[10]. IL-4 is a characteristic cytokine of Th2 cells and inhibits the inflammatory response caused by the shifting of cytokine network to Th1. Experiments show that the function of IL-4 is mainly to increase intracellular Bcl-2 protein expression. It is believed that IL-4 inhibits apoptosis by positive regulation of the apoptosis inhibitory gene Bcl-2.

Heat shock proteins are involved in some important cellular physiological activities, such as participation in protein folding, assembly, transport, and repair, and play important roles in maintaining the cells and functions. Heat shock protein is also known as 'molecular chaperone' and the material basis to protect cells[11]. According to the relative molecular mass and the different induction conditions, heat shock proteins can be divided into different families, including HSP100, HSP90, HSP70, HSP60, HSP47, calreticulin, and small heat shock protein[12]. HSP70 is related to stress response and is an important protein in gastric mucosal protection[13]. Studies show that HSP70 exists in human and animal gastric mucosa. Gastric mucosa quickly synthesizes HSP70 during exogenous stimuli (such as ethanol), which shows a protective effect in the acute gastric mucosal damage. The synthesis and transport of intracellular proteins will accelerate when the gastric mucosal epithelial cells are rapidly reconstructed. At this point, more HSP should be synthesized to play a 'chaperone' effect to help the correct folding of the nascent protein peptide chain. Research has shown that moxibustion at Zusanli (ST 36) can effectively control the release of TNF-α, IL-4 and HSP70 in the gastrointestinal tract[14-16].

The results suggest that moxibustion can improve the morphology of rat's gastric mucosal damage, and reduce the UI. Common peroneal nerve transection can produce significant interference in the effect of moxibustion on UI; moxibustion can regulate the serum TNF-α and IL-4 levels. The effect of HSP70 in gastric mucosa to protect the gastric mucosa was partly affected by nerve regulation, indicating that the common peroneal nerve pathway plays an important regulatory role in the action of moxibustion on gastric mucosal damage and protective factor expression. The effect of moxibustion in improving TNF-α and IL-4 levels in tissues is not obviously related with neuromodulation pathways, which may be related to the body fluid pathway. Common peroneal nerve is a part of the neural signaling pathway involved in the protective action of moxibustion at Zusanli (ST 36) on the gastric mucosa, and plays a role in the information transmission.

Conflict of Interest

The authors declared that there was no potential conflict of interest in this article.

Acknowledgments

This work was supported by National Natural Science Foundation of China (国家自然科学基金项目, No. 81303050); Hunan Provincial Outstanding Doctoral Dissertation Funded Projects (湖南省优秀博士论文资助项目, No. 2014-2016).

Statement of Human and Animal Rights

The treatment of animals conformed to the ethical criteria in this experiment.

Received: 11 September 2016/Accepted: 15 October 2016

References

[1] Chen G, Xiang J, Ouyang LZ, Li F, Xiang LJ, Chen Y, Yang Z, Yu J, Li TL, Peng L. Effect of moxibustion stimulation on repair of gastric mucosal lesions in rats after peroneal neurotomy. World J Gastroenterol, 2016, 24(2): 248-254.

[2] Cho SH. Effect of moxibustion on physiological indices and autonomic nervous symptoms in adults with prehypertension. J Korean Acad Nurs, 2010, 40(5): 686-694.

[3] Lee MS, Kang JW, Ernst E. Does moxibustion work? An overview of systematic reviews. BMC Res Notes, 2010, 3: 284-288.

[4] Chen ZF. Research of the Establishment of An Ideal Chronic Gastric Ulcer Model. Shantou: Master Thesis of Shantou University, 2012: 6-7.

[5] Li ZR. Experimental Acupuncture Science. Beijing: China Press of Traditional Chinese Medicine, 2007: 327-329.

[6] Jiang Y, Song CY, Wang GZ, Zhou YB, Chen BG, Lu QF, Wang SP. Study of the correlation of iNOS, TNF-α、IL-1β in gastric mucosa tissues in patients with Helicobacter pylori associated gastritis. Bengbu Yixueyuan Xuebao, 2012, 37(5): 556-558.

[7] Li ZS, Zhan XB, Xu GM. Gastric Mucosal Injury and Protection: Basic and Clinic. Shanghai: Shanghai Scientific and Technical Publishers, 2004: 4-5.

[8] Koyama S. Flow cytometric measurement of tumor necrosis factor-related apoptosis-inducing ligand and its receptors in gastric epithelium and infiltrating mucosal lymphocytes in Helicobacter pylori-associated gastritis. J Gastroenterol Hepatol, 2003, 18(7): 763-770.

[9] Brown JM, Attardi LD. The role of apoptosis in cancer development and treatment response. Nat Rev Cancer, 2005, 5(3): 231-234.

[10] Lou ZZ, Yang Q, Jiang XF, Zhang QQ, Munire Muhetaer, Gao L. The correlation between IL-4 and IgE levels presented in Xinjiang Uighur and Han patients with allergic rhinitis. Xinjiang Yike Daxue Xuebao, 2012, 35(4): 439-441, 456.

[11] Hahm KB, Park IS, Kim YS, Kim JH, Cho SW, Lee SI, Youn JK. Role of rebamipide on induction of heat shock protein and protection against reactive oxygen metabolite-mediated cell damage in cultured gastric mucosal cells. Free Radic Biol Med, 1997, 22(4): 711-716.

[12] Pawlowska Z, Baranska P, Jerczynska H, Koziolkiewicz W, Cierniewski CS. Heat shock proteins and other components of cellular machinery for protein synthesis are up-regulated in vascular endothelial cell growth factor- activated human endothelial cells. Proteomics, 2005, 5(5): 1217-1227.

[13] Welch WJ. Mammalian stress response: cell physiology, structure/function of stress proteins and implications for medicine and disease. Physiol Rev, 1992, 72(4): 1063-108l.

[14] Wang XM, Lu Y, Wu LY, Yu SG, Zhao BX, Hu HY, Wu HG, Bao CH, Liu HR, Wang JH, Yao Y, Hua XG, Guo HY, Shen LR. Moxibustion inhibits interleukin-12 and tumor necrosis factor alpha and modulates intestinal flora in rat with ulcerative colitis. World J Gastroenterol, 2012, 18(46): 6819-6828.

[15] Tracey KJ. Physiology and immunology of the cholinergic antiinflammatory pathway. J Clin Invest, 2007, 117(2): 289-296.

[16] Yi SX, Yu J, Chang XR, Peng Y, Lin YP. Effect of quercetin blocking HSP70 expression on pre-moxibustion suppressing gastric mucosal cell apoptosis. Zhongguo Zhongyiyao Xinxi Zazhi, 2009, 16(10): 30-33.

Translator: Yang Yan-ping (杨燕萍)

