The clinical efficacy of sepsis with early intervention of electroacupuncture

Ling-Cong Wang, Jian-Nong Wu *

Department Intensive Care Unit, The First Affiliated Hospital of Zhejiang Chinese Medical University, Hangzhou 310006, China
wu_jiannong@163.com

Abstract: Objective: to investigate the clinical efficacy of early intervention of electroacupuncture on sepsis. **Methods:** the patients with sepsis were chosen from ICU, First Affiliated Hospital, Zhejiang Chinese Medicine University from January, 2009 to June, 2011. All patients were randomly divided into two groups: treatment group and the control group. The control group was based on conventional treatment, such as anti-infective, anti-shock, respiratory support and nutritional support therapy; the treatment group was the combination of conventional treatment and daily electroacupuncture therapy, and the selecting points were Zusanli (ST 36), Tien Chu, Shangjuxu (ST 37) and Xiajuxu (ST 39) for three days. There were no significant differences about age, gender and APACHE Ⅱ score between the patients of two groups. The following indicators were observed in the two groups before and after treatment: C-reaction protein (CRP), IL-6, TNF-α, APACHE Ⅱ score, HLA-DR of $CD14^+$ mononuclear cells, the hospitalization days in ICU, the duration of ventilator and the 28-day mortality. **Results:** the CRP after treatment was significantly lower than that before treatment in the two groups ($P<0.01$), the IL-6 and TNF-α after treatment were significantly lower than that before treatment in the treatment group ($P<0.05$, $P<0.01$), the CRP, IL-6 and TNF-α of treatment group were significantly lower than that of control group after treatment ($P<0.05$). The HLA-DR of $CD14^+$ mononuclear cells after treatment was significant higher than that before treatment in the treatment group ($P<0.01$), and the HLA-DR of $CD14^+$ mononuclear cells of treatment group was significantly higher than that of control group after treatment ($P<0.05$). The APACHE Ⅱ score after electroacupuncture treatment was significantly lower than that before treatment in the treatment group ($P<0.05$). However, there were no significant differences in the duration of ICU stay, the duration ventilator and the 28-day mortality between the two groups. **Conclusion:** the early intervention of electroacupuncture can reduce the blood CRP, IL-6, TNF-α and APACHE Ⅱ score and improve the HLA-DR of $CD14^+$ mononuclear cells in patients with sepsis.

[Ling-Cong Wang, Jian-Nong Wu. **The clinical efficacy of sepsis with early intervention of electroacupuncture.** *Life Sci J* 2013;10(3):1900-1903]. (ISSN: 1097-8135). http://www.lifesciencesite.com. 282

Key words: electroacupuncture; sepsis; ST 36; ST 37; ST 39

1.Introduction

Sepsis is one of the main causes of death in critically illness patients, the mortality of sepsis is 28.6% (Dellinger et al., 2008), therefore, reduction of death from sepsis is a common challenge of clinicians. The acupuncture of traditional Chinese medicine (TCM) can dual-directional regulate nerve-endocrine-immune system with less side effects, which has been paid more and more attention. It has been proved that acupuncture on ST 36 of parasympathetic nerve could significantly promote gastrointestinal motility, improve immune function and reduce inflammation. In this study, we will investigate the clinical efficacy of electroacupuncture on patients with sepsis.

2. Materials and methods

2.1 Research objects

The patients with sepsis were chosen from ICU, First Affiliated Hospital, Zhejiang Chinese Medicine University from January, 2009 to June, 2011. All patients were accord with the diagnostic criteria of sepsis "Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock, 2008". The exclusion criteria were as followings: patients who didn't agree with the research; patients who used non-steroidal anti-inflammatory drugs within 30 days; patients who took part in other research. The research was approved by ethics committee of First Affiliated Hospital, Zhejiang Chinese Medicine University. Sixty-eight patients were divided into two groups according the random allocation table of SPSS software: control group and treatment group.

2.2 Treatment methods

The control group: according to the conventional treatment, such as anti-infective, anti-shock, respiratory support and nutritional support therapy; the treatment group was the combination of conventional treatment and daily electroacupuncture therapy, and the selecting points were Zusanli (ST 36), Tien Chu, Shangjuxu (ST 37) and Xiajuxu (ST 39). Using KWD-808 Ⅰ multifunctional acupuncture instrument, continuous wave, frequency: 4 Hz. One time on morning and night, 60 min each time, the therapy was

maintained for 3 days.

2.3 Outcome measures

The following indicators were observed in the two groups before and after treatment: C-reaction protein (CRP), IL-6, TNF-α, APACHE Ⅱ score, HLA-DR of $CD14^+$ mononuclear cells, the hospitalization days in ICU, the duration of ventilator and the 28-day mortality.

2.4 Statistical analysis

By doing the normality test, the continuous variables followed a normal distribution and were expressed as mean ± standard deviation (SD). Statistical analysis was performed using paired two-tailed t test to compare the variables between groups. Then statistical significant of differences was examined by paired-samples T Test in the corresponding group between before and after treatment. The 28-day mortality was analyzed with x^2 test. A $P<0.05$ was considered statistically significant. Statistical analysis was performed using SPSS software (SPSS 17.0, SPSS Inc., USA).

3.Results

3.1 General information

68 patients met the criteria and randomly divided into treatment group and control group according to sequence of hospitalization. 18 patients exited the experiment because of death, automatic discharge and changes of treatment. 26 patients eventually completed the experiment in treatment group, including 19 males and 7 females, the age was 73.50±8.96 years old, and the APACHE Ⅱ score was 16.25±2.19; 24 patients finished the experiment in the control group, including 16 males and 8 females, the age was 69.88±8.96 years old, and the APACHE Ⅱ score was 16.46±2.42. There were no significant differences about age, gender and APACHE Ⅱ score between the patients of two groups ($P>0.05$).

3.2 Comparison of inflammatory indicator in the two groups

The CRP after treatment was significantly lower than that before treatment in the two groups ($P<0.01$), the IL-6 and TNF-α after treatment were significantly lower than that before treatment in the treatment group ($P<0.05$, $P<0.01$), the CRP, IL-6 and TNF-α of treatment group were significantly lower than that of control group after treatment ($P<0.05$). The details are shown in Table 1.

Table 1. Comparison of CRP,IL-6 and TNF-α before and after treatment in two groups（x±s）

	group	Before treatment	After treatment	t	P
CRP(mg/d)	Control group	113.32±28.51	103.29±24.25	6.10	<0.01
	Treatment group	112.29±23.59#	82.19±15.54*	10.66	<0.01
IL-6(pg/ml)	Control group	34.45±5.40	32.60±4.38	1.91	0.069
	Treatment group	31.67±4.55#	21.85±2.51*	11.45	<0.01
TNF-α (fmol/ml)	Control group	32.37±7.20	30.96±3.59	1.25	0.22
	Treatment group	31.14±8.48#	23.06±2.11*	7.11	<0.01

#P>0.05, *P<0.05 compared to control group.

3.3 Comparison of HLA-DR of $CD14^+$ mononuclear cells and APACHE Ⅱ score

The HLA-DR of $CD14^+$ mononuclear cells after treatment was significant higher than that before treatment in the treatment group ($P<0.01$), and the HLA-DR of $CD14^+$ mononuclear cells of treatment group was significantly higher than that of control group after treatment ($P<0.05$). The APACHE Ⅱ score after electroacupuncture treatment was significantly lower than that before treatment in the treatment group ($P<0.05$). The details are shown in Table 2.

Table 2. HLA-DR on APACHE II and CD14+ cells before and after treatment in two groups（x±s）

	group	Before treatment	After treatment	t	P
APACHEⅡ(%)	Control group	16.25±2.19	17.33±4.10	-1.17	0.25
	Treatment group	16.46±2.42#	15.19±2.17#	2.07	0.049
HLA-DR(%)	Control group	54.20±6.74	55.29±7.79	-0.75	0.35
	Treatment group	54.43±6.86#	65.36±5.06 *	-8.16	<0.01

#P>0.05, *P<0.05 compared to control group.

3.4 Comparison of the duration ventilator, ICU stay and 28-day mortality

There were no significant differences in the duration of ICU stay, the duration ventilator and the 28-day mortality between the two groups ($P>0.05$). The details are shown in Table 3.

Table 3. Comparison the duration of ICU stay and the duration ventilator（x±s）

	Control group	Treatment group	t	P
ICU stay(days)	28.38±13.62	23.92±9.20	3.88	0.55
Ventilator time (days)	25.38±12.15	22.50±8.82	1.61	0.21

4. Discussion

For Chinese medicine, sepsis is a whole new concept; there is no corresponding disease in TCM. Therefore, there is no available dialectical system, but the sepsis belongs to febrile disease. The TCM physician speculated the mechanism of sepsis was intrinsic toxic heat, accumulation of blood stasis, deficiency of healthy qi and obstruction of fu-qi. The main therapy methods were heat-clearing and toxin-relieving therapy, promoting blood circulation therapy and comprehensive therapy. TCM believed that deficiency of healthy qi is the root cause of sepsis, so improving the healthy qi has become the hotspot in recent years(Li and Li 2010).

The venous blood of patients were collected in day 1, 4, 7, 14 and 28 after diagnoses, the expression of HLA-DR of $CD14^+$ mononuclear cells were detected with flow cytometry, and the APACHE Ⅱ score was recorded until sepsis disappear. 64 patients were enrolled in this experiment, and 18 patients exited the experiment. From day 4, the HLA-DR of $CD14^+$ mononuclear cells in treatment group was significantly higher than that in control group (P<0.001), and survival rate of patients whose HLA-DR>30% was significantly higher than those whose HLA-DR<30%. The expression of HLA-DR of $CD14^+$ mononuclear cells negatively correlated with APACHE Ⅱ score. We believed that the low expression of HLA-DR of $CD14^+$ mononuclear cells suggested that patients were in a state of immune suppression, and the expression of HLA-DR of $CD14^+$ mononuclear cells can be used to determine the severity of sepsis and assess prognosis(Wu et al.,2006). Our study found that subcutaneous injection of 1.6 mg thymosin a1 for one week could improve the HLA-DR level of $CD14^+$ mononuclear cells of patients with severe hospital acquired pneumonia, and shorten the ICU stay and duration of mechanical ventilation; however, the mortality, the timing of the start of treatment, the course of treatment and dose need further study to confirm. Our study suggests that improving the HLA-DR level of $CD14^+$ mononuclear cells benefits for patients with sepsis(Lei et al.,2005).

In 2009, we found that electroacupuncture at ST 36 could reduce the apoptosis of thymocytes in sepsis rat model which was induced by cecal ligation and puncture; the mechanism may be related to the synthesis and release of vasoactive intestinal peptide by pituitary and peripheral blood of rats(Lei et al., 2009). In recent years, some clinical and experimental studies found that acupuncture at ST 36 could enhance immune function and reduce the apoptosis of lymphocytes. Wang *et al* (2006) found electroacupuncture at ST 36 and appendix points could inhibit the apoptosis of thymocytes induced by traumatic stress, which could improve the dysfunction of immune function. Zhang *et al* (2005) proved that electroacupuncture at ST 36 could protect immune organ and inhibit apoptosis of thymocytes in rats with morphine withdrawal. It also has been proved that electroacupuncture at ST 36 could protect organ damage caused by proinflammatory cytokines, decrease the ALT, CREA, TNF-α, nitric oxide and myeloperoxidase activity, and reduce organ edema and dysfunction in rats with sepsis induced by cecal ligation and puncture, which has certain preventive effect for MODS (Hu et al.,2010; Hu et al.,2009). Other findings suggest that electroacupuncture pretreatment at the ST 36 and Neiguan (PC6) acupoints attenuated the LPS-induced inflammatory response and mitigated acute kidney injury (Gu et al., 2011). The above studies show acupuncture at ST 36 can enhance immune function.

In recent years, it is believed that electroacupuncture benefits to human beings. Liu *et al* (2011) found that electroacupuncture at PC6 could alleviate the development of liver injury and dysfunction in endotoxic rats. Song *et al* (2012) found that electroacupuncture at specific acupoints could modulate systemic inflammatory responses and improve survival via its impact on the autonomic nervous system in a rat model of sepsis. Zhao *et al* (2011) found that electroacupuncture can decrease the serum TNF-α and IL-6 contents, and down-regulate pulmonary NF-κB expression level in LPS induced endotoxaemia rats.

Zusanli and Tien Chu are the sea points of stomach channel of foot-yang ming, which is the important point of gastrointestinal function regulation; Shangjuxu is the lower sea point of colon, Xiajuxu is the lower sea point of small intestine, which are essential points for regulation of digestive function. Acupuncture at these four points can dredge meridian and move the bowels. Electroacupuncture at Zusanli can alleviate hepatic edema and dysfunction in septic rats, which might be related with the completeness of cranial nerve (Shi et al.,2010) In this study, early electroacupuncture at ST 36, Tien Chu, ST 37 and ST

39 of patients with sepsis could reduce the CRP, IL-6, TNF-α and APACHE Ⅱ score, improve the HLA-DR of $CD14^+$ mononuclear cells; however, there were no significant differences in the duration of ICU stay, the duration ventilator and the 28-day mortality between the two groups, which might be correlated with strengthening the immune system and inhibition of inflammation.

Early electroacupuncture at ST 36, Tien Chu, ST 37 and ST 39 of patients with sepsis could reduce the CRP, IL-6, TNF-α and APACHE Ⅱ score, improve the HLA-DR of $CD14^+$ mononuclear cells.

Correspond to:Jian-Nong Wu
Department Intensive Care Unit, The First Affiliated Hospital of Zhejiang Chinese Medical University, 54# Youdian Road, Hangzhou 310006, China.
Tel.:+86-571-870717326;
Fax:+86-571-87071732;
Email: wu_jiannong@163.com

References

1. Dellinger RP, Levy MM, Carlet JM, Bion J, Parker MM, Jaeschke R, Reinhart K, Angus DC, Brun-Buisson C, Beale R, Calandra T, Dhainaut JF, Gerlach H, Harvey M, Marini JJ, Marshall J, Ranieri M, Ramsay G, Sevransky J, Thompson BT, Townsend S, Vender JS, Zimmerman JL, Vincent JL. Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock: 2008. Intensive Care Med. 2008;34:17-60.
2. Li HT, Li YH. The treatment for sepsis by traditional Chinese medical science. Shaanxi J Tradit Chin Med 2010;31:124-6.
3. Wu YC, Zh X, Fang Q. Observation of the expression of CD14+ monocyte human leukocyte antigen DR in septic patients. Chin J Crit Care Med 2006; 26: 249-51.
4. Lei S, Wu YC, Chen JH. Application of thymosin alpha1 to the patients with severe hospital acquired pneumonia. Chin J Crit Care Med 2005; 25: 716-9.
5. Lei S, Xu YG, Jiang RL. Effects of electro-acupuncture at 'Zusanli' on the apoptosis of thymocytes in rats with sepsis. The journal of traditional Chinese medicine.2009; 24:1369-71.
6. Wang J, Sun J, Wang YQ. Effect of electroacupuncture on thymocyte proliferation and apoptosis in surgical trauma-stress rats. Acupuncture Research 2006;31:12-4.
7. Zhang RJ, Song XG, Tang ZL. Experimental study on the effect of electroacupuncture in resisting apoptosis of thymocytes in rats with morphine abstinence syndrome. Acupuncture Research 2005;20; 30:94-6.
8. Hu S, Zhang LJ, Bai HY, Tian YJ. Effect of electro-acupuncture at Zusanli point on tumor necrosis factor- a induced- multiple organ dysfunction in rats with sepsis. Chinese Journal of Pathophy siology 2010;26: 353-6
9. Hu S, Zhang LJ, Bai HY, Bao CM. The Protective effect of electroacupuncture at Zusanli Point on Proinflammatory factors indueed-hepatic in rats with sepsis. J Med Res 2009;38: 25-8.
10. Gu G, Zhang Z, Wang G, Han F, Han L, Wang K, Liu J, Li W. Effects of electroacupuncture pretreatment on inflammatory response and acute kidney injury in endotoxaemic rats. J Int Med Res. 2011;39:1783-97.
11. Liu HW, Liu MC, Tsao CM, Liao MH, Wu CC. Electro-acupuncture at 'Neiguan' (PC6) attenuates liver injury in endotoxaemic rats. Acupunct Med. 2011; 29:284-8.
12. Song JG, Li HH, Cao YF, Lv X, Zhang P, Li YS, Zheng YJ, Li Q, Yin PH, Song SL, Wang HY, Wang XR. Electroacupuncture improves survival in rats with lethal endotoxemia via the autonomic nervous system. Anesthesiology. 2012;116:406-14.
13. Zhao YX, He W, Gao XY, Rong PJ, Zhu B.Effect of electroacupuncture of auricular concha on inflammatory reaction in endotoxaemia rats. Zhen Ci Yan Jiu. 2011;6:187-92.
14 . Shi X, Zhang LJ, Bai HY, Bao CM, Hu S, Guan L. Effects of electroacupuncture on hepatic blood flow and lipid peroxidation in septic rats]. Zhongguo Zhen Jiu. 2010;30:397-400.
13. Zhao YX, He W, Gao XY, Rong PJ, Zhu B.Effect of electroacupuncture of auricular concha on inflammatory reaction in endotoxaemia rats. Zhen Ci Yan Jiu. 2011;6:187-92.
14. Shi X, Zhang LJ, Bai HY, Bao CM, Hu S, Guan L. Effects of electroacupuncture on hepatic blood flow and lipid peroxidation in septic rats]. Zhongguo Zhen Jiu. 2010;30:397-400.

8/23/2013