Gao F, Xu XK, Liang YL, *et al*. Effect of low-frequency electroacupuncture on pancreatic endocrine system in patients with simple obesity. J Acupunct Tuina Sci, 2017, 15(3): 209-213
DOI: 10.1007/s11726-017-1002-2

Clinical Study

Effect of low-frequency electroacupuncture on pancreatic endocrine system in patients with simple obesity

低频电针对单纯性肥胖症患者胰岛内分泌系统的影响

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Abstract

Objective: To observe different efficacies of low-frequency electroacupuncture (EA) on pancreatic endocrine system in male and female patients with simple obesity due to spleen deficiency-related dampness.

Methods: A total of 80 simple obesity patients were assigned to a male group (n=37) and a female group (n=43). Both groups received a 30-minute low-frequency EA at Yinlingquan (SP 9), Sanyinjiao (SP 6), Zusanli (ST 36), Fenglong (ST 40), Quchi (LI 11), Tianshu (ST 25), Zhongwan (CV 12), Shuifen (CV 9), Qihai (CV 6) and Guanyuan (CV 4). The treatment was done once a day, and 10 times made up a course of treatment. Patients in both groups were treated for 2 courses. Then the changes in body mass index (BMI), serum insulin, insulin antibodies and leptin level in the two groups were observed and analyzed.

Results: After treatment, the BMI, serum insulin, insulin antibodies and leptin levels were significantly reduced in both groups (P<0.01 or P<0.05); the BMI and serum insulin concentration were more significantly reduced in the male group than those in the female group (both P<0.01); and the leptin level was more significantly reduced in the female group than that in the male group (P<0.01).

Conclusion: EA can significantly regulate BMI and pancreatic endocrine system in both men and women with simple obesity; however, there is a gender difference: better effect for men in reducing BMI and serum insulin and better effect for women in reducing serum leptin level.

Keywords: Acupuncture Therapy; Electroacupuncture; Obesity; Sex Characteristics; Body Mass Index; Insulins; Insulin Antibodies; Leptin

【摘要】目的：探讨低频电针对男、女脾虚湿盛型单纯性肥胖症患者胰岛内分泌系统调节作用的差异性。**方法：**共纳入单纯性肥胖症患者80例，男性组37例，女性组43例，采用低频电针刺激两组患者的阴陵泉、三阴交、足三里、丰隆、曲池、天枢、中脘、水分、气海和关元，留针30 min，每天治疗1次，10次为1疗程，治疗2个疗程。观察两组患者治疗前后身体质量指数(BMI)及血清胰岛素、胰岛素抗体及瘦素的含量变化，并进行比较分析。**结果：**治疗后，两组患者BMI及血清胰岛素、胰岛素抗体及瘦素含量均较治疗前明显下降(P＜0.01或P＜0.05)；男性患者BMI及血清胰岛素含量较女性患者降低明显(均P＜0.01)；女性患者血清瘦素含量较男性患者降低明显(P＜0.01)。**结论：**电针对男女单纯性肥胖症患者BMI及紊乱的胰岛素内分泌系统有明显的调节作用，但存在一定的性别差异。在降低BMI及血清胰岛素方面，男性优于女性；在减低血清瘦素方面，女性优于男性。

【关键词】针刺疗法；电针；肥胖症；性别特征；身体质量指数；胰岛素；胰岛素抗体；瘦素

【中图分类号】R246.1　　**【文献标志码】**A

The number of obesity patients increases with improvement in living standard. Acupuncture is playing an increasing role in preventing, treating and reducing obesity and improving people's quality of life (QOL)[1-2]. Over the recent years, animal experiments have shown a gender difference in acupuncture effect for weight loss[3-5]. To further investigate the regulation effect of acupuncture on simple obesity in both men and women,

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we've observed and analyzed the EA effect on BMI, serum insulin, insulin receptors and leptin levels in men and women with simple obesity due to spleen deficiency coupled with dampness between March 2014 and October 2015. The results are now summarized as follows.

1 Clinical Materials

1.1 Diagnostic criteria

They were based on the *Diagnostic and Therapeutic Evaluation Criteria for Simple Obesity* stipulated in the 5th National Academic Conference on Simple Obesity in 1997[6].

1.1.1 Diagnosis in Western medicine

A body overweight of ＞20% standard body weight (a body overweight of ＜20% standard body weight: overweight; 20%-30%: mild obesity; 30%-50%: moderate obesity; ＞ 50%: severe obesity); a fat percentage (F%) of ＞30% (F% in men: 25%-30% is overweight; 30%-35% is mild obesity; 35%-45% is moderate obesity; and ＞45% is severe obesity. F% in women: 30%-35% is overweight; 35%-40% is mild obesity; 40%-50% is moderate obesity; and ＞50% is severe obesity). A BMI of ＞25 (25-26: overweight; 26-30: mild obesity; 30-40: moderate obesity; and ＞40: severe obesity). Patients can be diagnosed if they have 2 or more of the 3 above items.

1.1.2 Diagnosis in Chinese medicine

Spleen deficiency coupled with dampness: Edema, fatigue, weakness, limb heaviness, scanty urine, a poor appetite and abdominal fullness. The pulse is deep and thready. The tongue is pale red with a thin, greasy coating. Patients can be diagnosed if they have 2-3 symptoms and typical tongue and pulse conditions.

1.2 Inclusion criteria

Those who met the diagnostic criteria in Western and Chinese medicine; aged between 18 and 40 years; duration between 1 and 10 years; having not received any other weight-loss therapies prior to and during the treatment and were willing to accept follow-up visits/interviews; having no organic conditions; and willing to participate in the study and sign the informed consent.

1.3 Exclusion criteria

Secondary obesity confirmed by a medical history, physical examination or lab test; breast-feeding, pregnant women or women who plan to be pregnant or 1 year within childbirth; having complications of severe, primary diseases involving the cardio-cerebrovascular, hepatic, renal and hemopoietic systems, mental disorders or compromised immune system; having diabetes, connective tissue diseases, malignant tumor, systemic failure, hemophilia or hemorrhagic tendency; having participated in other clinical trials in the recent month; and those not suitable for this study.

1.4 Statistical management

The SPSS 13.0 version software was used for statistical management. The measurement data in normal distribution were expressed in the form of mean ± standard deviation ($\bar{X} \pm s$). The *t*-test was used for intra-group comparison before and after treatment. Independent sample *t*-test was used for inter-group comparison. Non-parameter test was used for data in abnormal distribution. Two-tailed tests were used for all statistical analysis. A *P* value of less than 0.05 indicated a statistical significance.

1.5 General materials

The 80 patients were from the Outpatient Departments of Hebei University of Chinese Medicine and Hebei Institute of Traditional Chinese Medicine Hospital. There were no between-group statistical differences in baseline data (all $P>0.05$), indicating that the two groups were comparable.

Table 1. Between-group comparison in baseline data

Group	*n*	Mean age ($\bar{X} \pm s$, year)	Mean duration ($\bar{X} \pm s$, year)	BMI ($\bar{X} \pm s$, kg/m^2)
Male	37	23.14±2.49	3.46±1.50	28.65±1.48
Female	43	23.74±3.87	3.65±1.41	28.10±1.27

2 Treatment Methods

Patients in the two groups received the same treatment.

Points: Zhongwan (CV 12), Shuifen (CV 9), Qihai (CV 6), Guanyuan (CV 4), 2-4 Ashi points on the abdomen and bilateral Yinlingquan (SP 9), Sanyinjiao (SP 6), Zusanli (ST 36), Fenglong (ST 40), Quchi (LI 11) and Tianshu (ST 25).

Method: The patients were asked to take a supine lying position. Filiform needles of 0.30-0.34 mm in diameter and 40-75 mm in length were used to puncture Zhongwan (CV 12) towards Shuifen (CV 9), Qihai (CV 6) towards Guanyuan (CV 4), Ashi point towards the other Ashi points (lift the needle tip to the layer of fat accumulation upon arrival of qi, and then puncture till the deeper layer). Then 2-3 pairs of points on one side (points on both sides were used alternately) were connected to the SDZ-II electric stimulator, using a continuous wave and a frequency of 2 Hz for a total of 30 min. The treatment was done once a day and 10 times made up a course of treatment. Patients were treated for 2 courses.

3 Outcomes Observation

3.1 Observation items and methods

3.1.1 Body height and weight

The body height and weight were measured by a specially-assigned person using the same measuring

apparatus before and after treatment. Then the BMI (kg/m^2) was calculated.

BMI (kg/m^2)＝Body weight (kg)÷Height (m)^2.

3.1.2 Serum biochemical items

The insulin, insulin receptors and leptin levels were observed before and after treatment.

A 5 mL of venous blood was drawn before and after treatment and injected into a tube of 30 μL and 40 μL aprotinin containing 10% ethylenediaminetetraacetic acid disodium (ETDA-2Na). After completely mixed (4 ℃), the solution were kept at –20 ℃ following a 10-minute centrifugation (3 000 r/min). The insulin concentration was measured using liquid equilibrium competitive radioimmunoassay. The insulin antibodies were measured using the liquid combined with radioimmunoassay. The leptin level was measured using the equilibrium method. The measurement was done in the Laboratory Center of Hebei University of Chinese Medicine.

3.2 Results

3.2.1 Between-group comparison of BMI

Before treatment, there were no between-group statistical differences in body weight and BMI (both $P > 0.05$), indicating that the two groups were comparable. After treatment, the body weight and BMI were significantly reduced in both groups (both $P < 0.01$), and there were between-group statistical differences (more significant in male group, both $P < 0.01$), (Table 2).

3.2.2 Between-group comparisons of insulin, insulin receptor and leptin levels

After treatment, the serum insulin, insulin receptor and leptin levels were significantly reduced in both groups ($P < 0.05$ or $P < 0.01$). There were between-group statistical differences in insulin concentration (more significant in male group, $P < 0.01$) and leptin level (more significant in female group, $P < 0.01$), (Table 3).

Table 2. Between-group comparisons of body weight and BMI before and after treatment ($\bar{X} \pm s$)

Group	*n*	Weight (kg)			BMI (kg/m^2)		
		Before treatment	After treatment	Difference value	Before treatment	After treatment	Difference value
Male	37	85.03±3.89	75.56±2.9[1)]	9.40±2.55[2)]	28.65±1.48	24.50±1.26[1)]	4.19±0.85[2)]
Female	43	69.86±3.82	63.30±4.24[1)]	6.77±2.31	28.10±1.27	25.45±1.45[1)]	2.65±0.93

Note: Intra-group comparison before and after treatment, 1) $P<0.01$; compared with the female group, 2) $P<0.01$

Table 3. Between-group comparisons of serum insulin, insulin receptor and leptin levels before and after treatment ($\bar{X} \pm s$)

Group	*n*	Insulin (uIU/mL)			Insulin receptor			Leptin (ng/mL)		
		Before treatment	After treatment	Difference value	Before treatment	After treatment	Difference value	Before treatment	After treatment	Difference value
Male	37	10.62±4.71	6.17±3.31[1)]	4.38±0.94[3)]	1.69±0.40	1.18±0.23[2)]	0.40±0.23	3.37±0.70	2.70±0.63[2)]	0.66±0.23
Female	43	11.85±4.62	9.86±4.54[1)]	2.07±0.77	1.82±0.41	1.35±0.30[2)]	0.47±0.26	10.19±1.42	6.30±1.49[1)]	3.49±1.09[4)]

Note: Intra-group comparison before and after treatment, 1) $P<0.01$, 2) $P<0.05$; compared with the female group, 3) $P<0.01$; compared with the male group, 4) $P<0.01$

4 Discussion

Simple obesity results when caloric intake exceeds energy expenditure. Patients mainly manifest as obesity or associated metabolic disorders[7]. In Chinese medicine, this condition can be differentiated into five patterns: spleen deficiency coupled with dampness, stomach heat coupled with dampness, liver qi stagnation, yang deficiency of the spleen and kidney, and internal heat due to yin deficiency. Clinically, spleen deficiency coupled with dampness is more common in obese population. As a result, this study targets this pattern. Today, sedentary lifestyle, work stress or over intake of high-calorie, high-fat and high-sugar food may affect the function of the spleen, resulting in phlegm-dampness, and subsequently, obesity. Consequently, points of the Spleen, Stomach, Large Intestine Meridians and of the Conception Vessel were selected to 'strengthen the spleen, resolve dampness, transform phlegm, unblock Fu organs, down-regulate turbidity and reduce fat'. Yinlingquan (SP 9) and Sanyinjiao (SP 6) fortify the spleen and stomach, resolve dampness and transform phlegm. Zusanli (ST 36), the lower He-Sea point of the stomach, strongly strengthens the spleen and stomach in promoting digestion and relieving food stagnation, and assists the function of Yinlingquan (SP 9) and Sanyinjiao (SP 6) through the internal-external connection between the Spleen Meridian and Stomach Meridian. Fenglong (ST 40), the Luo-Connecting point of the Stomach Meridian, connects the Spleen Meridian and Stomach Meridian, resolves phlegm and removes turbidity. Quchi (LI 11) is the He-Sea point of the Large

Intestine Meridian and Tianshu (ST 25) is the Front-Mu point of the large intestine. The two points regulate the large intestine, drain down the turbidity and reduce fat. Zhongwan (CV 12), the Front-Mu point of the stomach, strengthens the spleen, resolves phlegm, down-regulates stomach qi and removes turbidity. Shuifen (CV 9) strengthens the spleen and stomach and resolves water-dampness retention. Qihai (CV 6) and Guanyuan (CV 4) tonify the spleen and kidney, supplement Yang qi, transform qi and circulate water. Electroacupuncture (EA) acts to unblock meridians, harmonize qi and blood, and regulate yin and yang of the Zang-fu organs. Results of our previous animal experiment and pre-clinical trials have shown a significant effect of low-frequency EA on simple obesity with gender difference[8-9]. This study therefore observed the weight-loss efficacy and action mechanism of low-frequency EA in male and female patients.

Insulin is the only sugar-lowering hormone that promotes the synthesis of neutral fats in fat cells, increases the transport of glucose into body cells and stimulates glycogen synthesis. Insulin receptor may result in lipodystrophy, microvascular disease, insulin resistance, pharmacokinetic change of insulin, and insulin sensitivity or hypoglycemia[10]. Studies have found that there is probably a 'fat-pancreatic islets endocrine axis' between the fatty tissue and pancreatic islets[11] as well as a two-way feedback loop via leptin and insulin. In patients with obesity, the disordered 'fat-pancreatic islets endocrine axis' affects the function of leptin in inhibiting insulin secretion and results in hyperinsulinemia, and subsequently, insulin receptors, insulin resistance and hyperleptinemia (as a result of insulin stimulating leptin secretion in fatty tissue)[12-13]. In addition to hyperleptinemia and hyperinsulinemia, patients with obesity also have leptin resistance, insulin resistance and disturbance of carbohydrate metabolism[14], manifesting as increased food intake, decreased energy expenditure and weight gain.

Experimental results have shown significant reduction in blood sugar, insulin, insulin receptors and leptin in both male and female patients with simple obesity. This indicates that low-frequency EA can significantly improve the abnormal levels in blood sugar, insulin, insulin receptors and leptin in obesity patients. The mechanism might be associated with its correction of disordered 'fat-pancreatic islets endocrine axis'. As a result, it regulates the insulin/leptin resistance, reduces the levels of insulin receptors, stimulates insulin sensitivity, boosts energy expenditure and thus facilitates weight loss. However, there is a gender difference. EA showed a better effect for men in improving the serum insulin concentration, probably because of the positive correlation between androgen and insulin sensitivity[15]. Testosterone plays an important role in regulating insulin sensitivity, and low serum testosterone is commonly seen in diabetes and obesity[16]. Low testosterone levels may cause leptin and insulin resistance[17]. Androgen can reduce insulin-sensitizing hormone concentrations, induce the combination of leptin and leptin receptor expression in islet β cells, inhibit the insulin secretion in islet β cells and thus enhance the insulin sensitivity. On the other hand, EA showed a better effect for women in improving serum leptin, probably because of the negative correlation between serum leptin level and testosterone level[18]. Leptin directly acts on the ovary[19]. Ovary promotes the combination of leptin and transport proteins, which further combines with receptors through the blood-brain barrier and more sensitively regulate the hypothalamic-pituitary-ovarian axis. Since the level of insulin receptor decreases with the improvement in hyperleptinemia and hyperinsulinemia, there was no between-group statistical difference in the level of insulin receptor. Leptin is associated with body fat mass. Because women having the same BMI as men have significantly more fat mass, and men have a higher basal metabolic rate coupled with higher energy expenditure[20], the efficacy in men are better than that in women.

Conflict of Interest

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

Acknowledgments

This work was supported by Science and Technology Support Project of Hebei Provincial Administration of Traditional Chinese Medicine (河北省中医药管理局科技支撑项目, No. 2014015, No. 2017004); Youth Fund Project of Hebei University of Chinese Medicine (河北中医学院青年基金项目, No. QNZ2014023); Science and Technology Plan Project of Hebei Provincial Department of Science and Technology (河北省科技厅科技计划项目, No.16277704D); Science and Technology Research Project of Universities in Hebei Province (河北省高等学校科学技术研究项目, No. QN2015139).

Statement of Informed Consent

Informed consent was obtained from all individual participants included in this study.

Received: 13 September 2016/Accepted: 19 October 2016

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