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Serum IgG, IgA, IgM, and IgE Levels after Electroacupuncture and Diet Therapy in Obese Women

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Abstract: We investigated the effect of acupuncture therapy on obese women's body weight and peripheral blood levels of serum immunoglobulin G (IgG), immunoglobulin A (IgA), immunoglobulin M (IgM), and immunoglobulin E (IgE). Sixty-three healthy women were assigned into 3 groups: placebo electroacupuncture (n = 13; mean age, 40.5 ± 4.2 years; body mass index [BMI], 33.5 ± 4.2), diet restriction (n = 23; mean age, 42.9 ± 4.0 years; BMI, 34.6 ± 2.9), and electroacupuncture (n = 24; mean age, 40.1 ± 5.9 years; BMI, 33.9 ± 2.7). Electroacupuncture was applied to the Hunger and Shen Men ear points and to the LI 4, LI 11, St 36, St 44, and Ren 6 body points for 30 min once daily for 20 days. A restricted diet of 1400 kilocalories was given to participants in all 3 groups for 20 days. Weight was lost significantly in subjects in the electroacupuncture group compared to those in the diet restriction and placebo electroacupuncture groups ($p < 0.000$, Tukey test). Modulations in serum IgG ($p < 0.001$) were apparent in women treated with electroacupuncture compared with women treated with placebo electroacupuncture and restricted diet only. No significant changes were seen in serum IgA, IgM, and IgE levels among the 3 groups. Our results suggest that electroacupuncture can be effectively used to treat obesity. We also observed a modulating effect of serum IgG, which is associated with weight loss, in patients in the electroacupuncture group.

Keywords: Electroacupuncture; Obesity; IgG; IgA; IgM.

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Introduction

Electroacupuncture stimulation is one of the most popular forms of complementary medicine in the world (Richardson and Vincent, 1986). EA applied to specific anatomical loci in clinical and experimental studies has proved to be successful in the treatment of stress induced physical disorders and immunodeficiency (Vasilenko *et al*., 1989). Besides increasing the resistance to infection, EA also alleviates the autoimmunity and hypersensitivity in clinics (Cheng, 1997). Acupuncture application has been shown to increase levels of endomorphine-1, beta endorphin, enkephalin, and serotonin in plasma and brain tissues (Fu, 2000; Jin *et al.*, 1996; Takeshige *et al.*, 1993; Pan *et al.*, 1996; Petti *et al.*, 1998; Cabioglu and Ergene, 2006).

Treatments for obesity include restricted diet, regulation of physical activity, behavior treatment, pharmacotherapy, surgery, acupuncture, or the combination of these methods (Cabioglu and Ergene, 2005; 2006; Cabyoglu *et al*., 2006; Lyznicki *et al*., 2001; Ernst, 1997; Richards and Marley, 1998). Application of electroacupuncture on specific acupuncture points has been shown to cause weight loss in obese people (Cabioglu and Ergene, 2005; 2006; Richards and Marley, 1998; Zhan, 1993). Clinical and experimental studies have shown that electroacupuncture applied to certain acupuncture points on the human body has favorable effects in treating stress-induced immunodeficiency (Cheng *et al*., 1997) and physical disorders and inflammatory diseases (Sun and Xu, 1993). Combined electroacupuncture stimulation and moxibustion at the St 36 (Zusanli) acupuncture point has been shown to activate the defense systems (Vasilenko *et al*., 1989) and enhance cellular immune functioning in patients with malignant tumors (Rogers *et al*., 1992). Clinical and experimental studies have shown that sequential electrical stimulation of certain acupuncture points on the human body, such as the St 36 point, favorably affects stress-induced immunodeficiency and physical disorders (Vasilenko *et al*., 1989). Mediation of endogenous opioid peptides including beta endorphin and enkephalin is widely believed to be the major mechanism of action of acupuncture (Fu, 2000; Jin *et al*., 1996). The existence of receptors for the endogenous opioid peptides has been established in the cells of the immune system (Han *et al*., 1999). It has been determined that endogenous opioids (Jin *et al*., 1996) increased in plasma and brain tissues through acupuncture application effects on the levels of serum immunoglobulin.

In this study, we aimed to investigate the effect of electroacupuncture, diet only, and placebo electroacupuncture on body weight and peripheral blood levels of serum IgG, IgA, IgM, and IgE in obese women.

Materials and Methods

Subjects

Informed consent for electroacupuncture application was obtained from all study participants, and the study protocol was approved by our institutional ethics committee. The study included women aged 35 to 50 years with a body mass index (BMI) between

Table 1. Subject Characteristics

	Groups		
	Placebo EA	**Diet**	**EA**
Age	40.5 ± 4.2	42.9 ± 4.0	40.1 ± 5.9
Weight	77.7 ± 6.2	84.0 ± 4,6	83.7 ± 6.5
Body Mass Index	33.5 ± 4.2	34.6 ± 2.9	33.9 ± 2.7

EA: Electroacupuncture.

30 and 40. Sixty-three healthy women participated and were assigned into 3 groups: placebo electroacupuncture (n = 13; mean age, 40.5 ± 4.2 years; BMI, 33.5 ± 4.2), diet restriction (n = 23; mean age, 42.9 ± 4.0 years; BMI, 34.6 ± 2.9), and electroacupuncture (n = 24; mean age, 40.1 ± 5.9 years; BMI, 33.9 ± 2.7). No statistical significant differences were found with regard to mean values of age, body weight, and BMI among 3 groups (Table 1).

Selected Ear and Body Acupuncture Points

Hunger and Shen Men were selected as ear points and Hegu (LI 4), Quchi (LI 11), Zusanli (St 36), Neiting (St 44), and Ren 6 were selected as body points (Fig. 1).

Ear points:

1. The Hunger ear point is located at the junction of a line drawn horizontally from the apex tragus and one drawn vertically from the intertragic notch.
2. The Shen Men point is located at the point one third of the way up the lateral side of the upper edge of the triangular fossa.

Stimulation of the Hunger point creates an increased feeling of fullness and it suppresses hunger (Millar *et al.*, 1990). Stimulation of the Shen Men point regulates cerebral cortex functioning and it has a sedative effect (Asomoto and Takehige, 1992).

Body points:

1. The LI 4 body point is located at the dorsal face of the hand between the first and second metacarpal bones and in the middle of the radial side of the second metacarpal bone (Fig. 1).
2. The LI 11 point is located between the Lu 5 (Chise) point and the lateral epicondyle of the humerus at the end of the transverse cubital line when the elbow is flexed. When the arm is at maximum flexion, this point is the most lateral point of the elbow transverse curve (Fig.1).
3. The St 36 point is 3 cun below the lower edge of the patella, between the tibialis anterior muscle and the flexor digitorum communis muscle (Fig. 1).
4. The St 44 point is between the second and third phalanges on the foot and at the lateral and distal side of the second metatarsophalangeal joint (Fig. 1).
5. The Ren 6 point is 1.5 cun below the umbilicus, on the midline of the abdomen (Fig. 1).

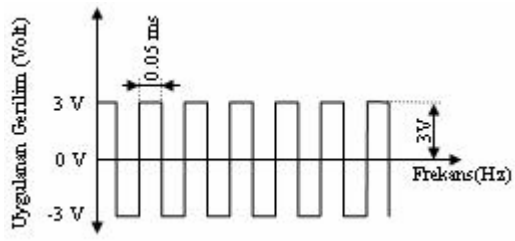

Figure 1. Characteristics of current applied with electroacupuncture.

Stimulation of the LI 4 and LI 11 points has a regulatory effect on intestinal motility (Wang and Kain, 2001). Stimulation of St 36 and St 44 increase excitability of the satiety center in the ventral medial nucleus of the hypothalamus (Zhao *et al*., 2000). In people who have hypoactive gastrointestinal motility, electroacupuncture applied to the St 36 point modulates gastrointestinal motility causing an increase in bowel movement; in people who have increased bowel motility, electroacupuncture produces a decrease in bowel movement.

Electroacupuncture Application

Electroacupuncture was applied for 30 min from 8:00 am to 8:30 am for 20 days. Body electroacupuncture was performed every day, and ear electroacupuncture was performed every other day. After electroacupuncture application, permanent ear needles were placed in the Hunger points. The body acupuncture needles were 2.5 cm long and the ear acupuncture needles were 1 cm long, with a 0.22 mm diameter. Electrical stimulation was administered using a pulse generator (Biotron instrument) at a frequency of 2 Hz at 3 V for 0.05 ms with positive and negative alterations in square wave form. Electrodes were connected to the Hunger and Shen Men points on both ears and on LI 4 and LI 11 with St 36 and St 44 on the body, symmetrically, in pairs. Acupuncture alone was applied on the Ren 6 points.

Placebo electroacupuncture application was performed with the acupuncture needles inserted into 2 ear points that were unrelated to weight loss; the needles were inserted superficially into selected body points that were not acupuncture points but were near the body acupuncture points used for the electroacupuncture group.

Diet Program

A 1400 kilocalorie diet was prepared for all women in the 3 groups. A diet of 1400 kilocalories was chosen to give a diet over their basal metabolism. Subjects continued their routine daily activities. The diet regimen was explained to the patients prior to the study, and their full consent was obtained. Calorie intake was monitored everyday for participants in the diet restriction, placebo electroacupuncture and electroacupuncture groups during the study.

Preparation of Samples

Venous blood samples (4 ml) were collected from each participant before and after therapy. Blood samples were centrifuged at 1000 rpm for 10 min. Supernatants were obtained and stored at −80°C for further analyses.

Weight and Height of Subjects

Weights of the subjects were measured with standard scales (sensitivity ± 0.5 kg) before breakfast. Heights of the subjects were measured with a steel rule (sensitivity ± 0.5 cm). The BMIs of the subjects were calculated by dividing the weights (kg) to the squares of the corresponding heights (m^2).

Determination of Serum IgG, IgA, IgM, and IgE Levels

Serum IgG, IgA, IgM, and IgE levels were determined by the nephelometric method using a Dade Behring kit (Marburg Gmb H D-35041, Marburg, Germany). Normal values were as follows: IgG, 8 to 17 g/L; IgA, 0.85 to 4.5 g/L; IgM, 0.6 to 3.7 g/L, and IgE, 0 to 100 IU/mL. Serum IgG, IgA, IgM, and IgE levels were measured by the BN 100 apparatus.

Statistical Analyses

The differences before and after electroacupuncture, diet only, and placebo electroacupuncture were calculated. The modulating effect of electroacupuncture was measured by before and after treatment. IgG levels were compared with a paired t-test. Differences in weight loss among the groups were assessed with a one-way analysis of variance and the Tukey test. Values for $p < 0.05$ were considered statistically significant.

Results

Weight Loss

A 2.71% decrease in body weight was observed in the placebo electroacupuncture group (mean body weight before therapy, 77.7 ± 6.2 kg vs. mean body weight after therapy, 75.6 ± 6.2 kg). A 2.98% decrease in body weight was observed in the diet restriction group (mean body weight before therapy, 84.0 ± 4.6 vs. mean body weight after therapy, 81.5 ± 4.7). A 4.9% decrease in body weight was observed in the electroacupuncture group (mean body weight before therapy, 83.7 ± 6.5 kg vs. the mean body weight after therapy, 79.6 ± 6.7 kg). A statistically significant greater loss of weight occurred in participants in the electroacupuncture group than in participants either in the diet restriction or the placebo electroacupuncture groups ($p < 0.000$, Tukey test) (Table 2).

Table 2. Changes in Weight Loss in Subjects after Placebo EA, EA, and Diet Therapy

Groups		Placebo EA	Diet	EA
Weight	1st day	77.7 ± 6.2	84.0 ± 4,6	83.7 ± 6.5
	20th day	75.6 ± 6.2	81.5 ± 4.7	79.6 ± 6.7
	T	27 000***	26 584***	47 728**
Body Mass Index	1st day	33.5 ± 4.2	34.6 ± 2.9	33.9 ± 2.7
	20th day	32.56 ± 1.2	33.6 ± 2.8	32.3 ± 2.7
	T	20.053***	25.745***	43.846***

Table 3. Changes in Serum IgG, IgA, IgM and IgE Levels in Subjects after Placebo EA, EA, and Diet Therapy

Groups		Placebo EA	Diet	EA
IgG	1st day	12.65 ± 2.55	12.88 ± 3.10	12.15 ± 3.51
	20th day	14.31 ± 8.90	13.14 ± 2.57	12.81 ± 1.57
	T	–0.969^{ns}	0.275^{ns}	4.858***
IgA	1st day	2.18 ± 0.87	2.19 ± 0.80	2.09 ± 1.10
	20th day	2.16 ± 0.78	2.15 ± 0.73	2.11 ± 1.11
	T	0.297^{ns}	0.447^{ns}	0.966^{ns}
IgM	1st day	1.19 ± 0.36	1.40 ± 0.71	1.18 ± 0.52
	20th day	1.18 ± 0.36	1.28 ± 0.56	1.13 ± 0.51
	T	–0.124^{ns}	0.025^{ns}	–1.493^{ns}
IgE	1st day	88.30 ± 84.04	81.71 ± 73.28	79.08 ± 72.83
	20th day	79.29 ± 94.33	67.54 ± 59.78	65.46 ± 59.35
	T	0.753^{ns}	1.969^{ns}	1.952^{ns}

ns: Not significant. $^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$, EA: electroacupuncture.

Serum IgG, IgA, IgM, and IgE Levels

IgG levels apparently were modulated in participants in the electroacupuncture group, while there were no changes in IgA, IgM, or IgE values (Table 3).

Discussion

When compared with placebo electroacupuncture and diet restriction, significant weight loss was accomplished in obese women by applying electroacupuncture. In addition, levels of serum IgG were modulated with electroacupuncture application compared to the other 2 treatments. To our knowledge, this is the first report in the English literature to document a change in serum IgG levels via electroacupuncture application in obese women.

Qunli and Zhicheng (2005) investigated the therapeutic effects of acupuncture at ear, body, and the combination in the treatment of obesity. In total, 195 obese subjects were

divided into 3 groups: body (n = 64), ear (n = 55), and combined ear and body (n = 76) acupuncture groups. In that study, the effects of body and body plus ear were superior to those of ear acupuncture, and the combined use of ear and body acupunctures was better than that of body acupuncture alone. In that study, after 20 days of treatment, 46% of the subjects in the combined ear and body acupuncture group lost 5 kg, 35% lost 5 kg in the body acupuncture group, and 27% lost 5 kg in the ear acupuncture group. In our study, after 20 days of treatment, patients with electroacupuncture on both the body and ear lost 4.2 kg of body weight.

Acupuncture has been used to treat diseases that affect the body's immune system such as inflammatory diseases and malignant tumors (Wu *et. al*., 1994). IgG may have great protective action (Brandtzaeg, 1973). Since IgG plays an important role in bacterial and viral defense, it may be of value in preventing infectious diseases. If acupuncture stimulation can affect the regulation of immunoglobulin levels, it is not surprising that acupuncture would be effective in treating immune diseases as well as disturbances in other organs of the body as well.

Yang and colleagues (1989) investigated changes in immunoglobulin levels in the serum, saliva, and gingival sulcus fluid following long and short electroacupuncture application in 70 volunteers. The authors applied electroacupuncture to only endocrine points on both ears in addition to body points Hegu (LI 4) and Xiaguan (St 7). The results of that study demonstrated that 30 min and 24 hours after acupuncture treatment, saliva IgA levels were significantly increased in volunteers with previously low levels of IgA; however, IgA levels were decreased in those who previously had high levels. When acupuncture was applied daily for 2 weeks, the authors observed that saliva IgA levels were significantly increased approximately 20% compare to the pretreatment value. 30 min after treatment, short duration acupuncture stimulation was shown to significantly decrease IgG levels in serum and gingival sulcus fluid. On the other hand, when applied daily for 7 days, long duration acupuncture stimulation significantly increased IgG levels in both serum and gingival sulcus fluid. We applied electroacupuncture to Hunger and Shen Men points on both ears in addition to body points LI 4, LI 11, St 36, St 44, and Ren 6 in obese women for 20 days, and observed that levels of serum IgG were modulated, but no changes were observed in the levels of serum IgA, IgM, or IgE.

Yu and associates (1997) applied electroacupuncture to the Zusanli (St 36) acupuncture point in rats for 60 min once a day over 3 days. Electroacupuncture application was performed with 1 to 5 mV at 1 Hz for 1 ms. Levels of interleucin-2, interferon gamma, and the activity of natural killer cells in the spleen were increased with this application. In another study on rats, Yu and associates (1998) applied electroacupuncture, with 3.5 to 5 mV at 1 Hz for 0.05 ms. to the St 36 point for 30 min for 3 days and observed that the activity of natural killer cells in the spleen and levels of beta endorphin and interferon gamma in serum were increased. When 10 mg/kg of naloxone was injected before electroacupuncture, the increases in natural killer cell activity and interferon gamma were lessened. The authors concluded that electroacupuncture applications increased beta endorphin secretions in the spleen. In turn, natural killer cell activity and interferon gamma levels were also increased. In our study, we applied electroacupuncture to the Zusanli

(St 36) and other acupuncture points for 20 days in obese women and observed that levels of serum IgG were modulated.

The effects of acupuncture on the immune system are related to the effects of beta endorphin, methionine enkephalin, and leucine enkephalin. In addition, leukocytes contain pro-opiomelanocortin mRNA. Due to this, leukocytes can synthesize corticotropin and beta endorphin from pro-opiomelanocortin. Besides, endogenous opioid receptors have been found on B lymphocytes, T lymphocytes, natural killer cells, granulocytes, monocytes, platelets, and the terminal complement complex. Chemical and physical similarities have been observed between neuroendocrine system opioid receptors and immune system opioid receptors (Khansari *et al.,* 1990).

Endorphins and enkephalins increase the activity of natural killer cells, the generation of cytotoxic T lymphocyte, the chemotaxis of monocytes, and the production of interferon gamma, interleucin-1 (IL-1), interleucin-2 (IL-2), interleucin-4 (IL-4), and interleucin-6 (IL-6). Jankovic and Millar have concluded that endogenous opioids produce an immunomodulatory effect (Jankovic, 1994; Millar *et al*., 1990). In studies by those authors, the immunomodulatory effect of acupuncture was associated with an increase in endogenous opioid levels.

Kho and colleagues (1991) evaluated changes in IgA, IgM, and IgG levels and total and differential leukocyte counts in the peripheral blood of 29 male patients taken during and 6 days after upper abdominal surgery performed under 2 different anesthetic techniques. Ear and paravertebral points were stimulated, and anesthesia was supplemented with small doses of fentanyl in Group 1 and moderate doses of fentanyl in Group 2. After surgery, a decrease in the levels of immunoglobulin, and in lymphocyte and eosinophil counts, and an increase in leukocyte and neutrophil counts were seen in both groups. No recovery was observed in IgA, IgG, leukocyte, neutrophil, and lymphocyte counts in both groups until the last assessment on the sixth day after surgery, whereas IgM and eosinophil counts recovered by the fourth day. Acupuncture and transcutaneous stimulation analgesia for major abdominal surgery did not influence the immune system of the body either during or after surgery as measured by the concentrations of immunoglobulin, as well as total and differential WBC counts.

Kho and associates (1990) investigated the patterns of adrenaline, noradrenalin, corticotropin, beta endorphin, hydrocortisone, and those of immunoglobulins (i.e, IgA, IgG, and IgM), and total and differential leukocyte counts in peripheral blood, during and 6 days after thyroid surgery. This study comprised 20 patients treated with acupuncture and anesthesia by supplementing small doses of pethidine. In all cases, 4 ipsilateral ear points — Shenmen, Jiaogan, Jing, and Neifenbi — to the thyroid nodules were selected for acupuncture. The needles were connected to a battery-powered stimulator and stimulation was applied (4 Hz, 20 mA, and 20 volts). During surgery, an increase in the levels of adrenaline, noradrenalin, corticotropin, beta endorphin, hydrocortisone, and a decrease in immunoglobulin were observed, whereas leukocytosis, a decreased percentage of eosinophils and a reduced percentage of neutrophils, were demonstrated by the leukocyte counts. After operation, the levels of noradrenalin and beta endorphin remained elevated, whereas adrenaline, corticotropin, and hydrocortisone levels gradually returned to normal

values. Immunoglobulin levels and eosinophil counts returned to the original values within 24 hours, and neutrophil and lymphocyte counts returned to the original values within 2 days. During thyroid surgery with only general anesthesia, immunoglobulin levels had not returned to normal values 3 days after the surgery (Cohnen, 1972), whereas in Kho and associates' study, immunoglobulin levels returned to the original values within 24 hours. In this study, the immunoglobulin levels that had decreased during surgery owing to acupuncture anesthesia returned to normal values in a shorter time, while beta endorphin levels remained elevated.

In our study, we observed modulated immunoglobulin levels in serum when 2-Hz electroacupuncture was applied in obese woman. Analgesia and the observed immunomodulatory effect induced by electroacupuncture are thought to be related to the release of endogenous opioids, dynorphin, and beta endorphin.

Endorphin and enkephalin increase the activity of natural killer cells; the generation of cytotoxic T lymphocytes; the chemotaxis of monocytes; and the production of interferon gamma, IL-1, IL-2, IL-4, and IL-6. IL-2, IL-4, and IL-6 functions stimulate the proliferation of B-lymphocytes (Carosella *et al*., 1989; Nies *et al*., 2002; Bertolini and Benson, 1990). IFN-gamma stimulates the production of IgG subclasses that activate the complement pathway and promote opsonization (Estes *et al*., 1994). Interferon gamma, interleukin-2, interleukin-4, and interleukin-6 affect immunoglobulin by increasing B-cell proliferation and antibody synthesis. In studies on this subject (Jankovic, 1994; Millar *et al*., 1990), it has been concluded that endogenous opioids create an immunomodulatory effect. At the same time, electroacupuncture stimulation produces an immunomodulatory effect (Hahm *et al.*, 2004). It is thought that the immunomodulatory effect of electroacupuncture may result from the increase in levels of endogenous opioids.

Application of electroacupuncture with restricted diet in obesity treatment is more effective than restricted diet alone. In this study, levels of serum IgG were modulated and were associated with weight loss in the electroacupuncture applications. In obesity treatment, electroacupuncture is preferred, as it provides both weight loss and immunomodulation.

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