Effects of acupoint catgut embedding therapy paired with dietary intervention on tumour necrosis factor-α levels and abdominal circumference in patients with obesity

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Abstract. Obesity is associated with a decreased quality of life and is a risk factor for the development of other diseases. Furthermore, obesity is associated with a chronic inflammatory status that contributes to the development of metabolic dysfunction and metabolic syndrome. Acupuncture assists weight loss through the suppression of appetite and the reduction of the risk of metabolic syndrome. The aim of this study was to determine the effectiveness of acupoint catgut embedding therapy combined with dietary intervention on serum tumour necrosis factor-α (TNF-α) levels and abdominal circumference. This study was a randomised, double-blind, controlled clinical trial involving 36 patients with obesity who were randomly divided into the following groups: catgut embedding method combined with dietary intervention (case group) and sham acupuncture combined with dietary intervention (control group). The results showed a significant difference in TNF-α levels before and after treatment within the case group and a significant difference in abdominal circumference change between the two groups. Acupoint catgut embedding combined with dietary intervention has significant effects on serum TNF-α levels and abdominal circumference in patients with obesity.

1. Introduction
Obesity is defined as the presence of excessive adipose tissue relative to the muscle mass (20% or more than the ideal body weight) [1,2]. Obesity occurs as a result of excessive accumulation of fat tissue, potentially leading to several health problems [3]. Recent evidence suggests that obesity is associated with chronic low-grade inflammatory status that contributes to the development of metabolic dysfunction and metabolic syndrome [4]. Based on abdominal circumference, the overall prevalence of obesity in adults was 26.6% [5]. Based on the outpatient nutritional status report from the Cipto Mangunkusumo Hospital in Jakarta, the prevalence of patients with excessive nutrition intake in Adult URJT 3rd Floor was 49.5%, and in RSCM Kencana it was 54.5% [6].

Obesity is associated with chronic low-grade inflammation, particularly in the adipose tissue, which is characterised by the accumulation of macrophages [7]. The adipose tissue acts as an endocrine organ that secretes adipokines, including tumour necrosis factor-α (TNF-α) and interleukin-6 (IL-6). These cytokines worsen glucose intolerance by decreasing adiponectin secretion [1,5].
Obesity management includes dietary interventions, physical activity, behaviour modification, pharmacotherapy and surgical interventions [8]. According to several studies, acupuncture is an effective obesity therapy [9]. Several acupuncture methods can be used to treat obesity, one of which involves catgut insertion at various acupoints [10]. This method provides acupoint stimulation for a longer duration of 15–18 days [11].

A systematic review and meta-analysis of obesity therapies showed that catgut embedding therapy was superior over manual acupuncture, drugs, electroacupuncture and sham for weight loss and BMI reduction [12]. Body acupuncture reportedly decreased TNF-α, IL-6 and high-sensitivity C-reactive protein levels while improving kidney function and lipid profiles [13].

This study sought to determine the effectiveness of acupoint catgut embedding therapy and dietary intervention on serum TNF-α levels and abdominal circumference in patients with obesity.

2. Methods
This was a randomised, double-blind, controlled clinical trial. The study was conducted from 18 April 2016 to 19 May 2016 at the Medical Acupuncture Polyclinic of Dr. Cipto Mangunkusumo Hospital, Jakarta. The study population included outpatients diagnosed with obesity at the Medical Acupuncture Polyclinic of Dr. Cipto Mangunkusumo Hospital, Jakarta, who met the following inclusion criteria: age 18–60 years, male or female, BMI: 25.0–39.9 kg/m², willing to sign the informed consent and willing to follow the research to completion. The exclusion criteria included subjects receiving anti-inflammatory therapy (steroidal or non-steroidal); subjects with hypertension, diabetes mellitus, rheumatoid arthritis, chronic digestive disorders (for > 3 months) and history of liver and kidney disorders; history of liver and kidney disorders; and subjects with contraindications for acupoint catgut embedding, including those with medical emergencies, pregnancy, malignancies, blood-clotting disorders, anticoagulant medications, history of animal protein allergies, infections and injury to the location where the catgut would be embedded. In addition, we excluded patients who were receiving drug therapy for weight loss (orlistat, lorcaserin, phentermine-topiramate and weight-loss supplements). Subjects who did not complete the research procedures or who experienced syncope or pre-shock during the acupoint catgut embedding therapy were discontinued.

The subjects were randomly assigned to one of the following two groups: the acupoint catgut embedding combined with dietary intervention group (case group) and sham acupuncture combined with dietary intervention group (control group). Acupoint catgut embedding therapy involves embedding 1-cm long chromic catgut needles, sized 3.0, by inserting a 21-G needle as deep as 1.5 cm into the acupoints of CV12 Zhongwan, CV6 Qihai, bilateral ST25 Tianshu and unilateral SP6 Sanyinjiao alternately. The embeddings were performed twice with a 2-week interval. Sham acupuncture involves superficial skin surface compression using the tip of a 21-G needle, without puncturing the skin. The sham procedure was similar to the acupoint catgut embedding therapy; however, the catgut suture was not inserted using the tip of the 21-G needle and there was no needle insertion at the acupoints. Sham acupuncture was also performed twice with a two-week interval. Dietary intervention involved a reduction in daily calorie intake by 500 calories.

We objectively measured serum TNF-α levels and abdominal circumference. The measurements were performed at the beginning and at 2 weeks post-treatment. All the measurements were performed by an independent evaluator team.

The collected data were entered into a database and analysed statistically using IBM SPSS version 20. Normally distributed data were analysed using unpaired t-test. If the data were non-normally distributed, a pre-test transformation was performed. If the data transformation resulted in a non-normal distribution, Mann–Whitney U test was performed. p < 0.05 indicated significance.

3. Results
There was no significant difference (p > 0.05) regarding gender, initial body weight, BMI, initial TNF-α levels and initial abdominal circumference between the two groups (see Table 1); however there was a significant difference regarding age (p < 0.05).
Table 1. Subject characteristics.

| Characteristic                  | Acupoint Catgut Embedding with Dietary Intervention (n = 18) | Sham Acupuncture with Dietary Intervention (n = 17) | Total (n = 35) | p-value |
|--------------------------------|-------------------------------------------------------------|--------------------------------------------------|----------------|---------|
| Age (years) Mean (SD)          | 36.2 (9.3)                                                  | 44.0 (7.3)                                      | 40.0 (9.1)     | 0.01*   |
| Gender                         |                                                             |                                                 |                |         |
| Male. n                        | 3                                                            | 3                                                | 6              | 0.93**  |
| Female. N                      | 15                                                           | 14                                               | 29             |         |
| Initial BW (kg) Mean (SD)      | 78.7 (7.2)                                                  | 77.1 (12.2)                                     | 77.9 (9.8)     | 0.64*   |
| BMI (kg/m²) Mean (SD)          | 30.9 (2.9)                                                  | 31.4 (3.7)                                      | 31.1 (3.3)     | 0.61*   |
| Initial TNF-α levels (pg/ml)   | 3.8 (3.1–5.9)                                               | 3.8 (3.3–5.3)                                   | 3.8 (3.1–5.9)  | 0.77*** |
| AC (cm) Median (Min.–Max.)     | 101.5 (91.5–115.0)                                          | 100.0 (93.0–121.0)                              | 100.0 (91.5–121.0) | 0.63*** |

* = Unpaired t-test; ** = χ² test; *** = Mann–Whitney U test

BW, body weight; BMI, body mass index; TNF-α, tumour necrosis factor-alpha; AC, abdominal circumference

Table 2. The comparison between groups regarding initial and final TNF-α levels.

| Variable                        | Acupoint Catgut Embedding and Dietary Intervention | Sham Acupuncture and Dietary Intervention | p-value |
|---------------------------------|----------------------------------------------------|------------------------------------------|---------|
| Δ TNF-α Levels (pg/ml)          | 2.0 (0.6)                                           | 2.1 (0.8)                                 | 0.64*   |

* = Unpaired t-test

TNF-α, tumour necrosis factor-alpha

There was no significant difference regarding ΔTNF-α levels before and after treatment between the two groups (see Table 2; p = 0.64; Confidence Index 95% −0.62 to 0.39).

Table 3. The comparison of mean initial and final TNF-α levels in both the groups.

| TNF-α Levels (pg/ml)            | Z       | P       |
|---------------------------------|---------|---------|
| Acupoint Catgut Embedding and Dietary Intervention Group (Initial vs Final) | −3.724  | <0.01   |
| Sham Acupuncture and Dietary Intervention Group (Initial vs Final)       | −3.622  | <0.01   |

Z = Wilcoxon test
There was a significant increase in the mean TNF-α levels before and after treatment in both the groups (acupoint catgut embedding and dietary intervention group, p < 0.01; Z = −3.724 and sham acupuncture and dietary intervention group, p < 0.01; Z = −3.622) (Table 3).

**Table 4.** The comparison between groups regarding initial and final abdominal circumference difference.

| Variable                      | Acupoint Catgut Embedding Therapy and Dietary Intervention | Sham Acupuncture and Dietary Intervention | p-value |
|-------------------------------|-----------------------------------------------------------|------------------------------------------|---------|
| Δ Abdominal Circumference (cm)| 7.5 (3.4)                                                 | 3.6 (3.0)                                | <0.01*  |

*= Unpaired t-test

There was a significant difference regarding change in abdominal circumference before and after treatment between the two groups (Table 4; p < 0.01; Confidence Index 95% 1.68–6.13).

**Table 5.** The comparison of mean initial and final abdominal circumference in both the groups.

| Abdominal Circumference (cm) | Z       | P    |
|------------------------------|---------|------|
| Acupoint Catgut Embedding and Dietary Intervention (Initial vs Final) | −3.727  | <0.01|
| Sham Acupuncture and Dietary Intervention (Initial vs Final) | −3.184  | <0.01|

Z = Wilcoxon test

There was a significant decrease in the mean abdominal circumference before and after treatment in both the groups (acupoint catgut embedding and dietary intervention group, p < 0.01; Z = −3.727 and sham acupuncture and dietary intervention group, p < 0.01; Z = −3.184) (Table 5).

4. Discussion
To the best of our knowledge, this is the first study in Indonesia to determine serum TNF-α levels following acupoint catgut embedding technique in patients with obesity. The concomitant dietary intervention involved reducing each subject’s daily calorie intake by 500 calories. The acupoint catgut embedding therapy was chosen because it was easy to perform, provided a longer and stronger stimulation and involved longer intervals between therapies [12]. Studies have shown the efficiency of acupoint catgut embedding therapy in maintaining body weight and changing the levels of several haematological markers [14].

We selected the study acupoints based on systematic reviews and meta-analyses conducted by Guo et al. where CV12 Zhongwan, CV6 Qihai, ST25 Tianshu and SP6 Sanyinjiao were the most widely used acupoints for obesity therapy; these are also referred to as anti-obesity points [12]. According to Silva et al. SP6 Sanyinjiao exerts anti-inflammatory effects [15].

BMI is an important indicator of nutritional status. In this study, the diagnosis of obesity was based on the IMT criteria of Asia-Pacific. The BMI range used to define obesity in this study was 25.0–39.9 kg/m². We chose this range because in individuals with BMI up to 40 kg/m², adipocytes increase in size and in individuals with BMI > 40 kg/m², there is an absolute increase in the total number of fat cells [1].
Serum TNF-α levels are positively correlated with adipose tissue volume and are associated with metabolic syndromes, cardiovascular diseases, insulin resistance and diabetes [13]. In this study, we excluded subjects with chronic inflammation and those receiving anti-inflammatory therapies (steroidal or non-steroidal). We sought to determine TNF-α levels in patients with obesity, but without other disorders that could elevate TNF-α levels.

High TNF-α levels are associated with pathological conditions related to insulin resistance syndrome. Therefore, we conclude that elevation in TNF-α levels plays an important role in the development of insulin resistance. One study suggested that TNF-α levels became elevated in individuals with obesity and decreased after weight loss [16]. However, other studies found no association of TNF-α levels with obesity, insulin resistance and impaired glucose tolerance [16].

This study found that TNF-α levels increased after both acupoint catgut embedding therapy and sham acupuncture, both of which were combined with dietary intervention. These findings stand in contrast to those of Ismail et al. [13], who reported that TNF-α levels decreased after acupuncture treatment. We measured TNF-α levels within a month after therapy, whereas Ismail et al. performed their measurements 6 months after therapy. Therefore, additional studies are needed to determine TNF-α levels following acupuncture.

TNF-α is involved in lipid metabolism. TNF-α lowers the uptake of free fatty acids, reduces triglyceride synthesis (lipogenesis) and increases lipolysis. In patients with obesity, elevated TNF-α levels contribute to increased basal lipolysis [17].

The insertion of needles at acupoints stimulates peripheral nerve fibres to regulate the autonomic control of internal organs and to coordinate the actions of sympathetic and parasympathetic nerves. Sympathetic inputs inhibit gastric emptying, whereas parasympathetic inputs increase intestinal peristalsis to reduce food absorption [2,18,19]. The insertion of needles at the acupoints incites local tissue injury and biochemical reactions by releasing various inflammatory and immune response mediators. Tissue injury involves biochemistry processes resulting in a therapeutic response at local and systemic levels [20]. In response to acupuncture, there is an infiltration of immune cells, such as macrophages. Macrophages are responsible for the production of majority of cytokines in the adipose tissue, including TNF-α and IL-6. Inflammation and tissue injury are communicated to the brain through nerve pathways, causing the brain to generate a local inflammatory response [21-23]. Increased TNF-α levels cause phosphorylation and suppress perilipin expression through MAPK p44/42 dan JNK. Perilipin is a phosphoprotein found in adipocytes on the droplet surface of the triacylglycerol that acts as a gatekeeper, preventing lipase from the triacylglycerol hydrolysis to facilitate the release of free fatty acids. Decreased perilipin expression leads to increased lipolysis [24].

Peripheral stimulation of acupoints stimulates the central nervous system, releasing catecholamines from the hypothalamus, which bind with β-adrenergic receptors. In response to this, phosphorylated protein kinase A activates hormone-sensitive lipase and increases adipose triglyceride lipase levels of mRNA, leading to lipolysis [25,26].

Our results suggest that acupoint catgut embedding and sham acupuncture, both combined with dietary intervention, result in lipolysis by increasing TNF-α levels. However, additional studies on the long-term effect of acupoint catgut embedding on TNF-α levels are needed.

Abdominal obesity contributes to type 2 diabetes and cardiovascular diseases. Abdominal circumference is an anthropometric parameter used to measure intra-abdominal fat and is linked to metabolic disease risk [27]. In this study, we observed a decrease in abdominal circumference in both the groups. The difference between the initial and final abdominal circumference (Δ abdominal circumference) in the acupuncture group was 7.5 (3.4) cm, whereas in the sham acupuncture group, it was 3.6 (3.0) cm. Thus, the change in abdominal circumference was significantly different between the two groups (p < 0.01; CI 95% 1.68–6.13). From this result, it can be concluded that acupoint catgut embedding therapy was more effective in reducing abdominal circumference than sham acupuncture.
As seen in Figure 1, acupoint catgut embedding therapy was more effective in increasing leptin receptor activity and in decreasing insulin levels, fat tissue mass and leptin levels.

Several side effects were associated with acupoint catgut embedding therapy; these included hematoma and pain in two subjects, pain alone in one subject and a nodule at the SP6 Sanyinjiao point in one subject. The hematoma and pain disappeared, without treatment, after a few days. Antibiotics were given to the subject who reported the nodule, which disappeared in 5 days.

A main limitation of this study was its short period (1 month). Consequently, we were unable to determine the effects of acupoint catgut embedding therapy on TNF-α levels in patients with obesity after achieving an ideal body weight.

5. Conclusion
The combination of acupoint catgut embedding therapy and dietary intervention affected serum TNF-α levels and abdominal circumference in patients with obesity. There was no significant difference between TNF-α levels before and after treatment in both the groups (p = 0.64; CI 95% −0.62 to 0.39 pg/ml). However, there was a significant difference in abdominal circumference before and after treatment in both the groups (p < 0.01; CI 95% 1.68–6.13 cm).

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