High-protein diet in morbidity obesity patient before bariatric surgery

Tratamiento nutricional hiperproteico precirugía bariátrica en obesidad mórbida

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Abstract

Objective: Compare the effectiveness of a hyperproteic hypocaloric feeding plan with a normoproteic on body composition, biochemical parameters and inflammatory cytokines in obese pre-bariatric surgery patients in the integral treatment. **Method:** Seventy-six pre-bariatric surgery patients with body mass index (BMI) ≥ 40 kg/m² were studied. One group was treated with a hyperproteic hypocaloric diet and compared with a normoproteic hypocaloric diet. Biochemical parameters, anthropometric parameters, body composition and levels of tumor necrosis factor (TNF), interleukin (IL)-6 and IL-1 β in serum were evaluated at the initiation of treatment and after 4 months. **Results:** In both groups studied, a decrease in weight, BMI and fat mass was observed, as well as an increase in muscle mass compared to baseline ($p < 0.05$), no differences showed between the groups studied. No change was found in the biochemical parameters and serum levels of TNF and IL-6 before and after 4 months of treatment, nor among the groups evaluated ($p > 0.05$). Serum IL-1 β levels decreased after treatment with only a normoprotein hypocaloric diet ($p = 0.02$). **Conclusions:** Hyperproteic hypocaloric diet does not show advantages in weight reduction and body fat or in muscle mass gain compared to the normoproteic hypocaloric diet in patients with morbid obesity bariatric pre-surgery in the integral treatment.

Key words: Morbid obesity. High-protein diet. Bariatric surgery.

Resumen

Objetivo: Comparar la efectividad de un plan de alimentación hipocalórico hiperproteico con otro normoproteico sobre la composición corporal, los parámetros bioquímicos y las citocinas inflamatorias en pacientes obesos precirugía bariátrica sometidos a un tratamiento integral. **Método:** Se estudiaron 76 pacientes con un índice de masa corporal (IMC) ≥ 40 kg/m² previamente a la cirugía bariátrica. Un grupo fue tratado con una dieta hipocalórica hiperproteica y se comparó con una dieta hipocalórica normoproteica. Se evaluaron parámetros bioquímicos, parámetros antropométricos, composición corporal y valores de citocinas inflamatorias en suero al inicio y después de 4 meses de tratamiento. **Resultados:** En ambos grupos se observó una disminución de peso, de IMC y de masa grasa, así como un incremento de la masa muscular respecto al momento basal ($p < 0.05$), sin diferencias entre los grupos estudiados. No se encontraron cambios en los parámetros bioquímicos

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ni en las concentraciones séricas de factor de necrosis tumoral (TNF) e interleucina (IL)-6 antes y después de 4 meses de tratamiento, ni entre los grupos evaluados ($p > 0.05$). Las concentraciones séricas de IL-1 β disminuyeron únicamente con la dieta hipocalórica normoproteica ($p = 0.02$). **Conclusiones:** La dieta hipocalórica hiperproteica no muestra ventajas en la reducción de peso y grasa corporal, ni en la ganancia de masa muscular, en comparación con la dieta hipocalórica normoproteica en pacientes con obesidad mórbida precirugía bariátrica sometidos a un tratamiento integral.

Palabras clave: Obesidad mórbida. Dieta hiperproteica. Cirugía bariátrica.

Introduction

Obesity and overweight are currently defined as an abnormal or excessive accumulation of fat of multifactorial etiology that can be detrimental for health, and that develops by an interaction of the influence of genetic, social, behavioral, psychological, metabolic, cellular and molecular factors¹.

According to data from the World Health Organization, the prevalence of obesity in the world has doubled between 1980 and 2014. In 2016, more than 1900 million adults aged 18 years or more had overweight, out of which more than 650 million were obese; 13% were obese women.² In Mexico, results of the 2016 National Survey on Health and Nutrition report a prevalence of overweight and obesity in adults aged 20 years or more of 72.5%, with predominance of the female gender³.

Overweight and obesity as a result of an imbalance between energy and physical activity entails adipocyte hypertrophy and hyperplasia, which overloads its functional capacity, thus causing adipocyte angiogenesis and hypoxia and immune system cell recruitment, such as pro-inflammatory macrophages that infiltrate adipocytes^{4,5}. This macrophage infiltration activates signaling pathways that drive to cytokine production, such as tumor necrosis factor (TNF), interleukin 1 β (IL-1 β) and interleukin 6 (IL-6), which combined with C-reactive protein drive to a state of chronic low-grade inflammation and anti-inflammatory markers inhibition, as well as to a decrease in insulin receptors density and an increase in β 3 receptors, which leads to lipolysis. These effects drive to an increased risk for the development of cardiovascular conditions, type 2 diabetes and metabolic syndrome^{5,6}.

Changes in lifestyle, dietary regimens and increases in physical activity can be the first line of therapy in decreasing obesity and its complications⁷. Various studies show that there are nutritional factors that can modulate the immune system, including caloric intake⁸, types of fats⁹⁻¹¹, carbohydrates^{12,13} and the amount of proteins¹², which have a positive impact on

inflammatory markers, body composition modifications and biochemical markers reduction.

Nutritional intervention has been shown to be a low cost and high effectiveness intervention in weight reduction⁷. However, so far there is not enough data that allow generating recommendations on which is the best distribution of macronutrients, which would give us a guideline to implement management protocols aimed at the obese patient. The purpose of this study was to assess the effectiveness of a hypocaloric, high-protein nutrition plan on the changes in body composition, lipid profile, insulin resistance and inflammatory cytokines in patients with morbid obesity prior to bariatric surgery, in comparison with a hypocaloric, normoproteic nutrition plan.

Method

Study population

Men and women older than 18 and younger than 50 years with a body mass index (BMI) ≥ 40 kg/m², with or without comorbidity, who agreed to participate in the study and signed the informed consent letter were included. Subjects with autoimmune diseases, chronic kidney disease, pregnant women or subjects on pharmacological treatment with steroids, non-steroidal anti-inflammatory drugs or immunomodulator agents were not included. The protocol was approved by the Committees of Research, Research Ethics and Biosafety of Hospital Juárez de México with registration number HJM 0121/16.

Study design

The study group had a hypocaloric, high-protein nutrition plan (HP group: 50% carbohydrates, 25% protein and 25% lipids) and the control group had a hypocaloric, normoproteic nutrition plan (NP group: 55% carbohydrates, 15% protein and 30% lipids). Both groups received 500 calories less than usual consumption, estimated by 24-hour reminder, during a

4-month period. Both groups were comprehensively treated, which included specialized medical treatment, individual and family psychological and nutritional support and an exercise regimen.

Preoperative specialized medical examination consisted of consultation with the internist and endocrinologist doctors every 2 months, consultation with the cardiovascular specialist and preoperative assessment by the bariatric surgery department and, finally, a lung function evaluation by spirometry.

Preoperative individual psychological management was by monthly consultation, which consisted of an initial mental exam by means of a structured interview, continuing with Beck's depression inventory anxiety and depression questionnaire and followed by a therapy focused on cognitive-behavioral solutions. Preoperative and postoperative family psychological management was carried out monthly using systemic family therapy, with the family function index being used as evaluation instrument.

Adherence to the nutritional treatment was assessed monthly using the 24-hour reminder instrument and anthropometric (weight) and body composition (fat and lean mass percentage) measurements. In addition, an educational intervention was carried out, which included workshop sessions every 2 months with educational activities, focused on eating habits modification.

The preoperative exercise program consisted of aerobic exercise four to five times per week for 30 minutes at moderate intensity (60 to 70% of maximum heart rate), and was complemented with resistance exercise twice weekly with three series of 10, working different muscles with 5 to 10% of body weight.

Determination of biochemical parameters, inflammatory cytokines and body composition

A 5-mL sample of peripheral blood was taken at baseline and after 4 months of treatment for biochemical markers determination (fasting glucose, fasting insulin, total cholesterol, high-density lipoprotein [HDL] and low density-lipoprotein [LDL] cholesterol) by colorimetric enzymatic reaction with automated equipment (ADVIA 1800 analyzer, Siemens), and insulin resistance using the homeostatic model (HOMA).

A 4-mL sample of peripheral blood was taken to determine serum IL-6, IL-1 β and TNF concentrations (in pg/mL) using the capture beads method (Human

Inflammatory Cytokine Kit, BD Cytometric Bead Array) for flow cytometry (BD Accuri C6).

Body composition was determined at baseline and at end of the intervention (fat mass percentage and lean mass percentage) by bioimpedance (Tanita MC-780). The group with the high-protein diet underwent renal function testing at baseline and at the end of nutritional treatment

Statistical analysis

Normality of the groups was determined with the Kolmogorov-Smirnov test and between-group mean comparison was carried out using Student's t-test for independent samples or Mann Whitney's test. The study variables were compared before and after the nutrition treatment in the groups using paired Student's t-test or Wilcoxon test. Statistical analysis was performed with the SPSS statistical package, version 20.0, with a p-value ≤ 0.05 being regarded as a statistically significant difference.

Results

Of the 120 patients who attended the Obesity and Metabolic Disorders Clinic during the period from August 2016 to August 2017, 76 met the inclusion criteria, participated in the study and signed their consent letter. The NP group was made up of 39 patients, out of which 77% were women ($n = 30$) and 23% were men ($n = 9$), with an mean age of 35.1 ± 8.01 years. The HP group consisted of 37 patients, out of which 81.1% ($n = 30$) were women and 18.9% were men ($n = 7$), with a mean age of 35.7 ± 7.64 years. Three participants were excluded for treatment abandonment by personal decision, one in the NP group and two in the HP group; no patient experienced adverse effects deriving from the diet.

No significant differences were found at treatment baseline in terms of age, weight, BMI, percentage of fat and muscle, blood pressure, biochemical parameters and serum cytokines between study groups (Table 1).

Weight and body composition

The NP group had a baseline weight of 120.2 ± 19.26 kg and a final weight of 115.21 ± 18.99 kg ($p < 0.001$), and a baseline BMI of 45.32 ± 6.02 kg/m² and a final BMI of 43.48 ± 6.12 kg/m² ($p < 0.001$), which represented a loss of 4.1% on average during 4 months

Table 1. Study population demographic data at comprehensive treatment baseline

	NP group (n = 39)	HP group (n = 37)	p
Age (years)	35.15 ± 8.01	35.78 ± 7.64	0.7272
Weight (kg)	120.20 ± 19.26	120.17 ± 22.36	0.9964
BMI (kg/m ²)	45.32 ± 6.02	46.14 ± 6.96	0.5834
Fat (%)	54.30 ± 7.23	55.07 ± 8.42	0.3695
Muscle (%)	45.39 ± 7.40	44.14 ± 8.07	0.3581
BP (mmHg)	100.29 ± 9.65	98.39 ± 11.81	0.2625
Glucose (mg/dL)	97 ± 34.27	109 ± 59.17	0.7287
HDL cholesterol (mg/dL)	38.13 ± 8.18	40.89 ± 11.42	0.2324
LDL cholesterol (mg/dL)	115.47 ± 29.57	115.53 ± 26.89	0.9916
Total cholesterol (mg/dL)	163.28 ± 31.06	167.48 ± 32.04	0.5602
IR (HOMA)	7.03 ± 3.78	6.77 ± 5.45	0.2428
TNF (pg/mL)	4.8 ± 1.47	9.3 ± 3.41	0.9089
IL-1-β (pg/mL)	10.5 ± 2.49	8.7 ± 2.29	0.6226
IL-6 (pg/mL)	3.7 ± 0.65	2.4 ± 0.56	0.8132
Comorbidity			
1	87.18%	78.38%	0%
2	53.84%	37.83%	-
< 3	23.07%	32.43%	-
	10.25%	8.10%	-

BMI: body mass index; BP: blood pressure; HDL: high-density lipoprotein; HP: hypocaloric, high-protein regimen; IL: interleukin; IR: insulin resistance; LDL: low-density lipoprotein; NP: hypocaloric, normoproteic regimen; TNF: tumor necrosis factor.

of treatment. The percentage of baseline fat mass was $54.30 \pm 7.23\%$ and final percentage was $51.29 \pm 8.07\%$ ($p = 0.0005$), and the percentage of baseline muscle mass was $45.39 \pm 7.40\%$ and final percentage was $48.78 \pm 8.19\%$ ($p = 0.0002$), which represented a decrease of 2.58% and an increase of 2.95%, respectively, after 4 months of treatment (Fig. 1).

The HP group started with an average weight of 120.17 ± 22.36 kg and finished with 113.83 ± 21.98 kg ($p = 0.001$), and baseline BMI was 46.14 ± 6.96 kg/m² and final 43.70 ± 6.94 kg/m² ($p < 0.001$), which represents a 5.27% weight loss, without statistical difference with the NP group ($p > 0.05$). Baseline fat mass percentage in the HP group was $55.07 \pm 8.42\%$ and final was $51.82 \pm 8.37\%$ ($p = 0.0001$), and the percentage of baseline muscle mass was 44.14 ± 8.07 and final was $48.29 \pm 8.93\%$ ($p = 0.0001$), which represented a 3.25% decrease and 3.74% increase, respectively, after 4 months of treatment. There were no significant differences in fat loss and muscle mass gain between groups ($p > 0.05$) (Fig. 1).

Figure 1. Effect of normoproteic and hyperproteic hypocaloric diets in morbidly obese subjects undergoing comprehensive treatment. Total fat mass percentage (A) and total muscle mass percentage (B) of morbidly obese patients undergoing a 16-week hypocaloric, normoproteic regimen (NP group, n = 39) or a hypocaloric, high-protein regimen (HP group, n = 37). Paired Student's t-test before and after treatment; p-values are shown in the graph.

Biochemical parameters

In the NP group, fasting glucose (baseline 97.34 ± 34.27 and final 93.6 ± 18.93 mg/dL; $p = 0.5179$), HDL cholesterol (baseline 38.13 ± 8.18 and final 38.30 ± 8.35 mg/dL; $p = 0.5110$), LDL cholesterol (baseline 115.47 ± 29.57 and final 110.41 ± 29.51 mg/dL; $p = 0.2227$), total cholesterol (baseline 163.28 ± 31.06 and final 160.73 ± 33.00 mg/dL; $p = 0.4103$) and IR (baseline 7.03 ± 3.78 and final 6.50 ± 3.66 ; $p = 0.4231$) showed no significant differences with the normoproteic diet after 4 months of treatment.

In the HP group, fasting glucose (baseline 109 ± 59.17 and final 96.43 ± 22.80 mg/dL; $p = 0.0584$), HDL cholesterol (baseline 40.89 ± 11.42 and final 41.56 ± 10.33 mg/dL; $p = 0.3202$), LDL cholesterol (baseline 115.53 ± 26.89 and final 109.30 ± 27.57 mg/dL; $p = 0.2435$), total cholesterol (baseline 167.48 ± 32.04 and final 164.40 ± 27.65 mg/dL; $p = 0.6554$) and IR (6.77 ± 5.45 and final 5.82 ± 3.90 ; $p = 0.1858$) showed no significant differences after treatment. The biochemical

Table 2. Biochemical parameters before and after comprehensive treatment in the study groups

	NP group (n = 39)			HP group (n = 37)		
	Baseline	Final	p	Baseline	Final	p
Glucose mg/dL)	97 ± 34.27	93.68 ± 18.93	0.5179	109 ± 59.17	96.43 ± 22.80	0.0584
HDL (mg/dL)	38.13 ± 8.18	38.38 ± 8.35	0.5110	40.89 ± 11.42	41.56 ± 10.33	0.3202
LDL (mg/dL)	115.47 ± 29.57	110.41 ± 29.51	0.2227	115.53 ± 26.89	109.30 ± 27.57	0.2435
Cholesterol (mg/dL)	163.28 ± 31.06	160.73 ± 33.00	0.4103	167.48 ± 32.0	164 ± 27.65	0.6554
IR	7.03 ± 3.78	6.50 ± 3.66	0.4231	6.77 ± 5.45	5.82 ± 3.90	0.1858

IR: insulin resistance; HDL: high density lipoprotein; HP: hypocaloric, high-protein regimen; LDL: low density lipoprotein; NP: hypocaloric, normoproteic regimen.

Table 3. Inflammatory cytokines before and after comprehensive treatment in the study groups

	NP group (n = 39)			HP Group (n = 37)		
	Baseline	Final	p	Baseline	Final	p
TNF (pg/mL)	4.8 ± 1.47	5.1 ± 1.96	0.8125	9.3 ± 3.41	4.8 ± 1.40	0.999
IL-1 β (pg/mL)	10.5 ± 2.49	7.8 ± 2.05	0.0234	8.7 ± 2.29	6.8 ± 1.90	0.3750
IL-6 (pg/dL)	3.7 ± 0.65	3.6 ± 0.70	0.999	2.4 ± 0.56	1.6 ± 0.48	0.2031

HP: hypocaloric, high-protein regimen; IL: interleukin; NP: hypocaloric, normoproteic regimen; TNF: tumor necrosis factor.

parameters showed no differences between the NP and HP groups ($p > 0.05$) (Table 2).

Inflammatory cytokines serum concentrations

In the NP group, IL-1 β serum concentrations decreased by 25% after treatment (baseline 10.5 ± 2.49 and final 7.8 ± 2.05 pg/mL; $p = 0.0234$), while TNF (baseline 4.8 ± 1.47 and final 5.1 ± 1.96 pg/mL; $p = 0.8125$) and IL-6 (baseline 3.7 ± 0.65 and final 3.6 ± 0.70 pg/mL; $p = 0.9999$) showed no statistically significant changes after 4 months of treatment. In the HP group, IL-1 β (baseline 8.7 ± 2.29 and final 6.8 ± 1.90 pg/mL; $p = 0.3750$), TNF (baseline 9.3 ± 3.41 and final 4.8 ± 1.40 pg/mL; $p = 0.9999$) and IL-6 (baseline 2.4 ± 0.56 and final 1.6 ± 0.48 pg/mL; $p = 0.2031$) serum concentrations had no significant changes after treatment with the high-protein diet. There were no significant changes between groups (Table 3).

Discussion

Hypocaloric diets with mild to moderate reduction of calories have an impact on weight reduction in patients with obesity. Various studies¹⁴⁻¹⁷ have reported

a weight reduction of between 5 and 10%, with decreased body fat and with a slight increase or preservation of muscle mass and an improvement in biochemical parameters in overweight or obese patients. We found a reduction of 4.1 and 5.2% in weight after 4 months of treatment in patients with morbid obesity, which is consistent with previous reports¹⁴⁻¹⁷.

Sacks et al.¹⁴ assessed four types of hypocaloric diets, two of them hyperproteic, in overweight or obese patients (BMI of 25 to 40 kg/m²) and without comorbidity, for 6 months, and found a similar weight reduction in all evaluated groups, with a decreased lipid profile and better insulin sensitivity regardless of macronutrient distribution. Our study also found a weight reduction regardless of protein distribution in the diet, without an improvement in lipid profile and insulin resistance being found; these differences might be due to the degree of obesity (morbid obesity) and to a higher insulin resistance in our patients with regard to the population studied by Sacks et al.¹⁴, in addition to the presence of comorbidity and a shorter intervention time (4 months).

Salas-Salvado et al.¹⁵ studied a similar population to that of our study (morbidly obese subjects), but with no comorbidity, with a strict hypocaloric (800 total calories) and high-protein diet with 10% more of

protein content, and found a reduction of biochemical parameters and inflammatory cytokines; our study found no differences in these parameters, probably because of the different study conditions and the heterogeneity of socio-economic, cultural and geographical characteristics.

Regarding inflammatory markers, in our study, patients showed a trend to a decrease, which was significant for serum IL-1 β concentrations for patients in the NP group. TNF, IL-1 β and IL-6 are known to be locally overexpressed in adipose tissue, sometimes being able to reach a systemic increase; therefore, we evaluated cytokines systemically, as a reflection of what it could be happening in the adipose tissue; however, very low cytokine values were detected, very close to the minimum level of detection of the used method, which might not be reflecting what occurs in the fatty tissue of morbidly obese subjects. On the other hand, serum cytokine concentrations are influenced by other conditions, such as diabetes, hyperuricemia and dyslipidemia, among others. In addition, as long as there are pro-inflammatory mediators, regulatory mechanisms are activated, such the release of IL-10 and Transforming Growth Factor (TGF)- β , which have anti-inflammatory properties, and release of TNF soluble receptor and IL-1 β antagonistic receptor, which neutralize the effects of their respective cytokines¹⁸.

Although the studies by Salas-Salvado et al.¹⁵ and Bruun et al.¹⁹ showed differences in serum cytokine concentrations, this apparent discrepancy with our study could be explained by the presence of comorbidity, the degree of obesity and the strict treatment regimen of the study patients. Future studies will be necessary to assess our treatment, with a longer intervention time when it comes to morbidly obese subjects.

Our findings add to the results found by other authors: the obese patient, by continuing with this condition, keeps presenting the inductors to trigger a low grade chronic inflammation, and this is more marked in morbidly obese subjects because they have a larger amount of fat mass. Finally, adherence to the dietary plan is the most decisive factor to achieve a significant weight loss. Therefore, these diets have the advantage of individually adapting respecting personal preferences, habits, culture and economic availability, and with higher likelihood of success in the long term.

Conclusion

The hypocaloric, high-protein diet shows no advantages in weight and body fat reduction or muscle mass

gain in comparison with the hypocaloric, normoproteic diet in patients with morbid obesity undergoing comprehensive treatment. The hypocaloric diet in patients with morbid obesity, regardless of macronutrient distribution, achieves weight reduction and improves body composition.

Conflict of interests

The authors declare that they have no conflicts of interests.

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