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Full Length Research Paper

From the Metabolic Syndrome to a Normal Status

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ABSTRACT

The aim of this study was to determine the effectiveness of a standard physical exercise protocol in terms of returning patients with signs of metabolic syndrome (MS) to a normal metabolic status. Patients showing signs of MS (45 adult females and 35 adult males, 20-50 years old) without any disability applied a combined treatment consisting of a hypocaloric diet (<2,500 kcal/day) and a program of physical exercise using a fitness bicycle. Prior to the exercise program and without any treatment, 23% showed a healthy lipid metabolism, 28% presented high LDL and low HDL, 14% showed an atherosclerotic index and LDL/HDL >3.5 for males and >2.5 for females, 5% exhibited values predictive of coronary risk (CHOL/HDL >5), and the remaining 30% had dyslipid syndrome types 2-4, with high cholesterol and triglyceride levels. After 3 months of standard physical effort, 64 patients (80%) exhibited normalized biochemical results and a normal health status. Of the patients who failed to respond to this standard physical exercise regimen, 16 (20%) might require drug-based treatment in addition to exercise and dieting. The diet/exercise combination presented in this study was effective for treatment of MS.

Keywords: Metabolic Syndrome, Qualitative Index HOMA, Waist-to-hip Ratio, Metabolic Equivalents, Body Mass Index.

INTRODUCTION

In all developed and some developing countries, the numbers of obese individuals diagnosed with insulin resistance (IR) have increased rapidly to >40% in recent years. IR is a patho-physiological state characterized by a subnormal physiological response to insulin concentrations. This state precedes the development of metabolic syndrome (MS). Insulin resistance is often considered a pre-diabetic condition [1]. However, studies have shown that the progression of pre-diabetes to diabetes can be prevented by a combination of weight loss and increased physical activity [2]. Although IR can be determined using a variety of methods, these are difficult to apply in everyday clinical practice; thus, it is easier to monitor other parameters of MS.

MS consists of multiple, interrelated risk factors of metabolic origin that appear to promote the development of atherosclerotic cardiovascular disease (ASCVD) and which are strongly associated with type 2 diabetes mellitus or the risk for this condition. The metabolic risk factors consist of atherogenic dyslipidemia (elevated triglycerides and apolipoprotein B, small LDL particles, low HDL cholesterol [HDL-C] concentrations), elevated blood pressure, elevated plasma glucose, a prothrombotic state, and a proinflammatory state [3]. Over the past decade, various criteria for the diagnosis of MS have been proposed. In 2001, the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) proposed a simple set of diagnostic criteria based on common clinical measures, including waist circumference, triglycerides, HDL-C, blood pressure, and fasting glucose level. The presence of defined abnormality in any three of these five measures constitutes a diagnosis of MS. The ATP III criteria for MS have been widely used in both clinical practice and epidemiological studies.

The World Health Organization (WHO) has slightly different criteria for metabolic syndrome, including high insulin levels, elevated fasting blood glucose, or elevated

post-meal glucose alone with at least two of the following criteria: abdominal obesity (defined as a waist-to-hip ratio greater than 0.9), a body mass index of ≥30 kg/m2 or a waist measurement >37 inches, lipid l panel showing a triglyceride level ≥150 mg/dl or an HDL cholesterol >35 mg/dl, blood pressure ≥ 140/90 (or receiving treatment for high blood pressure) [4].

SCOPE

The aim of this study was to determine the effectiveness of a standard physical exercise protocol that would return patients with clinical and paraclinical signs of MS to a normal metabolic status without any specific treatment for dyslipid syndromes. The patients were randomly selected outpatients who were aiming to obtain a normal body mass index (BMI), waist-to-hip ratio (WHR), and normal levels of lipid parameters.

METHODS

Patients who presented at general practitioners with clinical and paraclinical signs of MS, had no other disability and had not received specialized treatment for this syndrome, and who, based on the advice of their physicians, presented with medical letters to the Department of Endocrinology of the Ambulatory County Hospital Targu Jiu, were considered for inclusion in this study. The patients had been advised by a specialist physician to volunteer for combined treatment consisting of a hypocaloric diet (<2,500 kcal/day) and a program of physical exercise on a fitness bicycle. The fitness bicycle used (Pegas-Pedalux 3, Factory City Brasov, Romania) allowed the investigator to record the intensity of physical effort. During the physical exercise, the average heart rate (HR) was 110-136 bpm. Some patients with advanced obesity (30%) did not agree to participate in the standard exercise regimen; they were not included in the study.

In this experiment were following biochemical parameters with signs of MS:

- Blood glucose >120 mg/dl, as a sign of insulin resistance in non-diabetic obese persons.
- HOMA Qualitative Index (the relationship between liver fat and fasting serum insulin concentrations) >2, indicating liver fat and insulin resistance. Liver fat was measured by tomography [5].
- Liver enzymes: aspartate aminotransferase (AST), alanine aminotransferase (ALT) gamma glutamyl transpeptidase (GGT), alkaline phosphatase (ALP) levels 20-40 units above normal as a sign of fatty liver, and an AST/ALT ratio <1 in non-alcoholic fatty liver and serum cholinesterase > 9000 U/L, as signs of liver dysfunction [6].
- Elevated uric acid [7], interleukin-18, C-reactive protein [8], and adipokines [9, 10, 11], and a lipid profile characterized by elevated plasma cholesterol and triglycerides (TGs), increases in cholesterol only (pure or isolated hypercholesterolemia), increases in TGs only (pure or isolated hypertriglyceridemia or a low high-density lipoprotein level, which contributes to the development of atherosclerosis) [12].

Formerly, ideal weight (IW) was calculated using the Lorenz formula, which was developed in 1929 and exists as two versions, one for males and the other for females. Body weight must be known before its application: For females, IW (kg) = H (cm) – 100 – [H (cm) – 150] / 2; for males, IW (kg) = H (cm) – 100 – [H (cm) – 150] / 4. More recently, ideal weight has been recommended to be calculated as a function of height in centimeters (H) and age (A). Using the new formula (Bull's algorithm, also known as the EMBED Equation 3 method): for males, IW = 50 + 0.75(H – 150) + [(A– 20) / 4], and for females, IW 0.9.

The schedule of physical exercise was accompanied by a daily dietary energy intake reduction of 400 kcal (Table 1 below).

Note: Inclusion criteria of MS, based on clinical signs of metabolic risk factors can be prevented if the persons do not register:

- Obesity with a BMI >26 for females and >30 for males, calculated as [weight (kg)]/[height (m2)].
- Waist circumference >90 cm for females and >85 cm for males, measured half-way between the xyphoide appendix and the navel.
- Waist-to-hip ratio (WHR) >0.95 for females and >0.85 for males, calculated as waist circumference/hip circumference (measured between the two trochanters).

The target heart rate (THR), which determined the intensity of the exercise, was generally recommended based on the resting heart rate (HR at rest) and the heart rate during physical effort (HRP), which had to be 60–80% of the values characteristic of aerobic metabolism. The THR ranges were calculated using the Karvonen approach, as follows: THR = (HRP × 50%) + HRR. For a value of 60% of aerobic metabolism, the THR is ((180 − 70) ×0.60) + 70 = 136 bpm [13]. Metabolic equivalents (METs) are useful when walking exercises are recommended by physicians. By definition, a MET is the energy or level of oxygen used at rest (1 MET = 3.5 VO2 mL/kg/min). However, recent studies indicate that the average resting MET level in subjects with coronary heart disease is 23–36% less than the standard value of 3.5 mL/kg/min [14]. Patients showing signs of MS (45 females and 35 males, aged 20-50 years), were assessed using a biochemical analyzer (Hitachi 912,

Table 1. Calories per day with respect to age and weight with normal physical activity

Male, age	Cal/kg	Calories	Female, age	Cal/kg	Calories
25	46	3200	25	40	2500
45	40	3000	45	39	2200
65	38.5	2550	65	38	1800

Table 2. Energy expenditure during aerobic–anaerobic exercises performed by athletes on the fitness bicycle

No., Sex	Mean age	Mean weight (kg)	V_{O2}/min	Heart rate (BPM)	Respiratory rate/min	Index O_2/ pulse	Respiratory eq.	kcal / min	Watts
15 Males	29	65	3.1	120-130	35	18.7	21.4	13.6	212
10 Males	25	63	2.7	144-150	40	17.1	24.2	12.6	196
20 Males	17	61	2.2	140-150	45	14.1	30.3	10.4	179
12 Females	23	52	2.1	140-150	50	13.3	32.5	9.7	147
18 Females	20	50	2.0	150-160	60	9.5	38.1	8.3	122
5 Females	17	48	1.9	150-160	60	8.8	38.8	7.8	114

Legend: V_{O2} = oxygen consumption, L/min, Index oxygen pulse = V_{O2} 2/heart beat (>18.7 for ideal performance), Respiratory equivalent = expiratory volume/ V_{O2} (≤28±3 for ideal performance), Expiratory volume = current volume × heart rate., Current volume = 37% of body weight (kg).

Roche Diagnostics USA); the principal biochemical parameters for lipid metabolism: total cholesterol (CHOL), triglycerides (TGs), HDL-CO, and LDL- CO were evaluated. This assessment was performed both before and after the physical exercise /diet treatment. The total energy expended, Q (kcal), was calculated by the theoretical equation Q (kcal) = oxygen consumption (VO2) □ isocalorific coefficient (4.83 kcal) = [(5.8 □ W) + (151 +10.1 □ P) □ 4.83], where W represents the patient's weight (kg) and P is the power of pedaling on the stationary bicycle (Watts/sec) (15). The lipid energetic consumption, QL (kcal) was estimated using the equation Q1 = VO2 – [17.35 □ 4.83 □ total muscle mass of body (MSC)]. For efficient exercise, lipid energy consumption exceeds 7 kcal/min, when MSC = 20% from W. The energy consumption per minute for jogging was calculated as E (kcal) = 0.8 □ v + 0.5, where v is the jogging speed (3.5-6.5 km/h). In a parallel study, a control group consisting of 75 young healthy individuals (45 males and 30 females, mean age 21.8 years) who were members of a sporting club (Tennis Club of Bucharest) were assessed using the same type of ergonomic bicycle. The maximum effort capacity (VO2max) and calorie consumption (Q) of the healthy individuals, in comparison with the patients in the cohort study, were determined using an identical physical effort schedule (Table 2).

RESULTS

Before participating in the standard exercise program, based solely on the biochemical tests, 23% of the patients showed a healthy lipid metabolism, 28% presented high LDL (mean 189 mg/dL, SD 2.13) and low HDL (mean 30 mg/dL, SD 2.66), indicating onset of the atherosclerotic process, another 14% showed an atherosclerotic index and LDL/HDL > 3.5 for males, and >2.5 for females, a further 5% showed predictive coronary risk (CO/HDL >5), and the remaining 30% were patients with dyslipid syndrome types 2-4, in conjunction with high cholesterol (360 mg/dL, SD 2.26) and triglyceride (mean 255 mg/dL, SD 3.10) levels. Two 5- to 6-km jogging sessions per week led to the use of an additional 200-300 kcal/session. Energy consumption during exercise according to age was calculated using a mean value, 10 kcal/min

After 3 months of following the exercise regimen, 64 (80%) patients obtained a normal BMI and a good WHR (Table 3), a normal health status (normal HOMA

Table 3. Clinical parameters of patients with risk factors for MS, before and after participation in the standard physical effort program

No. cases	Sex (M / F)	Mean age	Height (cm)	Weight (kg)	BMI before program	BMI after program	WHR before program	WHR after program
19	M	50	1.72	95	32.7	27.5	1.96	0.85
27	F	48	1.68	88	31.3	27.6	1.95	0.80
16	M	35	1.69	85	30.3	25.2	1.93	0.74
18	F	30	1.65	78	28.8	24.2	1.88	0.70

Table 4. Energy values of various types of effort in terms of heart rate and respiratory equivalent

	Target heart rate	Heart rate (beats/min)	V_{O2} (mL/min)	Energy consumption (kcal/min/kg)
Walking at 2 km/hour = 2 METs	Efficient/recovery zone – 60% to 70%	Heart rate at rest = 70-80 bts	1000	7
Walking at 3 km/hour = 4 METs	Aerobic zone – 70% to 80%	Aerobic zone = 120-160 beats	2000	14

Qualitative Index <2), and normalized biochemical results: total cholesterol (mean 169.5 mg/dL, SD 2.13, p = 0.005, reference interval = 114-225 mg/dL), triglycerides (mean 99 mg/dL, SD 2.92, p = 0.04, reference interval = 53-145 mg/dL), HDL (mean 63 mg/dL, SD 2.60, reference interval = 36-60 mg/dL) and LDL (mean 89 mg/dL, SD 2.88, reference interval = 48-130 mg/dL). Sixteen patients (20%) did not respond to the physical exercise regimen and retained high cholesterol or triglyceride levels and a BMI and WHR exceeding the normal limits.

DISCUSSION

The results described in this report are corroborated by a previous study of sedentary subjects who walked at a self-selected pace (10,000 steps per day, 3 days/week), and exhibited improved lipoprotein profiles and expression of genes involved in reverse lipid transport, without accompanying changes in body weight or total body fat. Furthermore, a study of 16 pairs of same-sex twins with discordant physical activity patterns found that greater levels of exercise were associated with lower total visceral fat, liver fat, and intramuscular body fat, with the active twin having on average 50% less visceral fat and 25% less subcutaneous abdominal fat than the inactive twin (16). Two comprehensive reviews found little evidence of an intensity threshold for changes in HDL cholesterol, LDL cholesterol, or triglycerides, although most studies did not control for exercise volume, frequency and/or duration, and were conducted using intensities ≥40% VO2max [17]. The American College of Sports Medicine (ACSM) recommends that most adults engage in moderate-intensity cardio-respiratory exercise for at least 30 min/day, at least 5 days per week, for a total of over 150 min of exercise per week (Table 3).

Physical exercise should comprise vigorous-intensity cardio-respiratory exercise for at least 20 min/day on at least 3 days per week (≥75 min/week), or a combination of moderate and vigorous intensity exercise to achieve a total energy expenditure of over 500–1,000 kcal/min per week [18] (Table 4).

This study focused on a specific treatment method for patients at risk of metabolic syndrome using a standard physical effort of 20 min per day for 5 days per week, according to the recommended activity regimen. This, combined with an appropriate diet, aims to prevent risk factors associated with MS and maintain a normal health status.

Although diet alone and in combination with exercise improves insulin sensitivity and other cardio-metabolic risk factors in older obese adults, exercise alone shows no such benefits, according to research presented at ENDO 2012: The Endocrine Society 94th Annual Meeting. The results of 93 participants (87%) who completed a trial showed that the insulin sensitivity index, as measured by an oral glucose tolerance test, improved in 70% of participants in the diet group and in 86% of those in the diet plus exercise group, whereas no improvements were observed in the exercise only and control groups ($p < 0.05$) [19].

CONCLUSION

The diet and exercise combination presented in this study proved to be an effective treatment for MS, and this or a similar regimen should be recommended by physicians to patients who show signs of MS. For patients who show limited results from exercising on a stationary bicycle (or other exercising methods), drug treatment, such as specific treatment for dyslipid disorder, administration of leptins, leptin genes, or promoter drugs may be necessary, in addition to physical exercise and maintenance of an appropriate diet.

Further studies, which should include an appropriate control group, are necessary to confirm these findings, which can be regarded at present as only a hypothesis derived from the signs and symptoms of MS.

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