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Physical activity has numerous beneficial effects on metabolic and inflammatory processes

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ABSTRACT

Obesity is a long-term multifactorial chronic disease, characterized by energy imbalance, due to an excess of caloric intake compared to energy expenditure and deregulation of other metabolic parameters, as, altered lipid profile, increased insulin resistance and chronic pro-inflammatory state. A healthy lifestyle, characterized by hypocaloric diet and physical activity, is important to reduce a chronic inflammation, oxidative stress and metabolic disorders typical of obesity. It is well known that the chronic inflammation state and oxidative stress are responsible for the aging and development of many diseases, such as cancer. In the light of these evidences, the aim of this study is to analyse body composition, metabolic profile and oxidative stress levels in obese patients subjected to a physical activity program before and after weight loss. We analysed the glycaemic and lipid profile, body composition such as visceral adipose tissue (VAT), fat mass (FM), and the dROMs serum levels via the Fenton's reaction. We found that in obese patients before physical activity intervention there are higher levels in dROMs serum levels, altered glycaemic and lipid profile and body composition compared to obese patients after physical activity intervention. In conclusion, the physical activity has numerous beneficial effects in obesity, modulating not only metabolic profile but also inflammatory and oxidative stress response.

Keywords: Obesity; Chronic diseases; Healthy lifestyle; Body composition; Metabolic profile.

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INTRODUCTION

Obesity contributes to reduced life expectancy, impaired quality of life, and disabilities, mainly in those individuals who develop cardiovascular diseases, type 2 diabetes, osteoarthritis, and cancer (Bray et al, 2017; Boutari et al, 2018; Mahmoud et al, 2018). This is a multifactorial disease characterized by an energy imbalance, due to that energy intake exceeds energy expenditure and by deregulation of other metabolic parameters as worse lipid profile, increased insulin resistance and a chronic pro-inflammatory state (Bray et al., 2017; Esposito et al., 2014; Moscatelli et al., 2016; Messina A. et al., 2016; Sessa et al., 2018). In the obese status there is an accumulation of visceral adipose tissue in the abdominal area of the body leading to develop the chronic inflammation state and oxidative stress, responsible for the aging and development of many diseases associated to obesity, such as cancer (Bukvic et al., 2010; Viggiano et al., 2009, 2010). Many data literature reported that the visceral adipose tissue (VAT) is extremely dangerous for health subject, in fact, it has been seen that abdominal fat has different characteristics compared to the subcutaneous fat, both from the cellular point of view and from the aspect of the effects that these cells exert on the endocrine-metabolic balance of the organism. The alteration in VAT leading to an imbalance production of adipokines by adipose tissue. Indeed, it is well known that the dysregulation in production of adiponectin and leptin by obese adipose tissue leading to a chronic inflammatory state (Monda et al., 2019; Moscatelli et al, 2015; Sperandeo et al., 2018; Viggiano et al., 2009).

Furthermore, the VAT is strongly involved in the production of pro-inflammatory and anti- inflammatory cytokines, indeed, the accumulation of visceral fat is also responsible of imbalance of immune cells which populated adipose tissue and then of production of cytokines (Polito et al., 2018; Messina et al., 2015; Monda et al., 2018; Viggiano et al., 2016). Fort these reasons, in obese condition, there is an important oxidative stress that are able to accelerate the risk of development of diseases associated to obesity (Patti et al, 2017; Viggiano et al., 2016).

In obese status, there is also, an alteration in many genes involved in the repair of cellular damage, oxidative stress and inflammation. In this scenario, an healthy lifestyle is able to activate numerous metabolic pathways such as SIRT1 that deacetylates nuclear and cytoplasmic proteins that control apoptotic processes, and down-regulates the production of mediators of inflammation and reduces ROS production (Ziegler et al., 2003; Messina et al., 2018; Moscatelli et al., 2015; Precenzano et al., 2017). On the other hand, weight control due to a healthy lifestyle, is able to increase the production of anti-inflammatory cytokines such as adiponectin and to reduce other pro-inflammatory mediators (Francavilla et al., 2007; 2018; 2016; Salerno et al., 2018; Barone et al, 2017). In the light of these evidences, the aim of this study is to analyse body composition, metabolic profile and oxidative stress levels in obese patients subjected to a physical activity program before and after weight loss.

MATERIALS AND METHODS

Participants

Ten obese subjects (5 females, 5 males), aged between 40-50 years (mean 47 ± 2.5 years), volunteered to participate in the study. Written informed consent for participation in the study was obtained from every patient. This study was performed in accordance with the Declaration of Helsinki and approved by the local ethics committee The anthropometric and biochemical characteristics of the 10 included patients are evaluated at baseline and after three months of physical activity program. Blood tests were taken at baseline and 6 months, after a 12h fast. Fasting blood samples were collected at 8:00 am from an antecubital vein, using a 21G Vacutainer.

Physical activity protocol

As previously reported the physical activity program consist in the mixed exercise program (Polito et al 2020). The protocol consist in 90 minutes per week in 2 session for 6 months. In the first time obese subjects following an aerobic session, 20 minutes on treadmill (60-80% of VO2max). In the second step the patients are subjected to resistance exercise (65% of 1RM). The protocol provides transverse thrust movements, frontal traction movements of the upper limbs, distension of the lower limbs, trunk flexions for the abdominals and 3 stretching positions.

ROMs (Reactive Oxygen Metabolites) Test

In population of obese subjects before and after physical activity program , we performed the d-ROMs to evaluate total amount of hydroperoxides in serum via the Fenton's reaction. Hydroperoxides, consisting of lipids, carbonylated proteins, and oxidized nucleic acids, are one of the most important ROS involved in oxidative stress and their measurement is considered a reliable marker of oxidation in plasma. The test was performed with the Free Radical Analytical System 4 (FRAS 4): this is a photometric analytical system developed for the assessment of oxidative stress that measures plasma hydroperoxides concentrations using the d-ROMs test with a single drop of peripheral (finger) blood. The blood sample was collected by patient's finger (0.15 mL) in a heparinized microcuvette. Thanks to the centrifuge of the FRAS 4 Evolvo System, plasma was immediately isolated by centrifugation at 37°C for 60 s. The plasma was dissolved in an acidic buffer (pH 4.8) in which its hydroperoxides react with the transition metal ions liberated from the proteins in the acidic medium and was converted to alkoxy and peroxy radicals. Subsequently, a colourless chromogen was added (N,N-diethyl-para- phenylenediamine). These newly formed radicals oxidized this chromogen that changed into a radical cation producing a magenta coloured derivative. This colour is directly correlated with the concentration of hydroperoxides in the plasma sample that is proportional to the quantity of ROMs, according to the Lambert-Beer law. The photometer FRAS 4 Evolvo (absorption at 505 nm, Temperature 37°C) was used to measure the magenta colour in order to measure the hydroperoxide concentration. The d- ROMs value was expressed in the arbitrary unit U. CARR (Units Carratelli), as established by the manufacturer (1 U. CARR corresponds to 0.08 mg of H_2O_2/dL). Normal values range between 250 and 300 U. CARR and values higher than 300 U. CARR suggest increased oxidative stress (Valenzano et al, 2019).

Statistical analysis

Because this study used a "pre-post" design and the comparison of interest was the change from baseline to 6 months physical activity intervention, a two-tailed paired t test was used to test for statistical significance of outcome variables. Statistical analyses were performed using the StatView software 5.0.1.0. All data are presented as mean ± SE. A p value of $\leq .05$ was used for statistical significance.

RESULTS

Anthropometric and biochemical parameters of obese subjects before and after physical activity intervention.

Our results show a significant change in the anthropometric and biochemical parameters of obese subjects before and after physical activity intervention. First of all, anthropometric parameters such as weight and BMI are statistically reduced in obese subjects before and after physical activity program (Table 1). Furthermore, there is a strongly reduction of fat mass (FM) and visceral adipose tissue (VAT). Furthermore, there is a strongly modulation of all biochemical parameters, such as glycaemic and lipid profile and also in inflammation status such as CRP protein.

Table 1. Biochemical features of VLCKD subjects before and after weight-loss.

	VLCKD obese subjects		
	T0	**T 6 months**	***p-value***
Age	47 ± 2.5		*ns*
Weight (kg)	92.33 ± 7.1	80.73 ± 3.36	<*.001*
BMI (kg/m²)	31.19 ± 4.78	27.76 ± 3.62	<*.001*
VAT (g)	1451.55 ± 11.63	917.79 ± 14.92	<*.001*
FM (g)	39208.77 ± 132.55	27377.03 ± 117.48	<*.001*
TOTAL CHOLESTEROL(mg/dl)	225.13 ± 50.77	163.91 ± 32.93	<*.05*
HDL(mg/dl)	48.13 ± 7.14	46.76 ± 5.4	*ns*
LDL(mg/dl)	131.83 ± 16.48	103.57 ± 7.72	<*.05*
TRIGLYCERIDES(mg/dl)	125.54 ± 5.27	81.25 ± 6.14	<*.05*
Glycemia (mg/dL)	120.53 ± 7.18	85.37 ± 3.79	<*.05*
CRP mg/ml	*0.99 ± 0.1*	*0.45 ± 0.07*	<*.05*

Serum Reactive Oxygen Metabolites Test

We analysed reactive oxygen metabolites in serum of obese subjects before and after physical activity program by d-ROMs test. The results of the d-ROMs test showed different values: in the patients before VLCKD diet the value is statistically higher than to patients after VLCKD diet (632 U vs 295 U, p-value < .05); this finding suggests the decrease of oxidative stress in obese subjects after physical activity program.

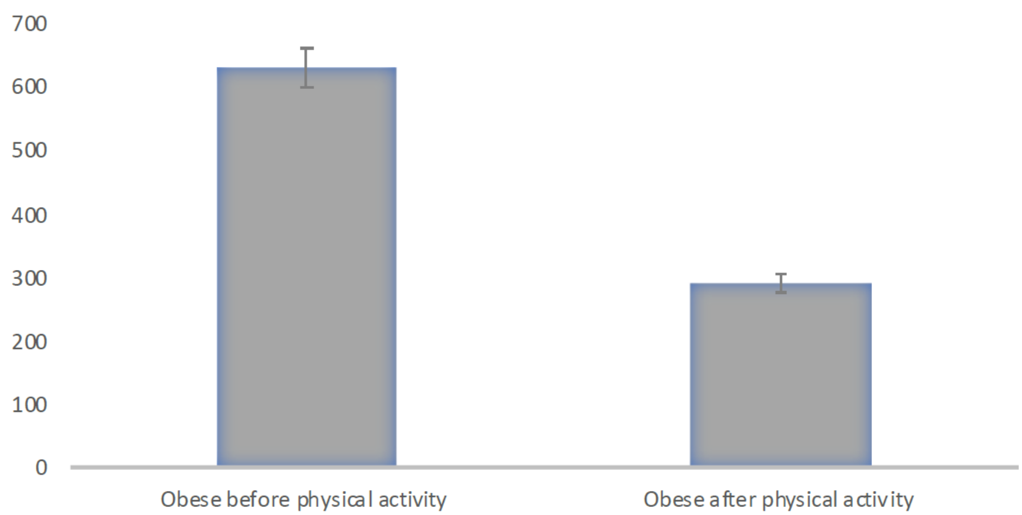

Figure 5. d-ROMs serum levels are strongly modified by physical activity program in obese subjects.

DISCUSSION

Obesity is a chronic disease associated to insulin resistance, diabetes mellitus and altered lipid profile. Furthermore, there are many serious obese-diseases correlated, such as liver diseases, immune disease and cancer (Bianco et al., 2018; Cavaliere et al., 2018, 2019; Ledda et al., 2017; Pomara et al., 2014; Santacroce et al., 2008). The principal characteristic of obesity is the accumulation of visceral fat mass in the abdominal area leading to develop of hyperinsulinemia and insulin resistance and responsible of chronic low-inflammation (Mahmoud et al., 2018; Francavilla et al., 2018; 2013; 2015; Fineschi et al., 2006; Pomara et al., 2005; Schiavone et al., 2017; Vicchio et al., 2020; Guarnieri et al., 2020). For these reasons, in this study, we analysed anthropometric and biochemical parameters in obese subjects before and after physical activity program. In particular, after 6 months we found the statistically decreased of weight loss, BMI, fat mass, and visceral adipose tissue and the ameliorating of all anthropometric and biochemical parameters is very significantly. In particular the strongly reduction of d-ROMs and of weight-loss may be associated also to the strongly reduction of visceral adipose tissue. The reduction of visceral adipose tissue leads to a decrease of chronic inflammation, blocking pro-inflammatory cytokines production and enhancing anti-inflammatory production. Moreover, it is well known that with the reduction of visceral fat mass, there is an increase of lean mass and skeletal bone preservation. These finding is of foremost relevance, reinforcing the beneficial effect of a physical activity in obesity treatment. Indeed, as reported by Moro T. et al, physical activity improves some health-related biomarkers, decreases fat mass, and maintain muscle mass in resistance-trained (Moro et al., 2016; Giuditta et al., 2008; Eyman et al., 2019; Mazzeo et al., 2013; Bertozzi et al., 2017; Ledda et al., 2016; Neri et al., 2016). The VAT accumulation associated to production of pro-inflammatory cytokines is a characteristic of chronic low inflammation of obese subjects and is strongly involved also in oxidative stress and ROS production (Spagnolo et al., 2019; Ventura et al., 2018; Mondello et al., 2018; Sapienza et al., 2017; Barone et al., 2017; Monda et al., 2018). For these reasons, in our study, we also analysed the effects of physical activity program in obese subjects on ROS production. As previously reported there is a strong reduction in d-ROMs serum levels and then in oxidative stress in obese subjects after physical activity program. Indeed, many data literature reported that healthy lifestyle such as correct nutrition and physical activity are able to reduce ROS production, increasing SOD 1 and SOD 2 and reduced pro-inflammatory cytokines production, increasing anti-inflammatory mediators production (Gualniera et al., 2017; Maio et al., 2002; Orban et al., 2014; Pomara et al., 2016; Messina A et al., 2018; 2017; Messina G. et al., 2015). In conclusion, given these results, physical activity program in obese conditions is able to ameliorate anthropometric and biochemical parameters and to reduce oxidative stress responsible of aging and many serious diseases obese-associated such as cancer.

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