Original Article

Acupuncture Improves Intestinal Absorption of Iron in Iron-deficient Obese Patients: A Randomized Controlled Preliminary Trial

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Abstract

Background: Obesity has an adverse effect on iron status. Hepcidin-mediated inhibition of iron absorption in the duodenum is a potential mechanism. Iron-deficient obese patients have diminished response to oral iron therapy. This study was designed to assess whether acupuncture could promote the efficacy of oral iron supplementation for the treatment of obesity-related iron deficiency (ID).

Methods: Sixty ID or ID anemia (IDA) patients with obesity were screened at Beijing Hospital of Traditional Chinese Medicine and were randomly allocated to receive either oral iron replacement allied with acupuncture weight loss treatment (acupuncture group, $n = 30$) or oral iron combined with sham-acupuncture treatment (control group, $n = 30$). Anthropometric parameters were measured and blood samples were tested pre- and post-treatment. Differences in the treatment outcomes of ID/IDA were compared between the two groups.

Results: After 8 weeks of acupuncture treatment, there was a significant decrease in body weight, body mass index, waist circumference, and waist/hip circumference ratio of patients in the acupuncture group, while no significant changes were observed in the control group. Oral iron supplementation brought more obvious improvements of iron status indicators including absolute increases in serum iron (11.08 ± 2.19 μmol/L vs. 4.43 ± 0.47 μmol/L), transferrin saturation (11.26 ± 1.65% vs. 1.01 ± 0.23%), and hemoglobin (31.47 ± 1.19 g/L vs. 21.00 ± 2.69 g/L) in the acupuncture group than control group (all $P < 0.05$). Meanwhile, serum leptin (2.26 ± 0.45 ng/ml vs. 8.13 ± 0.55 ng/ml, $P < 0.05$) and hepcidin (3.52 ± 1.23 ng/ml vs. 6.77 ± 0.84 ng/ml, $P < 0.05$) concentrations declined significantly in the acupuncture group than those in the control group.

Conclusion: Acupuncture-based weight loss can enhance the therapeutic effects of iron replacement therapy for obesity-related ID/IDA through improving intestinal iron absorption, probably by downregulating the systemic leptin-hepcidin levels.

Key words: Acupuncture; Iron Absorption; Iron Deficiency; Obesity; Randomized Controlled Trial

Introduction

Obesity is a public health problem that has reached epidemic proportions affecting countries worldwide.[1,2] Obesity is associated with an increased risk of type 2 diabetes, hypertension, cardiovascular disease, dyslipidemia, and some cancers. In addition, there is increasing evidence that obesity contributes to the development of micronutrient deficiencies, in particular iron deficiency (ID) or ID anemia (ID/IDA). Studies have demonstrated that obesity adversely impacts iron nutritional status.[3,4] A recent study in Mashhad, Iran, detected low serum iron (SI) levels in 56.1% of obese children compared to only 10.4% of normal weight children.[5] The prevalence of ID has been shown to increase with increasing body mass index (BMI).[6,7] The mechanisms linking obesity and ID are not fully understood. Potential explanations for this

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association include poor dietary iron intake, increased iron requirements, and/or impaired iron absorption in obese individuals.[8] Of these potential explanations, impaired iron absorption has been generally accepted, as obese individuals have been shown to have markedly lower absorption of isotope-labeled iron compared to normal weight individuals.[9-11] Obesity may promote ID/IDA by inhibiting intestinal iron absorption.[12] This can further lead to diminished response to oral iron replacement therapy or dietary iron fortification,[11] rendering obesity-related ID/IDA an iron refractory disorder.

The absorption of dietary iron begins with iron uptake into the enterocyte by divalent metal-ion transporter-1. After entering enterocytes, iron can be used for metabolic purposes, stored within intracellular ferritin, or exported across the basolateral membrane through ferroportin-1 (Fpn1) into the bloodstream. Fpn1 is the sole known iron exporter of enterocytes.[13] Intestinal iron efflux through Fpn1 is tightly modulated by a systemic iron regulatory hormone, hepcidin, which is produced mainly by the liver. Hepcidin acts as a negative regulator of iron absorption by binding to Fpn1 on the basolateral membrane of duodenal enterocytes, inducing its internalization and degradation.[14] Higher circulating hepcidin concentrations have been detected in overweight and obese children with ID/IDA.[15,16] Furthermore, a recent study involving obese children observed improvements in iron status and absorption along with a reduction in serum hepcidin after a 6-month weight loss program.[17] These results strengthen the hypothesis that the poor iron status that frequently occurs in obese individuals may be due to hepcidin-mediated inhibition of dietary iron absorption.

Leptin is an adipocyte-secreted hormone that inhibits food intake and stimulates energy expenditure. Leptin has been shown to promote the expression of hepcidin and has a strong direct correlation with plasma hepcidin levels.[18] Leptin plasma concentrations are particularly elevated in obese humans.[15] In obese children exposed to a weight loss program, leptin reduction was associated with hepcidin reduction.[17] Leptin may play an important role in controlling hepcidin production in the setting of obesity.

The refractory nature of obesity-related ID/IDA requires investigation of complementary and alternative approaches. Weight loss programs have been associated with improvement in iron absorption and iron status; however, most of the conventional weight loss measures are difficult to implement (such as dieting and exercise) or have serious potential side effects (such as surgery or medication treatment). Acupuncture is growing in popularity worldwide as an effective weight loss tool with almost no adverse events. Treatment of obesity by acupuncture may lead to a reduction of plasma leptin levels and weight loss.[19,20] However, it is not known whether acupuncture-based weight loss can play a role in the treatment of obesity-related ID/IDA. We hypothesize that acupuncture may have the potential to improve obesity-induced iron malabsorption by regulating the leptin-hepcidin axis. To test this, a randomized controlled clinical trial was conducted.

Methods

Patient recruitment and iron deficiency/iron deficiency anemia screening

Obese patients (age: 20–55 years) visiting the Acupuncture Department at the Beijing Hospital of Traditional Chinese Medicine for obesity treatment were recruited from May 2013 to October 2015. Body weight (BW), waist circumference (WC), and waist/hip circumference ratio (WHR) were measured or calculated. According to the definition proposed by the International Life Science Institute Working Group of Obesity in China, patients with a BMI ≥28.0 kg/m^2 were considered obese and therefore they were eligible for the study.[21] Patients were excluded from the study if they were morbidly obese or had hepatobiliary disease, gastrointestinal tract disease, hematologic disease, or inflammatory disease. The enrolled patients underwent ID/IDA screening tests. Fasting venous blood samples were collected and tested for: (1) SI; (2) total iron-binding capacity (TIBC); (3) soluble transferrin receptor (sTfR); and (4) hemoglobin (Hb). Transferrin saturation (TS) was calculated according to the following formula: TS (%) = SI/TIBC. ID was diagnosed if the patients had one or more of the following results: TS <15%; sTfR >3.2 mg/L; or SI <10.7 μmol/L. IDA was diagnosed if the patients had a Hb <130 g/L (males) or Hb <120 g/L (females). Although low serum ferritin (SF) concentration is a sensitive indicator of ID, ferritin is also an acute-phase protein that can increase in respond to the chronic low-grade inflammation of obesity and potentially masks a diagnosis of ID in obesity; thus SF was not used in this study. The blood samples were also used to measure serum hepcidin, leptin, and soluble leptin receptor (sLR) levels to judge the patients' systemic hepcidin and leptin secretion status.

The cyanmethemoglobin method was used to measure Hb. The ferrozine method was used to measure SI and TIBC (DiaSys Diagnostic Systems Co., Ltd., Germany). Levels were detected with an automatic biochemical analyzer (Beckman Co., USA). An ELISA kit was used for measuring sTfR, sLR, hepcidin, and leptin (BlueGene Biotech, USA) and was detected with a Multiskan Ascent Microplate Reader (Thermo Multiskan MK3, USA).

Sample size estimation and grouping

The primary goal of this study was to investigate the regulatory effect of acupuncture on the leptin-hepcidin system. According to the literature,[20] acupuncture can lower serum leptin levels up to 45%, while sham-acupuncture lowers them about 10%. Given an $\alpha = 0.05$ and $\beta = 0.10$, we computed that 28 patients were needed per group. For this study, approximately, 300 participants were initially recruited. After screening, sixty obese patients with ID/IDA were enrolled. A stratified randomization grouping method was used to classify the sixty patients based on gender

(male, female), age (under 40 years, 40 years, and over), and iron status (ID, IDA) and then randomized them to either the acupuncture auxiliary treatment group (acupuncture group for short) or the sham-acupuncture control group (control group for short). There were thirty patients in each group [Figure 1]. Enrollment and stratification were conducted by the trial investigator. The allocation sequence was generated by specially trained nurses in the Acupuncture Department of the hospital using random number tables; these nurses were independent from the trial investigators. Patients were consecutively assigned a random number in chronological order that allocated him or her to receive either real or sham acupuncture. All patients provided written informed consent to participate in the study. The study was approved and supervised by the Ethics Committee of Beijing Hospital of Traditional Chinese Medicine.

Patient treatment and outcome measures

Acupuncture group

The patients in the acupuncture group received acupuncture-based weight reduction and oral iron replacement therapy. The therapeutic scheme was as follows:

Acupoint selection

The following acupoints were chosen: Zhongwan (CV12), Guanyuan (CV4), Daju (ST27, bilaterally), and Fujie (SP14, bilaterally) on the abdomen; Zhigou (TE6) and Houxi (SI3) on the forearms and hands; and Fenglong (ST40), Rangu (KI2), Taibai (SP3), and Zulinqi (GB41) on the lower legs and feet. Stimulation of this set of acupoints has previously been associated with weight loss.[22]

Needling procedure

The patients were placed in the supine position. The skin was disinfected in the conventional manner, and a 0.3 mm × 40.0 mm HuaTuo stainless steel acupuncture needle was rapidly inserted to a depth dependent on the degree of obesity until a needling response (deqi, the sensation of heaviness in the area surrounding the locus of insertion) was felt. The needle was then twirled for 15 s with a mild reinforcing-reducing method and retained for 30 min with twirling again at the 15th min. Acupuncture was performed every other day for 6 weeks (divided into two treatment courses with a 5-day interval after the first 3 weeks) and twice per week thereafter for 2 weeks. Each patient received a total of 25 acupuncture sessions. All needling procedures were done by a specialized acupuncturist.

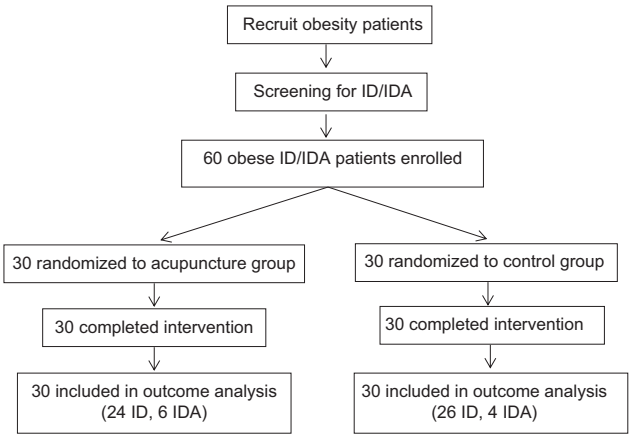

Figure 1: Flowchart of the study protocol. ID: Iron deficiency; IDA: Iron deficiency anemia.

Iron replacement

After 2 weeks of acupuncture treatment, oral iron replacement therapy was initiated. In this study, ferrous fumarate tablets (Beijing Double-Crane Pharmaceutical Co., Ltd, Beijing, China) was used as the iron supplement and was administrated weekly at a dosage of 5 mg iron/kg BW divided over three meals in a day. Iron replacement therapy continued for 6 weeks.

Control group

The patients in the control group received nonacupoint acupuncture (a type of sham acupuncture) and oral iron replacement therapy. The acupuncture points selected were 1–2 inches distal (above, below, or beside) from the real acupoints in the acupuncture group. The needling procedure and course of treatment were the same as the acupuncture group. Oral iron replacement therapy with ferrous fumarate tablets was identical to that of the acupuncture group and was initiated after the first 2 weeks of nonacupoint acupuncture. All participants in both groups were given counseling on maintaining a low-calorie diet.

Determination of efficacy

After 8 weeks of treatment, each patient's height, BW, BMI, WC, HC, and WHR were again measured or calculated. Fasting venous blood levels were retested for the same parameters of iron status that were measured at baseline. The changes between baseline and posttreatment iron parameters of the two groups were analyzed. The differences in therapeutic efficacy of oral iron replacement and weight loss between the groups were compared.

Quality control

The study was double blinded. The patients and examiners were both blinded to grouping. The acupuncturist was the only person not blinded to treatment group.

Statistical analysis

Statistical analysis was performed with SPSS software version 17.0 (SPSS Inc., Chicago, IL, USA). Data were presented as mean ± standard deviation (SD) for continuous variables and number (%) for categorical variables. Continuous variables were compared between the two groups using a two-sample independent *t*-test, paired *t*-test, or Wilcoxon rank test, where appropriate. Categorical variables were compared using Chi-square test. A $P < 0.05$ was considered statistically significant.

Results

Effects of acupuncture on obesity parameters

All patients completed the entire course of intervention; no patients dropped out or were lost to follow-up. In the

acupuncture group, there were 6 males and 24 females (age: 33 ± 6 years; BMI: 30.75 ± 2.16 kg/m^2). In the control group, there were 5 males and 25 females (age: 34 ± 7 years; BMI: 29.99 ± 1.69 kg/m^2). The two groups were similar in regards to age, gender, and BMI.

The effect of acupuncture on obesity was evaluated by the amount of weight lost[23] in the respective groups. Table 1 displays that 86.7% (26/30) of the patients in the acupuncture group achieved a weight loss of ≥3 kg compared to only 13.3% (4/30) of the subjects in the control group, this difference between the two groups was statistically significant ($P < 0.001$; Wilcoxon rank test).

In addition to BW, acupuncture also improved other parameters of obesity. BMI, WC, and WHR of patients in the acupuncture group significantly decreased (all $P < 0.05$), while no significant changes were observed in the control group [Table 2]. Neither group experienced obvious adverse reactions throughout the entire duration of treatment. A few patients experienced mild symptoms of upset stomach.

Influences of acupuncture on oral iron replacement treatment in obese patients with iron deficiency/iron deficiency anemia

Intragroup comparison

After oral iron replacement therapy, indicators of iron status improved in both the acupuncture and the control groups. Specifically, SI and Hb levels increased, while sTfR levels decreased. The differences before and after treatment were statistically significant in both groups ($P < 0.05$). In the acupuncture group, the TS level also significantly increased after treatment; however, in the control group, there was no significant difference in TS level before and after treatment. The results are shown in Table 3.

Intergroup comparison

Using a screening test for ID/IDA, 24 patients in the acupuncture group were diagnosed as ID and six were diagnosed as having IDA. In the control group, 26 had ID and four had IDA. Before treatment, there were no statistically significant differences in SI, TS, Hb, or sTfR levels between the two groups. After treatment, SI and TS levels in the acupuncture group were higher than those in control group and the differences were statistically significant [both $P < 0.001$, Table 3]. The sTfR levels of the two groups were comparable ($P = 0.090$). Hb concentrations after treatment were only re-measured for the six IDA patients in the acupuncture group and the four IDA patients in the control group, no statistically significant difference was found ($P = 0.214$) which was likely due to insufficient power from very few patients with IDA [Table 3].

Comparison of the degree of iron status improvement

To fully elucidate whether acupuncture helps treat obesity-driven ID/IDA, the net iron improvement in each group was analyzed and compared. After oral iron supplementation, the absolute increases in SI, TS, and Hb levels in the acupuncture group were greater than those in the control group (SI: 11.08 ± 2.19 μmol/L vs. 4.43 ± 0.47 μmol/L; TS: 11.26 ± 1.65% vs. 1.01 ± 0.23%; and Hb: 31.47 ± 1.19 g/L vs. 21.00 ± 2.69 g/L), these differences were statistically significant (all $P < 0.05$). The absolute decrease in sTfR levels, however, was similar between the two groups (6.38 ± 1.30 ng/ml vs. 4.20 ± 1.32 ng/ml, $P > 0.05$). Although the actual Hb concentrations of the two groups after oral iron therapy were not significantly different, the absolute change in Hb in the acupuncture group was much bigger than in the control group, this may signify the patients in the acupuncture group having a better response

Table 1: Effects of acupuncture on weight reduction of patients with simple obesity (n = 30 in each group)

Group	Cured (weight loss to within the standard weight or overweight range), *n* (%)	Significantly effective (weight loss ≥5 kg), *n* (%)	Effective (3≤ kg weight loss <5 kg), *n* (%)	Ineffective (weight loss <3 kg), *n* (%)	Total effective rate (%)
Acupuncture	0 (0.0)	16 (53.3)	10 (33.3)	4 (13.3)	86.7
Control	0 (0.0)	0 (0.0)	4 (13.3)	26 (86.7)	13.3

Table 2: Changes in anthropometric parameters as well as serum leptin, hepcidin, and sLR levels of obese patients after acupuncture

Variables	Acupuncture group (n = 30)		t	P	Control group (n = 30)		t	P
	Before treatment	After treatment			Before treatment	After treatment		
BW (kg)	86.83 ± 7.55	79.60 ± 7.42	3.222	0.002	86.71 ± 7.80	85.27 ± 8.14	−0.275	0.784
BMI (kg/m^2)	30.75 ± 2.16	28.61 ± 2.06	3.914	<0.001	29.99 ± 1.69	29.67 ± 2.31	−0.359	0.721
WC (cm)	99.17 ± 5.85	93.15 ± 4.07	3.088	0.003	97.94 ± 6.95	95.37 ± 4.30	1.054	0.296
WHR	0.99 ± 0.02	0.94 ± 0.04	−2.763	0.010	0.98 ± 0.06	0.97 ± 0.04	−0.530	0.632
Leptin (ng/ml)	7.59 ± 1.94	2.26 ± 0.45	10.390	<0.001	8.28 ± 1.38	8.13 ± 0.55	−0.402	0.691
Hepcidin (ng/ml)	7.60 ± 1.38	3.52 ± 1.23	4.801	<0.001	6.98 ± 0.89	6.77 ± 0.84	0.643	0.525
sLR (ng/ml)	2.88 ± 0.96	3.06 ± 0.62	0.742	0.465	2.98 ± 0.75	2.72 ± 0.83	−0.595	0.557

Values are expressed as mean ± SD. BW: Body weight; BMI: Body mass index; WC: Waist circumference; WHR: Waist/hip circumference ratio; sLR: Soluble leptin receptor; SD: Standard deviation.

Table 3: Effects of acupuncture on the efficacy of oral iron replacement therapy for ID/IDA in obese patients

Variable	Before iron replacement		*t*	*P*	After iron replacement		*t*	*P*
	Acupuncture group ($n = 30$)	Control group ($n = 30$)			Acupuncture group ($n = 30$)	Control group ($n = 30$)		
SI (μmol/L)	4.85 ± 1.09	4.72 ± 0.96	0.337	0.739	15.93 ± 3.28	9.15 ± 1.43	10.582	<0.001
TS (%)	9.51 ± 2.16	9.39 ± 1.98	0.141	0.889	20.77 ± 3.81	10.40 ± 2.21	−5.391	<0.001
sTfR (ng/ml)	14.39 ± 2.99	13.79 ± 2.74	0.579	0.567	8.01 ± 1.69	9.59 ± 1.42	1.054	0.090
Hb (g/L)	103.26 ± 6.06	108.53 ± 4.28	0.443	0.680	134.73 ± 7.25	129.53 ± 6.97	1.086	0.214

Values are expressed as mean ± SD. SI: Serum iron; TS: Transferrin saturation; sTfR: Soluble transferrin receptor; Hb: Hemoglobin; ID/IDA: Iron deficiency/iron deficiency anemia; SD: Standard deviation.

to iron supplementation. Taken in whole, these results suggested that acupuncture may synergistically reinforce oral iron replacement therapy for obese patients with ID/IDA.

Effects of acupuncture on systemic hepcidin, leptin, and soluble leptin receptor

Intragroup comparison

In the acupuncture group, serum leptin and hepcidin levels decreased after treatment. Compared with the baseline data, the differences were statistically significant ($P < 0.01$). No changes were observed in the serum sLR levels before and after treatment in the acupuncture group ($P = 0.465$). In the control group, the serum levels of leptin, hepcidin, and sLR were not different before and after treatment (leptin: $P = 0.691$; hepcidin: $P = 0.525$; sLR: $P = 0.557$). The results are presented in Table 2.

Intergroup comparison

Before treatment, there were no differences in the baseline serum levels of leptin, hepcidin, and sLR between the acupuncture and control groups (leptin: $P = 0.309$; hepcidin: $P = 0.152$; sLR: $P = 0.781$). After treatment, the serum levels of leptin ($P < 0.001$) and hepcidin ($P = 0.001$) in the acupuncture group were lower than those in the control group, but the serum sLR levels were comparable between the two groups ($P = 0.266$).

Double-variable correlation analysis was performed based on the baseline serum leptin and hepcidin levels and their changes after treatment in all the sixty patients. Leptin was found to be positively correlated with hepcidin ($r = 0.684$, $P < 0.01$; Pearson's test).

Discussion

ID and IDA are frequent findings in obese patients.[24,25] Patients with concurrent ID/IDA and obesity are doubly afflicted by health hazards.[26,27] Worse still, obesity-related ID/IDA is often refractory to oral iron therapy or dietary iron fortification due to impaired intestinal iron absorption. This study suggests that acupuncture may be a promising auxiliary measure for the treatment of ID/IDA in obese patients and may play a dual role in reducing weight and improving iron absorption.

One challenge in treating ID/IDA in obese patients is the poor efficacy of oral iron replacement due to decreased enteral iron absorption. Elevated hepcidin concentrations in obese patients provide a partial explanation for the diminished iron absorption. Obese adipose tissue is characterized by an increased production of several pro-inflammatory cytokines and adipokines not produced in healthy lean adipose tissue. These inflammatory markers may stimulate hepcidin production in the liver and subsequently impede iron absorption or directly impact iron absorption from the enterocyte.[28,29] This may explain why oral iron replacement therapy is relatively ineffective for obesity-related ID/IDA when weight reduction measures are not taken simultaneously. Our present study demonstrated that acupuncture may enhance the efficacy of oral iron replacement therapy in obese patients with ID/IDA, possibly through a mechanism associated with the effect of acupuncture on weight reduction. Many previous studies have investigated acupuncture-based weight reduction. Although results vary because of differences in study methods, participants, or acupuncture treatment protocols, most studies suggested that acupuncture-based weight loss is indeed effective.[30-34] Our results concur with those of the previous studies showing that acupuncture can reduce the BW, BMI, WC, and WHR of obese patients,[30-34] thus supporting the assertion that acupuncture has an anti-obesity effect, especially for abdominal or visceral obesity. Several recent studies have reported improvements in iron status in response to weight loss from restrictive bariatric surgery in adults[35] or exercise-based long-term weight loss intervention in children.[17,36] This study provides evidence for acupuncture-based weight reduction improving the iron status in obese patients with ID/IDA. Acupuncture weight loss has the following advantages: (1) it is a healthy mode of weight loss, (2) it takes effect quickly, and (3) it is easy to implement compared to an exercise-based weight loss measure given that obese patients with ID/IDA have impaired endurance.

Our results demonstrate that oral iron replacement therapy can improve the iron status in both the acupuncture and the control groups; however, there was a significant difference in the degree of improvement between the two groups. That is, the absolute changes in SI, TS, and Hb in the acupuncture group were markedly greater than those in the control group. Such a difference in treatment response to the same dose of enteral iron supplementation between the two groups reflects the different iron absorption capabilities of the patients. On one hand, these results validated the findings

of other investigators that obesity can inhibit intestinal iron absorption.[9-11] On the other hand, they suggest that acupuncture has the potential to improve iron absorption through enterocytes in obese patients.

The mechanism underlying the facilitation of iron absorption through acupuncture requires further elucidation. Our study suggests that acupuncture might promote intestinal iron absorption by downregulating the systemic leptin-hepcidin levels, and the decrease of leptin-hepcidin may be the result of weight reduction. By examining adipocyte numbers and size, Abdi *et al*.[30] demonstrated that acupuncture caused fat weight loss including subcutaneous fat and visceral fat; subcutaneous fat and visceral fat are the main sources of leptin production, and serum leptin levels are positively correlated with body fat content.[37] In our study, acupuncture weight loss was manifested by the reduction of WC and WHR, which provide an indication of body fat loss. In particular, the reduction of WC and WHR reveals a potential advantage of acupuncture for the treatment of abdominal obesity and reduction of visceral fat. Acupuncture may lead to reduction of body fat mass and consequent decline of circulating leptin, which allows the liver to secrete less hepcidin. As a result, iron absorption is less suppressed, and oral iron therapy can be more efficacious. The possibility that acupuncture directly regulates leptin secretion from adipose tissues cannot be ruled out. One study demonstrated that during acupuncture treatment, plasma leptin levels decreased prior to obvious weight loss, and no obvious weight loss effects were obtained in ob/ob mice with a genetic leptin defect.[38] Gene expression analyses have shown that acupuncture can lower elevated levels of leptin mRNA expression in the abdominal fat tissues of obese rats down to approaching the normal level.[19] The acupuncture-induced downregulation of leptin in obese patients may be a cause rather than a consequence of weight loss. Our results also showed that the serum levels of both leptin and hepcidin in the acupuncture group decreased, and there was a positive correlation between leptin and hepcidin levels. This appears to support the hypothesis that acupuncture-based weight loss can downregulate the leptin-hepcidin iron regulatory axis to improve intestinal iron absorption in obese patients. Of note, adipose tissues can also secrete hepcidin too,[39] so the acupuncture-induced decline in hepcidin may be partly attributed to body fat reduction rather than solely through the adipose leptin-hepatic hepcidin pathway. In addition, acupuncture may regulate hepcidin levels through other nonleptin-dependent mechanisms. For example, it has been reported that acupuncture can improve the chronic, low-grade inflammatory status of obese individuals,[40,41] reduce macrophage infiltration of fat tissues, and lower the expression of interleukin 6, tumor necrosis factor-α, and other inflammatory cytokines that are important stimulators of hepcidin syntheses.

sLR acts as a binding protein for leptin and is the major determinant of plasma leptin levels by stabilizing circulating leptin without increasing leptin gene expression.[42] Circulating sLR may play a role in leptin transport across the blood–brain barrier into the central nervous system, where leptin activates its signaling receptor, OB-Rb, and causes reduced food intake and increased energy expenditure. The sLR is synthesized by alternative splicing of OB-R mRNA (OB-Re) and/or ectodomain shedding of membrane-spanning receptors.[39] In humans, plasma levels of sLR are inversely related to adiposity.[43,44] In other words, the sLR level is decreased in obese patients.[45] This decreased production may lead to insufficient transport of leptin into the brain, and thus makes it difficult for leptin to exert its function on the central nervous system. Thus, leptin resistance in obesity may be caused by decreased sLR levels. A recent study reported that acupuncture treatment for obesity can increase the level of sLR;[46] however, no such effect was observed in this study. Based on our results, we speculate that acupuncture mainly stimulates the endocrine system of the body and is less likely to work on the central nervous system.

This study detected a higher SI level in the acupuncture group than the control group following oral iron supplementation, demonstrating acupuncture may enhance enteral iron absorption. Furthermore, a larger increase in TS as well as Hb level was achieved in the acupuncture group compared to the control group. The increase in TS is generally regarded as a consequence of the elevated circulating iron concentrations in the blood. Increased Hb is a result of increased iron in the erythrocytes. ID/IDA patients are also characterized by increased levels of sTfR because ID can induce higher expression of the transmembrane TfR from which sTfR is produced by proteolysis.[47,48] Hence, a decrease in sTfR levels primarily reflects an improvement in cellular iron status and is a more sensitive indicator than Hb. Oral iron replacement therapy led to a decrease in sTfR levels in both the acupuncture and control groups. Despite the lack of a significant difference between the two groups, the high sensitivity of sTfR in response to the iron improvement may play a part.

There are several limitations of our study. First, the sample size was relatively small. This made it impossible to perform subgroup analyses by demographic data and assessment of the probable influence of different clinical features such as type or degree of obesity on treatment effectiveness. Second, it was conducted at one single hospital and there was a lack of follow-up period after the treatment. Such limitations might affect the power of study and even result in biased or incomplete evidence. Third, our study did not evaluate long-term effects on iron status or weight maintenance. Future studies should address such issues and, in addition, examine the generalizability of the benefits observed in this study to other settings and refine the acupuncture-based adjunctive intervention protocol to further increase its efficiency and effectiveness.

In conclusion, acupuncture appears to enhance the therapeutic effects of oral iron replacement for obesity-related ID/IDA by improving intestinal iron absorption. Acupuncture-based weight loss may be a favorable and efficient adjuvant therapy to correct ID/IDA in obese patients.

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Conflicts of interest

There are no conflicts of interest.

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