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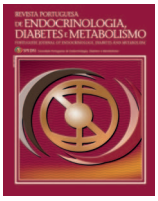

Artigo Original

Blood Pressure and Lipid Profiles Improvement in Patients with Obesity After Lifestyle Intervention-Induced Weight Loss

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INFORMAÇÃO SOBRE O ARTIGO

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A B S T R A C T

Introduction: Obesity, as a marker of metabolic syndrome, is frequently associated with hypertension and dyslipidemia, which improve with weight loss. The aim of this study was to verify the relationship between weight loss and blood pressure and lipid profiles improvement in patients followed in our project named "TObe", in which obese patients lose weight through an intensive medical intervention, involving Endocrinology and Nutrition.
Methods: Retrospective study with 213 patients with obesity, with twelve months of follow up in the "TObe" project and weight, body mass index (BMI), blood pressure and lipid profile assessment at 0 and 12 months. Data was collected from clinical appointments. Statistical analysis was performed with SPSSvs25, with a significance level of 0.05.
Results: One hundred sixty four (77%) were female and the mean age was 45.98±12.69 years. Baseline BMI was 39.55 (P25: 36.62; P75: 43.29) kg/m². Patients with hypertension (n=35), dyslipidemia (n=43) or both (n=64) were under medication and controlled. After twelve months, there was a weight reduction of 4.70 (1.40 – 9.35) kg, $p<0.001$, BMI reduction of 2.00 (0.60 – 3.98) kg/m², $p<0.001$, a systolic blood pressure (SBP) reduction of 3.53 ± 15.40 mmHg, $p=0.002$, a diastolic blood pressure (DBP) decrease of 1.71 ± 9.66 mmHg, $p=0.010$, a total cholesterol (Total-C) increase of 6.00 (11.00 – 24.00) mg/dL, $p=0.012$, a high density lipoprotein cholesterol (HDL-C) increase of 4.00 (0.00 - 10.00) mg/dL, $p<0.001$, and apolipoprotein A1 (Apo-A1) increase of 5.47 ± 19.09 mg/dL, $p=0.002$. BMI variation correlated positively with SBP and DBP variation (r=0.168; $p=0.024$ and r=0.286; $p<0.001$, respectively) and negatively with HDL-C variation (r=-0.160; $p=0.040$).
Conclusion: Clinically significant weight loss through lifestyle intervention allowed a reduction of SBP and DBP, and an increase in HDL-C, improving blood pressure and lipid profile, which may reduce the cardiovascular disease risk of patients with obesity.

Palavras-chave:
Estilo de Vida;
Metabolismo dos Lípidos;
Obesidade;
Perda de Peso;
Pressão Arterial.

Melhoria dos Perfis Tensional e Lipídico em Doentes com Obesidade Após Perda Ponderal Induzida por Medidas de Estilo de Vida

R E S U M O

Introdução: A obesidade, marcador de sindrome metabólica, associa-se frequentemente a hipertensão arterial e dislipidemia, que melhoram com a perda ponderal. Este estudo visa a relação entre perda ponderal e melhoria dos perfis tensional e lipídico em doentes seguidos no nosso projecto "TObe", no qual doentes com obesidade perdem peso através de uma intervenção médica intensiva por Endocrinologia e Nutrição.
Métodos: Estudo retrospectivo com 213 doentes com obesidade, com 12 meses de seguimento no projecto "TObe" e avaliação do peso, índice de massa corporal (IMC), pressão arterial e perfil lipí-

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dico aos 0 e 12 meses. Os dados foram colhidos do processo clínico e a análise estatística realizada através do programa SPSSvs25, com nível de significância de 0.05.

Resultados: Cento e sessenta e quatro eram do sexo feminino (77%) e a média de idades era de 45,98±12,69 anos. O IMC inicial era de 39,55 (P25: 36,62; P75: 43,29) kg/m². Doentes com hipertensão arterial (n=35), dislipidemia (n=43) ou ambas (n=64) encontravam-se medicados e controlados. Ao fim de 12 meses, verificou-se redução do peso de 4,70 (1,40 – 9,35) kg, $p<0,001$, do IMC de 2,00 (0,60 – 3,98) kg/m², $p<0,001$, da pressão arterial sistólica (PAS) de 3,53 ± 15,40 mmHg, $p=0,002$, da pressão arterial diastólica (PAD) de 1,71 ± 9,66 mmHg, $p=0,010$, aumento do colesterol total (C-Total) de 6,00 (11,00 – 24,00) mg/dL, $p=0,012$, aumento do colesterol de lipoproteinas de alta densidade (C-HDL) de 4,00 (0,00 – 10,00) mg/dL, $p<0,001$, e aumento da apolipoproteina A1 (Apo-A1) de 5,47 ± 19,09 mg/dL, $p=0,002$. A variação do IMC correlacionou-se positivamente com a variação da PAS e da PAD (r=0,168; $p=0,024$ e r=0,286; $p<0.001$, respectivamente) e negativamente com a variação do C-HDL (r=-0,160; $p=0,040$).

Conclusão: Uma perda de peso clinicamente significativa através de medidas de estilo de vida permitiu reduzir a PAS e a PAD, e aumentar o C-HDL, melhorando o perfil tensional e lipídico, o que pode reduzir o risco de doença cardiovascular de doentes com obesidade.

Introdution

Obesity is a major public health problem, with more than one third of the world population classified as overweight or obese. It is estimated that obesity prevalence in 2030 will reach 57.8% if the current trend continues.[1,2]

Chronic positive energy balance contributes to adipose tissue accumulation, which defines obesity.[1,3,4] But visceral fat is not only a depot for triglycerides, it is also an endocrine organ responsible for adipocytokines secretion and chronic low grade inflammation that ultimately leads to insulin resistance and metabolic syndrome. Therefore obesity is an important risk factor for metabolic and cardiovascular diseases, such as hypertension, dyslipidemia, type 2 diabetes, chronic kidney disease, ischemic heart disease, stroke, dementia, several malignancies, nonalcoholic fatty liver disease, asthma and obstructive sleep apnea.[3-8]

Hypertension world prevalence in 2015 was 30%-45% (20% in females and 24% in males).[6,7,9,10] In the USA, half of the patients with hypertension are obese and, on the other hand, one-third of the obese population has hypertension, compared to less than one-fifth of normal-weight individuals.[7,10] Small increments in blood pressure are associated with increased risk of cardiovascular disease, which aggravates if associated with obesity. On the other hand, obesity is a risk factor for hypertension, being responsible for 40% to 78% of the cases.[11-13] The pathophysiological mechanisms by which obesity promotes the development of hypertension are multiple and include altered concentrations of adipokines, inflammation, insulin resistance, oxidative stress, activation of sympathetic nervous system, altered hemodynamics, renal dysfunction, endothelial dysfunction, impaired sodium homeostasis and activation of renin-angiotensin-aldosterone system.[7,13-15] This obesity-related hypertension has important therapeutic implications: weight loss results in blood pressure reduction and it is advised as the first therapeutic approach.[6,7,9,12,13,16,17]

Obesity is also associated with an atherogenic lipid profile, leading to a further increased cardiovascular disease risk. The link between obesity and this atherogenic dyslipidemia may be the development of insulin resistance, which increases hepatic lipase activity, hepatic flow of dietary fatty acids, intravascular lipolysis, resistance of the adipose tissue to the anti-lipolytic effect of insulin and formation of smaller low density lipoprotein particle size.[18-20] Lipid profile associated with obesity is mainly characterized by increased triglycerides and decreased high density lipoprotein cholesterol levels.[17,19,21-24] Consequently, cardiovascular risk reduction guidelines recognize the importance of lifestyle modifications with weight loss to improve lipid profile and other comorbidities, decreasing morbidity and mortality ultimately.[17,25,26]

The aim of this study was to analyze blood pressure profile and lipid profile variations after weight loss through medical treatment and to determine the correlation between those differences and weight reduction.

Material and Methods

It was performed a retrospective, observational and analytical study with patients with obesity referred by general practitioners to our center, a tertiary and academic hospital, between January 2016 and July 2018. These patients were submitted to an intensive medical treatment program for obesity called "TObe Project – medical Treatment of Obesity".

This project involved a multidisciplinary team of Endocrinologists and Nutritionists that elaborated a follow up plan of one year. Endocrinology appointments were at 0, 2, 6 and 12 months. Nutrition appointments took place 2 weeks after the first Endocrinology appointment, 1 month after and scheduled thereafter so that there were 2 appointments between each of the Endocrinology's. The purpose of the first Endocrinology appointment was to collect the clinical history with emphasis in obesity evolution, risk factors and comorbidities, to execute physical examination to characterize obesity and search for endocrinopathies features, to assess body composition through bioelectrical impedance analysis (InBody®), to request blood and urine analysis to exclude obesity endocrine secondary causes and to evaluate risk factors and comorbidities such as diabetes or dyslipidemia. Each patient received a manual with information about the disease, its management and tables which could be filled with treatment adherence and its results. After this first appointment, the patient was encouraged to start nutritional and physical activity improvements. In Nutrition's first appointment it was again evaluated body composition through bioelectrical impedance analysis (Tanita®), collected nutritional history with the most frequently consumed foods in a day recall method, established the weight goal and a personalized dietary plan based in calorie restriction was provided. The diagnosis of an endocrinopathy was an exclusion criteria of the project. Patients without a secondary cause for obesity engaged nutritional and physical activity modifications, following a calorie restricted nutritional plan with an energy deficit of 500 Kcal and practicing 150 minutes of aerobic activity per week, namely 30 minutes walking, 5 times per week. If weight loss at 6 months was inferior to 5%, pharmacological and/or surgical treatment was considered. Patients under pharmacological treatment or referred to bariatric

surgery were excluded. At 12 months, the patients were clinically and biochemically reevaluated.

Nutritional status was evaluated through weight and body mass index (BMI) (weight (kg)/height² (m)), blood pressure profile by systolic blood pressure (SBP) and diastolic blood pressure (DBP) and lipid profile through total cholesterol (Total-C), low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C), triglycerides (TG), apolipoprotein B (Apo-B) and apolipoprotein A1 (Apo-A1).

These data were collected at 0 and 12 months and analyzed using the software IBM SPSS® version 25.0, with statistical significance set at p <0.05. For continuous quantitative variables, the existence of normal distribution was tested through histogram observation and kurtosis and skewness analysis. To describe variables, we used central tendency measures (mean and median) and dispersion measures (standard-deviation and percentiles 25-75) for quantitative variables and absolute numbers and percentages for qualitative variables. The Wilcoxon test was used to compare continuous variables with non-normal distribution within groups. The correlation between variables was determined with Spearman's correlation method.

The study was conducted in accordance with the amended Declaration of Helsinki and informed consent was collected from all the participants at the first appointment. It was approved by the ethical committee of Hospital de Braga at 13 of June of 2019 (Ref[a] 90_2019).

Results

From the 372 patients evaluated in this project in the referred time frame, 47 initiated pharmacological therapy, 14 were referred to bariatric surgery and 213 (57%) completed 12 months of our intensive lifestyle intervention program. Table 1 displays the characteristics of the population at baseline. At twelve months of follow up and nutritional and physical activity optimization, it was verified a significant reduction of weight, BMI, SBP and DBP, and an increase in Total-C, HDL-C and Apo-A1 (Table 2).

Table 1. Characteristics of the population of the study at baseline.

	Baseline
Feminine gender (n; %)	164; 77.00
Masculine gender (n; %)	49; 23.00
Age (n; m±SD years)	213; 45.98 ± 12.69
With HT (n; %)	35; 16.43
With dyslipidemia (n; %)	43; 20.19
With HT and dyslipidemia (n; %)	64; 30.05
Without HT or dyslipidemia (n; %)	71; 33.33

HT=hypertension; m=mean; SD=standard deviation

Patients lost a median of 4.90 (P25: 1.41; P75: 9.60) % of initial body weight, which represents a median of 4.70 (P25: 1.40; P75: 9.35) kg and a median reduction of BMI of 2.00 (P25: 0.60; P75: 3.98) kg/m² at twelve months. SBP decreased 3.53 ± 15.40 mmHg, DBP decreased 1.71 ± 9.66 mmHg, Total-C increased 6.00 (P25: 11.00; P75: 24.00) mg/dL, HDL-C increased 4.00 (P25: 0.00; P75: 10.00) mg/dL and Apo-A1 increased 5.47 ± 19.09 mg/dL.

It was detected a positive correlation between BMI variation and SBP variation (rho (181) 0.168; p=0.024) and DBP variation (rho (181) 0.286; p<0.001). A negative correlation between BMI variation and HDL-C variation throughout the twelve months was identified (rho (165) -0.160; p=0.040) (Table 3).

Table 2. Weight, body mass index, blood pressure profile and lipid profile at baseline and at twelve months of the intensive medical treatment program for obesity.

	Baseline	At twelve months	*p*
Weight (n; md(P25--P75)/n; m±SD kg)	213; 101.20 (92.50 – 112.60)	213; 97.77 ± 19.45	<0.001
BMI (n; md(P25--P75)/n; m±SD kg/m²)	213; 39.55 (36.62 – 43.29)	213; 37.81 ± 6.52	<0.001
SBP (n; md(P25-P75)/ n; m±SD mmHg)	188; 136.00 (125.00 – 147.00)	188; 133.27 ± 13.98	0.002
DBP (n; m±SD/n; md(P25-P75) mmHg)	187; 80.76 ± 10.68	187; 81.00 (73.00 – 87.00)	0.010
Total-C (n; md(P25--P75)/n; m±SD mg/dL)	166; 181.50 (161.75 - 210.00)	166; 190.32 ± 35.56	0.012
LDL-C (n; md(P25--P75)/n; m±SD mg/dL)	129; 113.50 (97.25 - 135.75)	129; 116.93 ± 31.97	0.156
HDL-C (n; md(P25-P75) mg/dL)	167; 49.00 (40.00 - 57.00)	167; 53.00 (45.00 – 62.00)	<0.001
TG (n; md(P25-P75) mg/dL)	169; 113.00 (86.50 – 151.00)	169; 114.00 (78.50 – 167.50)	0.744
Apo-B (n; md(P25--P75)/n; m±SD mg/dL)	134; 91.00 (78.00 – 109.00)	134; 92.82 ± 21.76	0.341
Apo-A1 (n; md(P25--P75) mg/dL)	133; 146.00 (128.50 – 163.00)	133; 151.00 (135.00 – 166.00)	0.002

BMI=body mass index; SBP=systolic blood pressure; DBP=diastolic blood pressure; Total-C=total cholesterol; LDL-C=low density lipoprotein cholesterol; HDL-C=high density lipoprotein cholesterol; TG=Triglycerides; Apo-B=apolipoprotein B; Apo-A1=apolipoprotein A1; m=mean; SD=standard deviation; md=median; P25=25th percentile; P75=75th percentile

Table 3. Correlation between body mass index variation and blood pressure and lipid profiles variation at the twelve months of the intensive medical treatment program for obesity.

	r	*p*
SBP variation (mmHg)	0.168	0.024
DBP variation (mmHg)	0.286	<0.001
Total-C variation (mg/dL)	-0.087	0.270
LDL-C variation (mg/dL)	-0.128	0.155
HDL-C variation (mg/dL)	-0.160	0.040
TG variation (mg/dL)	0.041	0.603
Apo-B variation (mg/dL)	0.083	0.341
Apo-A1 variation (mg/dL)	-0.033	0.710

SBP=systolic blood pressure; DBP=diastolic blood pressure; Total-C=total cholesterol; LDL-C=low density lipoprotein cholesterol; HDL-C=high density lipoprotein cholesterol; TG=triglycerides; Apo-B=apolipoprotein B; Apo-A1=apolipoprotein A1

In a subanalysis of the population with HT, it was verified a reduction of DBP of 2.24 ± 9.6 mmHg (p=0.032) at twelve months. There was a BMI reduction of 3.86 (P25: 1.4; P75: 37.2) kg/m² (p<0.001) that correlated with DBP reduction (rho (86) 0.304; p=0.004). In patients with dyslipidemia, HDL-C increased 4.00 (P25: -2.00; P75: 10.00) mg/dL (p<0.001). Although there was a reduction in BMI of 2.94 (P25: 1.4; P75: 34.9) kg/m² (p<0.001) in this group, there was no correlation with the verified HDL-C increase (rho (87) -0.169; p=0.118).

Discussion

The intensive medical treatment program for obesity "TObe Project – medical Treatment of Obesity" allowed a clinically significant weight loss at the twelve months period, with a median of weight loss of 4.90 (1.41 – 9.60) % of initial weight, corresponding to 4.70 (1.40 – 9.35) kg of weight and 2.00 (0.60 – 3.98) kg/m² of BMI.

Regarding the blood pressure profile, it was verified a reduction of both SBP and DBP at the one year of the project, but SBP suffered a greater reduction than DBP. In the population with HT, DBP suffered a reduction and correlated with weight loss.

This is in accordance with previous studies.[7,10,12,27,28] The look AHEAD study, a similar 12 months intensive lifestyle intervention for the treatment of obesity, with 5154 patients, showed comparable results: a weight reduction of 4.8 ± 7.6 kg, a mean SBP reduction of 4.76 mmHg and a mean DBP reduction of 2.40 mmHg.[10]

The positive correlation between BMI and blood pressure profile is well documented. Weight loss induces proportional reductions of SBP and DBP. Consequently, the extent of the improvement of blood pressure profile depends on the magnitude of weight loss, which is a result of the obesity treatment strategy adopted and its adherence.[10,12,17] Concerning lifestyle modifications, a reduction of at least 1 kg/m² of BMI at one year was inversely associated with the presence of uncontrolled hypertension,[12] patients losing more than 5% of initial weight had a greater improvement in blood pressure and a weight loss of 4 kg reduces systolic and diastolic by 4.5 and 3.2 mmHg, respectively.[16] In this study it was observed a lower degree of reduction of SBP and DBP for a superior median weight reduction of 4.70 kg, possibly related with the mixed population, that englobes patients with and without hypertension. Nevertheless, this association is observed in patients with and without hypertension, such as the population of this study.[10] This fact led to the reinforcement of the importance of weight loss as the first line of the hypertension treatment[9] and to the recommendation of maintaining a BMI inferior to 25 kg/m² for hypertension primary prevention.[13]

The mechanism under this weight loss effect in SBP and DBP seems to be related with the reduction of adipose tissue mass, which disrupts the pathophysiological pathways that lead to metabolic syndrome.[7,10] An explanation for the highest decrease in SBP than in DBP is yet to find. Concerning lipid profile, it was detected an elevation in Total-C, HDL-C and Apo-A1, twelve months after the beginning of the follow-up. However, only HDL-C variation correlated negatively with BMI difference over one year. In the group of patients with dyslipidemia, HDL-C suffered an elevation, though it did not correlate with BMI reduction.

In accordance with these results, it is considered that weight loss mediated by lifestyle modification results in HDL-C elevation.[19,22,23,29] Each kilogram of weight loss increases HDL-C by 0.009 mmol/L.[22]

Several studies confirmed that lifestyle modifications were responsible for HDL-C and Apo-A1 increase as the BMI decreased.[22,30] Nevertheless, there are differences in the HDL-C variation depending on the weight loss approach. In one study, although HDL-C increased with weight loss induced by caloric restriction and by physical exercise, Apo-A1 only increased in groups submitted exclusively to exercise.[30] Other authors verified that weight loss induced by aerobic exercise was more effective at increasing HDL-C than diet.[31-33] Diet composition is also an important determinant of HDL metabolism, with low-fat diets possibly leading to a HDL-C decrease, though without compromise of HDL function.[18,22,31,34] Once the patients of the present study had probably dissimilar diet and exercise adherence, it is not possible to detect these differences, but this fact, besides sample size, can explain why it was not detected a correlation between BMI and Apo-A1 variations, despite Apo-A1 increase.

The reasons why weight loss by lifestyle modification increases HDL-C and Apo-A1 are: diet induced triglycerides reduction leads to a decrease in the exchange of very low density lipoprotein triglyceride for esterified cholesterol in the HDL particle core, which increases HDL-C particle size; exercise increases the number of normal HDL-C particles; weight loss per se reduces HDL-C and Apo-A1 catabolism.[22,29,30,34]

Total-C variations with weight loss are not uniform, depending on the percentage of weight loss and timing of evaluation.[35] Schwartz *et al*[30] found that Total-C underwent a reduction after a 13 kg weight loss induced by a 3 months calorie-restrictive diet. Leenen et al showed that a weight loss of approximately 11 kg in 26 weeks was responsible for a Total-C reduction.[29] This study detected an increase in Total-C at the one year of weight loss, which might have been related with the lower weight loss verified but mostly with the timing of the evaluation. During the active weight loss phase it is observed an initial Total-C reduction, followed by a late increase that results from mobilization of adipose cholesterol reserves. This effect is more pronounced 6 months after the initiation of major weight loss, but it ceases after weight stabilization.[35] These facts, along with small sample size and the lack of data on the weight loss phase in which each patient was, could explain why Total-C did not correlate with BMI.

It is important to note that the obtained variations were within normal range, which could have resulted from the presence of metabolically healthy obese patients in the study population in unknown number, which could have diluted the benefits of weight loss. In these individuals, weight loss showed slightly improves in lipid profile, but within normal ranges.[18]

Regarding the limitations of this study, it is important to highlight: a small and non-calculated sample size; selection bias, with patients from one specific geographic area of our country, referred by general physicians to our hospital; no group control; missing values for some variables at zero and at twelve month evaluation; no method apart patient report to control the adherence to food plan and physical activity advised in the "TObe" program; no data concerning diet composition or type of physical exercise adopted by each patient; no data on whether the patients are in the active or passive weight loss phase; the population analyzed was composed by patients with and without hypertension/dyslipidemia; no recording if there was initiation of anti-HT or anti-dyslipidemia therapy in patients diagnosed during the project or alterations of these medications in patients previously diagnosed; no information about how many patients were metabolically healthy obese; the cardiovascular risk score was not evaluated at zero and twelve months once only 36 patients fulfilled the criteria for its calculation.

Conclusion

Clinical significant weight loss through lifestyle intervention in patients with obesity allowed an improvement in blood pressure profile and lipid profile at the twelve months.

The observed decrease in both SBP and DBP and the increase in HDL-C at one year of weight loss is responsible for a reduction of cardiovascular disease risk. For this reason, diet and physical activity induced weight loss is the first recommendation for

obesity, hypertension and dyslipidemia treatment, with important implications in morbidity and mortality of patients with obesity.

Clinicians must be aware of the possible late rise of Total-C with major and prolonged weight loss. This phenomenon ceases as the patients reach weight stability, without need of pharmacologic intervention.

Responsabilidades Éticas

Conflitos de Interesse: Os autores declaram a inexistência de conflitos de interesse na realização do presente trabalho.
Fontes de Financiamento: Não existiram fontes externas de financiamento para a realização deste artigo.
Confidencialidade dos Dados: Os autores declaram ter seguido os protocolos da sua instituição acerca da publicação dos dados de doentes.
Proteção de Pessoas e Animais: Os autores declaram que os procedimentos seguidos estavam de acordo com os regulamentos estabelecidos pelos responsáveis da Comissão de Investigação Clínica e Ética e de acordo com a Declaração de Helsínquia da Associação Médica Mundial.
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Ethical Disclosures

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Confidentiality of Data: The authors declare that they have followed the protocols of their work center on the publication of data from patients.
Protection of Human and Animal Subjects: The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).
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