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ORIGINAL CONTRIBUTIONS

Percutaneous Electrical Neurostimulation of Dermatome T6 for Appetite Reduction and Weight Loss in Morbidly Obese Patients

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Abstract
Background A continuous feeling of hunger is the major cause of dietary treatment failure in obese patients, making dietary leave. The aim of this study was to evaluate the effect of percutaneous electrical neurostimulation (PENS) of T6 dermatome on appetite, weight loss and dietary compliance.
Methods A prospective, randomized study was performed. The patients were randomized into two groups: those undergoing PENS of dermatome T6 associated with the implementation of a 1,200-Kcal diet (group 1) and those following only a 1,200-Kcal diet (group 2). A third group of obese patients (BMI >30 Kg/m^2) with fecal incontinence undergoing PENS of posterior tibial nerve was evaluated.
Results One hundred five patients were included in the study, 45 in groups 1 and 2, and 15 in group 3. The median pain perception after PENS of dermatome T6 was 1. There were no complications. Only the patients in group 1 experienced significant reductions of weight, BMI, and appetite. All of the patients in group 1 experienced appetite reduction compared to 20 % of the patients in group 2 and 30 % of the patients in group 3 ($p<0.001$). Weight loss ≥5 Kg was achieved in 76.7 % of the patients in group 1, 6.7 % of the patients in group 2, and 0 % of the patients in group 3 ($p<0.001$). Dietary compliance after 12 weeks was 93.3 % in group 1, 56.7 % in group 2, and 50 % in group 3($p=0.006$).
Conclusions PENS of dermatome T6 was associated with appetite reduction in all of the patients and, along with a proper diet, achieved a significantly greater weight reduction than diet alone.

Keywords Percutaneous electroneurostimulation · Dermatome T6 · Weight loss · Appetite reduction

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Introduction

About a third of the population in developed countries is obese to some degree. Obesity itself is a health risk factor that influences the development and progression of various diseases, such as dyslipidemia, ischemic heart disease, hypertension, diabetes mellitus type 2, and sleep apnea-hypopnea syndrome, thereby worsening the quality of life of patients, limiting their activities, and causing psychosocial problems. There is a direct relationship between body mass index (BMI) and morbidity and mortality risks in obese patients, which is derived from associated pathologies and results in making obesity itself a disease [1–3].

Dietary treatment associated with exercise is the first therapeutic step for obesity. However, to be effective, patient motivation is essential, though often lacking. Obese patients often tire of following a low-calorie diet for long-time periods. A continuous feeling of hunger is the major cause of dietary treatment failure [1, 4].

An implantable gastric stimulator (gastric pacemaker) has been used to treat obesity, with promising results in some initial publications, though these results have not been completely confirmed in posterior studies. This technique consists in applying cyclic electric pulses of 40 Hz every 4–12 min to the gastric wall. The stimulator induces gastric distention in the fasting state and inhibits postprandial antral contractions, thereby impairing stomach emptying, which may lead to early satiety and reduced food intake. The induction of gastric distension in the fasting state results in the activation of stretch receptors, causing satiety [5]. It has been observed that this technique achieves excess weight loss up to 40 % in approximately 1 year. This stimulator can be placed laparoscopically or endoscopically, techniques that carry a small risk to the patient but are still invasive [4–7]. The modulation of neuronal activities and release of certain hormones with an implantable gastric stimulator may also explain the reduction of appetite and the increase of satiety. A decrease in Ghrelin levels could be one mechanism that explains weight loss and appetite reduction after implantable gastric stimulation [8].

Percutaneous electroneurostimulation (PENS) was originally developed to treat urinary and fecal incontinence by stimulating the posterior tibial nerve. The mechanism of action involves the creation of a somatosomatic reflex (the posterior tibial nerve, the afferent pathway) that leads the electrical impulse to root S3, for which the efferent pathway is the pudendal nerve, which is responsible for the innervation of the anal sphincter [9, 10].

Based on the creation of a somato-autonomic reflex, the stimulation of sensory nerve terminals located in dermatome T6 may cause a reflex, for which the efferent pathways end in vagal nerve branches stimulating the gastric wall similarly to the gastric pacemaker.

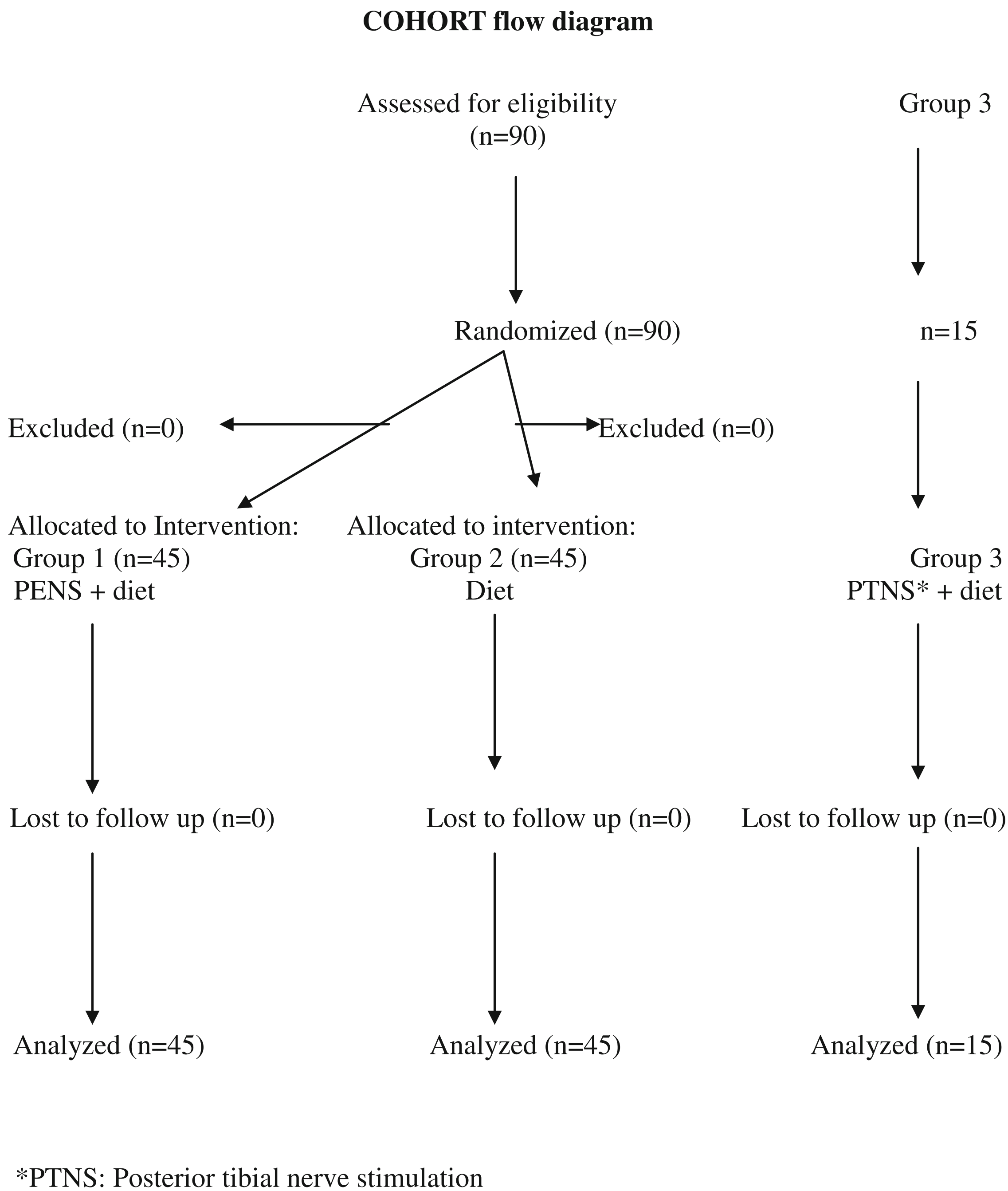
The aim of this study was to evaluate the effect of PENS of T6 dermatome on appetite, weight loss, and dietary compliance.

Patients and Methods

A prospective, randomized study was performed in the Bariatric Surgery Unit of the General University Hospital of Elche between January and June 2012. The calculated sample size was based on an expected weight loss of 6 Kg for the patients undergoing PENS of T6 dermatome and diet and 4 Kg for the patients following only dietary treatment; this calculation was based on the historical data (at our institution) of preoperative weight loss following a 1,200-Kcal diet. Using 80 % power and a significance level of $p < 0.050$, it was calculated that 45 patients were required in each arm of the study. The inclusion criteria were patients who were bariatric surgery candidates with BMIs of >40 or >35 Kg/m^2 with comorbidities associated with the obesity status and dietary treatment failure. The exclusion criteria were untreated endocrine disease causing obesity and serious psychiatric illness.

The patients were randomized into two groups using an Internet randomization module as follows: patients undergoing PENS of dermatome T6 in conjunction with the implementation of a 1,200-Kcal diet (group 1) and those following a 1,200-Kcal diet only (group 2).

To avoid the placebo effect associated to the intervention as a bias in the study, a third group was evaluated. This group included obese patients (BMI >30 Kg/m^2 before beginning the therapy) with fecal incontinence undergoing PENS of posterior tibial nerve for the treatment of incontinence. It was explained to these patients that this therapy might also help them to lose weight, reducing the appetite sensation, but they had to follow a 1,200-Kcal diet to achieve the weight reduction. The importance of weight reduction for the improvement of fecal incontinence was based on the results reported by Sileri et al. [11], who reported improvement of Fecal Incontinence Severity Index and Wexner Score after bariatric surgery. They also defended that obesity is an important risk factor for the development of diverse defecatory disorders, especially fecal incontinence.



Preoperative Protocol for Patients Planning to Undergo Bariatric Surgery at Our Institution

The potential surgical candidates were evaluated by a multidisciplinary team composed of surgeons, endocrinologists, psychiatrists, psychologists, anesthesiologists, endoscopists, radiologists, and specialized nurses. A preoperative diet, which had a total daily energy intake of 1,200-Kcal, was established for all the patients. According to the randomization, the patients assigned to the interventional group (group 1) underwent PENS of T6 dermatome apart from the 1,200-Kcal diet. A minimum weight loss of 5 Kg was considered the cut-off point for significant weight reduction. It was explained to the patients of groups 1 and 2 that they will undergo a bariatric procedure after finishing the treatment and that weight reduction is essential to minimize the surgical risk.

Diet is described in Table 1. Dietary compliance was evaluated by means of a food diary that the patients filled. A dietitian, who was in permanent contact with the patients, evaluated the food diary.

PENS Methodology

PENS of dermatome T6 was performed by surgeons from the General University Hospital of Elche. Urgent PC 200 Neuromodulation System® (Uroplasty, Minnetonka, MN, USA) was used. This device was originally developed to treat fecal and urinary incontinence. The participants underwent one 30-min session every week for 12 consecutive weeks. Each patient was placed in a supine position without anesthesia and PENS was delivered by a needle electrode inserted in the left upper quadrant along the medioclavicular line, 2 cm below the ribcage at a 90 ° angle towards the abdominal wall at a depth of approximately 0.5–1 cm. Successful placement was confirmed by the feeling of electric sensation movement at least 5 cm beyond the dermatome territory. PENS was undertaken at a frequency of 20 Hz at the highest amplify (0–20 mA) without causing pain.

Posterior tibial nerve PENS was performed by the same surgeons. Conditions were similar to PENS of dermatome T6, except in the needle electrode insertion, that in these patients was placed 3–4 cm cephalad and 2 cm backward to the medial malleolus, at a 60 ° angle towards the ankle joint. The same electroneurostimulator device Urgent PC 200 Neuromodulation System® (Uroplasty, Minnetonka, MN, USA) was used. Subjects underwent one 30-min session every week for 12 consecutive weeks.

Table 1 1,200-Kcal diet

Breakfast
- Skimmed milk (200 ml) or two natural yogurts
- Bread (200 g) or three cookies

Mid morning
- Fruit (100 g of apple, pear, orange, peach, or kiwi)

Lunch and dinner:
- *First course to choose from*:
  • Vegetables (200 g) spinach, chard, eggplant, watercress, endive, lettuce, cauliflower, mushrooms, leeks, asparagus, endive, cabbage, cucumber, peppers, tomatoes, alternating cooked or salad. Or 150 g green beans, beets, carrots, artichokes or Brussels sprouts
  • *Vegetables soup*
  • Soup pasta, semolina, rice or tapioca starch (15 g dry)
- *Second course to choose from*:
  • Fish (120 g)
  • Chicken, turkey, rabbit, veal (100 g)
  • Eggs (1 U)
- *Dessert*, *choice of*:
  • Fruit (100 g of apple, pear, orange, peach, or kiwi or 200 g melon, watermelon, or strawberries)
- Bread (30 g)

Snack:
200 ml of skimmed milk alone or with coffee or tea.
Olive oil for all day 30 cm^3 (two tablespoons).

Mean values of carbohydrates 51 %; proteins 23 %; fats 26 %

Variables

A specific protocol for data collection was created for this study. Age, gender, weight, BMI, excess weight, and appetite were recorded before the intervention. Pain perception after PENS was evaluated after the first PENS session in group 1. Weight, BMI, appetite, and diet compliance were analyzed after finishing the 12-week intervention. Complications secondary to PENS were also recorded. Appetite and pain were evaluated with a visual analog scale (VAS) that ranged from 0 (absence of perception) to 10 (maximal perception). Pain was recorded after the first episode of neurostimulation and appetite was investigated before beginning the treatment and after finishing the 12 sessions. A minimum weight loss of 5 Kg was considered clinically relevant.

Statistics

The statistical analysis was performed with the statistical software SPSS 19.0 for Windows. Quantitative variables that followed a normal distribution were defined by the mean and standard deviation. For non-Gaussian variables, median and range were used. Qualitative variables were defined by the number and percentage of cases.

A comparison of variables was performed with Student's *t* test, ANOVA and Pearson's correlation coefficient for quantitative variables following a Gaussian distribution. Nonparametric tests (Mann–Whitney *U* test, Kruskal–Wallis, and Spearman's rank–order correlation) were used for non-Gaussian variables. Student's *t* test and the Friedman test were used to compare paired variables.

A comparison of qualitative variables was performed with the chi-squared test; in cases with fewer than five observations in the cell, Fisher's exact probability method was used. Values of $p < 0.05$ were considered significant. This study was approved by the local Ethics Committee.

Results

One hundred and five patients were included in the study: 45 patients in group 1, 45 in group 2, and 15 in group 3. The sample consisted of 80 % women and 20 % men, with a mean patient age of 45.6±14.3 years (range 21–74 years). The distribution of age, gender, weight, BMI, excess weight, and

Table 2 Distribution of age, gender, weight, BMI, excess of weight and appetite between groups, before starting any treatment scheme

	Group 1	Group 2	p Value (groups 1 vs 2)	Group 3	p Value (groups 1 vs 3)
Age (years)	40.3±12.3	41.2±11.9	0.568	63.5+8.2	0.003
Gender (females/males)	80/20 %	80/20 %	1	80/20 %	1
Weight (Kg)	123.3±25.1	121.3±20.6	0.368	82.8±10.2	0.012
BMI (Kg/m^2)	46.1±7.5	45.3±6	0.424	32.5±2.4	0.009
Excess of weight (Kg)	56.9±21.3	54.7±19.6	0.296	20.8±9.7	0.008
Appetite (VAS)	6 (range 4–10)	6 (range 4–9)	0.876	5 (range 2–7)	0.498

Group 3 significantly differ from the other groups in age, weight, BMI, and excess of weight

appetite quantification before treatment between the groups is described in Table 2. When all three groups were simultaneously analyzed, significant differences could be observed in age (p=0.008), weight (p=0.026), BMI (p=0.015), and excess of weight (p=0.015).

The median pain perception after PENS of dermatome T6 was 1 (range 0–2) and 2 (range 1–4) after PENS of posterior tibial nerve. There were no complications in any of the groups.

When all three groups were simultaneously analyzed, significant differences between groups in weight loss (p=0.012), BMI loss (p=0.01), excess weight loss (p=0.012), and appetite (p=0.006) after finishing the treatment, could be observed. A 2×2 analysis is described in Table 3, revealing that group 1 significantly differed from the other groups in all the variables. Comparing pre- and post-interventional values, only the patients in group 1 experienced significant reductions of weight (mean 7.1 Kg, CI 95 %, 3.7–10.4, p=0.001), BMI (mean 2.7 Kg/m^2, CI 95 %, 1.4–4, p=0.001), excess percentage of weight loss (mean 10.7 %, CI 95 %, 5.9–15.4, p= 0.001) and appetite (median 3, CI 95 %, 1.5–4, p<0.001). Appetite reduction in each group is shown in Fig. 1. All of the patients in group 1 experienced appetite reduction compared to 20 % of the patients in group 2 and 30 % of the patients in group 3 (p<0.001). Moreover, 70 % of the patients in groups 2 and 3 reported an increase in appetite, leading them to abandon the diet in most cases. This appetite increase was secondary to the diet compliance. These patients probably lose weight so long as they followed the diet, but when they abandoned it, they possibly regained part of the lost weight.

After the interventions, clinically significant weight loss (≥5 Kg) was achieved in 76.7 % of the patients in group 1, 6.7 % of the patients in group 2, and 0 % of the patients in group 3 (p<0.001) (Fig. 2). Including all weight loss, all of the patients of group 1 lost weight (range 1.5–32.3 Kg) compared to 63.3 % of the patients in group 2 (range −2–9.5 Kg) and 40 % of group 3 (range (−1)–4 Kg). In group 1, one patient decided to abandon the bariatric surgery program at our institution after losing 32.3 Kg (65.3 % excess weight loss and final BMI 32.2 Kg/m^2) because she was extremely satisfied with the weight loss achieved.

The median treatment week in which decreased appetite was reported by the patients of group 1 was 1.5 (range 1–6). Dietary compliance after 12 weeks was 93.3 % in group 1, 56.7 % in group 2, and 50 % in group 3 (p=0.006) (Fig. 3). Dietary compliance in all the groups was associated with lower appetite quantification after treatment (p<0.001) and with weight loss (p=0.007) (Fig. 4). The two patients in group 1 who abandoned the diet experienced less weight loss (1.5 and 2 Kg). They left the study because of personal problems, not because they noticed an appetite increase or could not tolerate the hunger.

An inverse correlation could be established between weight loss and changes in appetite (Spearman −0.411; p=0.011).

Discussion

The effect of PENS has been widely demonstrated by the posterior tibial nerve neurostimulation in treating urinary and fecal incontinence, creating a somato-somatic reflex [9, 10]. To our knowledge, this is the first study reporting using PENS of dermatome T6 to reduce appetite and, consequently, obtain

Table 3 Weight loss, BMI loss, excess weight loss, and appetite after finishing the treatment

	Group 1	Group 2	p Value (groups 1 vs 2)	Group 3	p Value (groups 1 vs 3)
Weight loss (Kg)	7.1±1.5	2±1.1	0.008	0.8±0.3	0.001
BMI loss (Kg/m^2)	2.7±0.5	0.9±0.3	0.006	0.3±0.4	0.001
Excess weight loss (%)	10.7±2.6	3.2±1.8	0.008	0.4±0.4	0.001
Appetite (VAS)	1.5 (range 0–3)	5 (range 3–9)	0.001	4 (range 2–6)	0.002

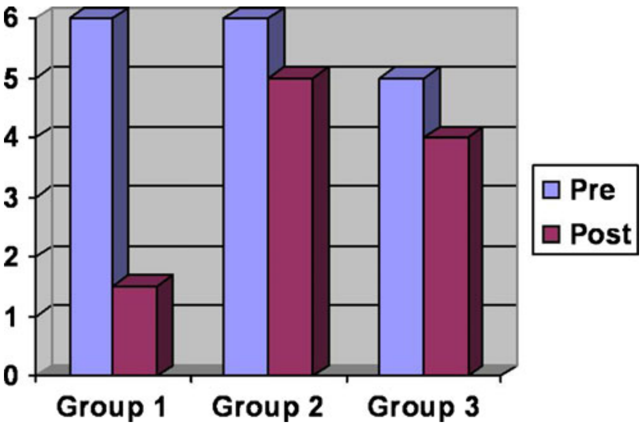


Fig. 1 Appetite quantification by VAS between the groups. A significant reduction of appetite was observed only in group 1 ($p = 0.002$)

a clinically significant weight loss. Pereira and Foster [12] observed an excess weight loss of 20 % associated with decreased appetite in two morbidly obese patients in whom spinal cord stimulators were set up at the T6 and T7 levels to control intractable lumbar pain and lumbosacral radiculitis secondary to lumbar disk herniation. These patients did not increase their physical activity or follow any type of diet; however, they experienced significant appetite reductions. The authors were the first to hypothesize that spinal cord stimulation could affect the stomach. Other authors have reported that transcutaneous electrical gastric stimulation may alter gastric motility, delay gastric emptying, and lead to postprandial satiety [13–15]. They believed that electrical stimulation was transmitted to the stomach through the abdominal wall when placing the electrode in the left upper quadrant of the abdomen. However, we think that it is more likely that the effect is produced by the creation of a somato-autonomic reflex rather than by transcutaneous transmission of the electrical stimuli, similar to the transcutaneous electrical stimulation of the posterior tibial nerve in treating incontinence [16]. Moreover, it is difficult to believe that electrical stimulus could have some effect when traversing a thick abdominal wall, which is present in morbidly obese patients, particularly considering the presence of adipose tissue, which is not a good electrical conductor. The same authors have also postulated that the effect of gastric stimulation, which is associated with the delay of gastric emptying, might also decrease Ghrelin segregation in the gastric fundus and inhibit appetite through the central nervous system [13–15]. Chen [5] reported that electric gastric stimulation with a gastric pacemaker may affect the central nervous system by segregating hormones in the stomach and regulating satiety and/or appetite, with Ghrelin being particularly involved in this mechanism.

It is widely known that the main reason for dietary treatment failure is that patients tire of following the diet after several weeks, usually regaining the weight loss achieved, or even exceeding it. Appetite is greater than willpower, and patients leave the dietary treatment [1, 4]. In our sample, we observed that appetite was associated with diet compliance, which, logically, was associated with weight loss. We have not analyzed the isolated effect of PENS of dermatome T6 without diet, but this therapy itself does not justify a relevant weight loss. As shown in this study, its main effect is appetite reduction; all of the patients presented with mild feelings of hunger or even the absence of hunger after PENS of

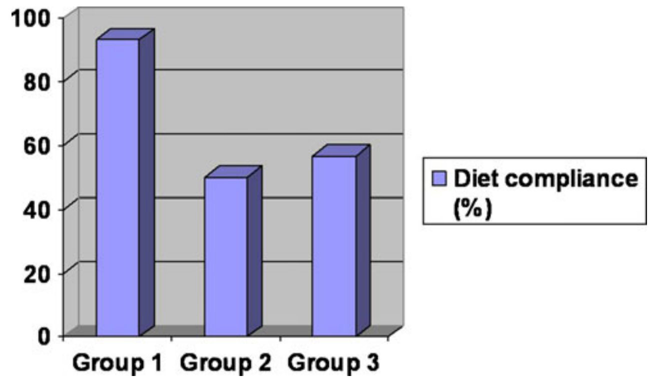


Fig. 3 Dietary compliance between groups. In group 1, dietary compliance was significantly greater compared to the other two groups

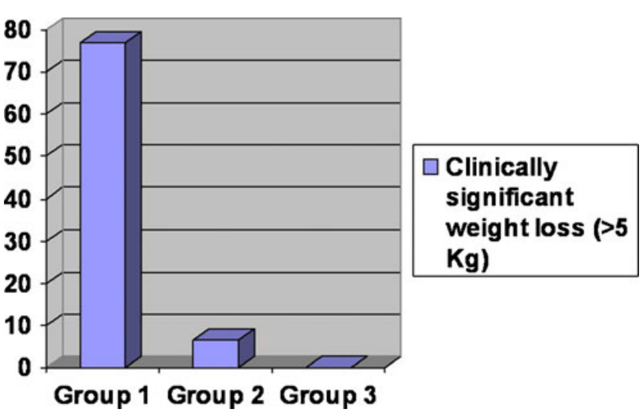


Fig. 2 Percentage of patients with clinically significant weight loss after treatment

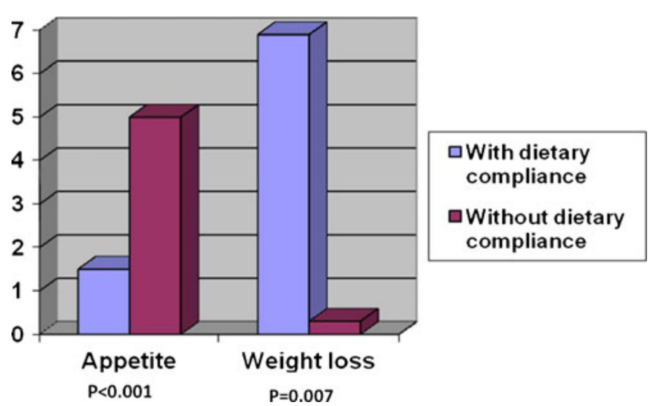


Fig. 4 Appetite quantification and weight loss in patients with and without dietary compliance

dermatome T6. However, some weight loss could be obtained just based on less food intake, secondary to the appetite reduction, although a specific low-calorie diet was not established.

The main limit of this study is the heterogeneity of group 3 when compared to groups 1 and 2. The aim of the inclusion of these patients was to evaluate the placebo effect based on the intervention of PENS. Despite performance of PENS in groups 1 and 3, significant differences regarding appetite reduction were obtained only in group 1 patients ($p<0.001$). Appetite reduction was similar among patients of groups 2 and 3. Referring to weight loss, statistical differences were only obtained in group 1. A comparison of weight loss can only be established between patients of groups 1 and 2, but not with group 3, because the latter presents lower BMI (not homogeneous groups), being more difficult for these patients to obtain the same weight loss.

In terms of bariatric surgery aims, an excess weight loss over 50 % with a final BMI of <35 Kg/m^2 is considered a satisfactory result of a bariatric technique [16]. Only one patient in group 1 achieved these goals before deciding to abandon the bariatric surgery program. In our patients, the therapy was planned to achieve a weight reduction before bariatric surgery to reduce the surgical risk. Therefore, after finishing the treatment with PENS of dermatome T6, the patients underwent a bariatric technique. In our opinion, PENS of dermatome T6 cannot be considered a bariatric approach; therefore, a mean weight loss of 7.1 Kg and a mean percentage of weight loss of 10.7 % are not enough for a morbidly obese patient. It remains unknown whether prolonging the therapy would add some additional effects and how long the effect of this therapy lasts. In the PENS of posterior tibial nerve for treating fecal or urinary incontinence, a secondary treatment period every 2 weeks over a 3-month period has been determined to add some benefits to the first treatment [17, 18].

All of the patients undergoing PENS of dermatome T6 in this study presented with BMIs of >35 Kg/m^2. The weight reduction obtained in these patients was not enough to alleviate their morbid obesity. However, in patients presenting with mild obesity or even overweight, this therapy would most likely help them lose their weight excess, returning to a normal weight status. Future studies must be conducted to confirm this hypothesis.

Conclusion

PENS of dermatome T6 was associated with an appetite reduction in all of the patients. After therapy, appetite was mild or even absent in all the patients. This therapy, along with a proper diet, achieved a significantly greater weight reduction compared to diet alone in morbidly obese patients. Dietary compliance surpassed 90 %. No complications were observed associated with the technique and pain sensation was nearly imperceptible.

ClinicalTrials.gov Identifier: NCT01792947

Conflict of Interests All authors (Jaime Ruiz-Tovar, M.D., Ph.D., Inmaculada Oller, M.D., Ph.D., María Diez, M.D., Lorea Zubiaga, M.D., Antonio Arroyo, M.D., Ph.D., and Rafael Calpena, M.D., Ph.D.) declare that they have no conflict of interests in the preparation of this manuscript.

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