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12 Weeks' aerobic and resistance training without dietary intervention did not influence oxidative stress but aerobic training decreased atherogenic index in middle-aged men with impaired glucose regulation

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ABSTRACT

Our aim was to determine whether 12 weeks' aerobic Nordic walking (NW) or resistance exercise training (RT) without diet-induced weight loss could decrease oxidative stress and atherogenic index of plasma (AIP), prevalence of metabolic syndrome (MetS) and MetS score in middle-aged men with impaired glucose regulation (IGR) ($n = 144$. 54.5 ± 6.5 years). In addition, we compared effects of intervention between overweight and obese subgroups.

Prevalence of MetS and AIP index decreased only in NW group and MetS score in both NW and RT groups but not in control group. The changes in AIP index correlated inversely with changes in plasma antioxidant capacity. The change in AIP index remained a significant independent predictor of the changes in MetS score after the model was adjusted for age, BMI and volume of exercise (MET h/week) in NW group. There were no changes in the other measured markers of oxidative stress and related cytokines (e.g. osteopontin and osteoprotegerin) in any of the groups.

Nordic walking decreased prevalence of MetS and MetS score. Improved lipid profile remained a predictor of decreased MetS score only in NW group and it seems that Nordic walking has more beneficial effects on cardiovascular disease risks than RT training.

1. Introduction

The metabolic syndrome (MetS) affects as many as 30% of the population, even 50% of severely obese adolescents in United States (Ford et al., 2004; Lim et al., 2013) and regardless of the criteria used for its definition, the prevalence of MetS is still rising in all western societies (Hollman and Kristenson, 2008; Ervin, 2009). The metabolic syndrome is a generalized diet- and obesity- related disorder, defined as a cluster of interrelated risk factors for cardiovascular disease and type 2 diabetes. In addition to unhealthy diet, there is growing evidence that a sedentary lifestyle, lack of physical activity and poor physical fitness play significant roles in the development of MetS.

Oxidative stress has a central role in MetS and its component pathologies like dyslipidemia, hypertension, insulin resistance

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Abbreviations: AIP, atherogenic index of plasma; BMI, body mass index; C, control group; CAD, coronary artery disease; CVD, cardiovascular disease; HDL, high density lipoprotein; HMW, human high molecular weight; IDF, International Diabetes Federation; IGR, impaired glucose regulation; IGT, impaired glucose tolerance; LDL, low density lipoprotein; LPO, lipid hydroperoxides; MDA, malondialdehyde; MET, metabolic equivalent of task; MetS, metabolic syndrome; NW, nordic walking group; OB, obese group; OGTT, oral glucose tolerance test; OPG, osteoprotegerin; OPN, osteopontin; ORAC, oxygen radical absorbance capacity; OX-LDL, oxidized LDL; OW, overweight group; ROS, reactive oxygen species; RT, resistance training group; SD, standard deviations; SE, standard errors; TGs, triglycerides.

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and obesity and may be a unifying factor in the progression of this disease (Hutcheson and Rocic, 2012). Increased oxidative stress, as measured by indices of lipid peroxidation and protein oxidation, have been shown in hyperglycemia, MetS and in both type 1 and type 2 diabetes (Atalay and Laaksonen, 2002). The serum levels of malondialdehyde (MDA) were elevated in overweight and obese subjects, especially in those who have clear abdominal adiposity (Sankhla et al., 2012). The same study further demonstrated that the increased oxidative stress was associated with adiponectin deficiency (Sankhla et al., 2012). Protein carbonyl levels, a marker of protein oxidation, were significantly higher in subjects with MetS than in controls (Armutcu et al., 2008).

Epidemiological studies have demonstrated that regular physical activity prevents type 2 diabetes, cardiovascular disease, and premature mortality (Laaksonen et al., 2002, 2004). There is a large body of epidemiological data demonstrating that exercise can decrease the incidence of oxidative stress-associated diseases (Katzmarzyk and Janssen, 2004; Tremblay et al., 2007). This beneficial effect is due to the fact that exercise-induced reactive oxygen species (ROS) production is necessary for achieving ROS-mediated adaptations.

MetS doubles the risk of cardiovascular disease, which is a result of complex interactions of several components of MetS (Després et al., 2008; Grundy, 2012). Patients having MetS often develop atherosclerosis, where oxidative stress plays central role in disease progression (Hutcheson and Rocic, 2012). Recently we have shown that Nordic walking (aerobic training) could lower total cholesterol and low density lipoprotein (LDL) cholesterol levels in middle aged men with impaired glucose regulation (IGR) (Venojärvi et al., 2013). In addition, small dense LDL is considered to be a risk marker for cardiovascular disease (CVD) (Kotani et al., 2012) and it is commonly accepted that the combination of high concentrations of triglycerides (TG) and low levels of high density lipoprotein cholesterol (HDL-C) can be referred to as atherogenic dyslipidemia. The logarithm of this ratio (log [TG/HDL-C]), also called atherogenic index of plasma (AIP) (Dobiásová and Frohlich, 2001), which is comparable with smaller LDL particles (Dobiásová and Frohlich, 2001; Soška et al., 2012). A high AIP, a surrogate of small LDL particle size, reflects obesity and hyperinsulinemia in men and is associated with high blood pressure and metabolic syndrome (Onat et al. 2010). Lippi and co-workers showed that the AIP index was significantly lower in highly trained subjects in comparison to sedentary subjects and lower AIP index was associated with increased aerobic physical activity in highly trained subjects (Lippi et al., 2006). The relationships between AIP and markers of oxidative stress and serum osteopontin (OPN) and osteoprotegerin (OPG) have not been studied in terms of the response to exercise intervention.

It has been reported that plasma OPN levels and adipose tissue and liver OPN mRNA expression were increased in overweight/obese patients (Gómez-Ambrosi et al., 2007; Bertola et al. 2009). It has been shown that there is a correlation between OPN and MDA, a marker of oxidative stress in patients with coronary artery disease (CAD) (Georgiadou et al., 2008) and also serum osteopontin levels were markedly higher in patients with nonalcoholic fatty liver disease than in controls (Yilmaz et al., 2013). Recently serum levels of osteoprotegerin have been shown to be linked to vascular calcification (Davenport et al., 2012). Similarly to adiponectin, the levels of osteoprotegerin were reduced in the obese subjects compared to lean subjects and correlated negatively with BMI (Ashley et al., 2011).

There are recent studies confirming that moderate regular exercise, alone or combined with caloric restriction, can improve insulin resistance, MetS, and cardiovascular disease risk factors (Otani, 2011), possibly by altering the systemic levels of inflammatory adipocytokines.

The primary aim of this study was to determine whether aerobic and/or resistance exercise training without accompanying diet-induced weight loss could decrease atherogenic index of plasma and the level of oxidative stress in middle-aged men with IGR. In addition, we evaluated if markers of oxidative stress would be associated with the AIP index and plasma OPG and OPN levels after this intervention and whether there would be differences between the overweight and obese subgroups at baseline.

2. Materials and methods

2.1. Study subjects

Overweight or obese male volunteers (40–65 years), who did not exercise regularly and who were interested in participating in the study and eligible for screening ($n = 313$), were recruited through advertisements in newspapers and in local occupational health care institutes. After a telephone interview, 267 of these men were recruited to participate in the screening tests.

The health status and suitability of the volunteers for the study were checked by a health and lifestyle questionnaire, physical examinations and a 75 g oral glucose tolerance test (OGTT). Inclusion criteria were male sex, age 40–65 years, BMI 25.1–34.9 kg/m^2 and fasting plasma glucose 5.6–6.9 mmol/l and/or 2-h plasma glucose 7.8–11.0 mmol/l. Exclusion criteria were previously detection of impaired glucose tolerance (IGT) and participation in a prescribed diet or an exercise program, participation in regular and physically vigorous activities, usage of any medication affecting glucose balance (e.g. peroral corticosteroid medication).

Finally, 144 volunteers were eligible to take part in the study (Trial No.: ISRCTN97931118). They were equally randomized into one of three groups: (1) a control group (C group, $n = 47$), (2) a Nordic walking group (NW group, $n = 48$) or (3) a resistance training group (RT group, $n = 49$). In addition we compared the overweight (OW group, $n = 60$) (BMI < 30) and obese (OB group, $n = 55$) (BMI $\geqslant$ 30) subjects at baseline and after the intervention. During the intervention period, some of the subjects dropped out due to private or medical reasons or difficulties in work arrangements and eventually some also due to motivational factors. As a result, 115 subjects completed the intervention as intended. The characteristics of the subjects are shown in Table 1. There was no difference in smoking habits between the groups. No differences in workload or physical activity levels during the past year before the study were detected among the three groups. The Ethical Committee of the Hospital District of Helsinki and Uusimaa in Finland approved the protocol of the study and all the subjects provided written informed consent.

2.2. Intervention

Participants were advised not to change their habitual diet or their other lifestyle factors during the intervention. If they had been physically active during their leisure-time, they were asked to continue with their activities. The aim of the intervention program was to be supplementary activity, not compensatory, and the time allocated should be taken from the inactive leisure time.

The control group, that had no supervised exercise during the intervention period, was advised, however, about the health benefits of exercise during the first test day. Both intervention groups trained three times per week for 60 min per session during 12 weeks, according to special exercise programs in which both the exercise intensity and load were increased such that the strain of the subjects was progressively increased after every 4 weeks of training. Training sessions were supervised by at least two physical education instructors.

The programs in the Nordic walking group consisted of warm-up exercises including walking for 5 min and stretching of the main muscle groups in addition to walking with poles. The programs were individually designed, but they started with guidance sessions advising on how to walk with walking poles. The aerobic exercise sessions were carried out at the strain levels increasing from 55% to 75% of heart rate reserve (weeks 1–4 at 55%, weeks 5–8 at 65% and weeks 9–12 at 75%). Individual target heart rates were calculated by using measured resting heart rate and the maximal heart rate estimated with the formula 210 – (0.65 × age in years) (Jones, 1998). Heart rate was monitored during training with Polar F4 (Polar Electro Oy, Kempele, Finland) heart rate monitors and the target heart rate range was progressively increased as described. Either the walking speed was increased or the length of uphill part was prolonged so that the intended target heart rate was achieved. After the pole walking session the main muscle groups were stretched during 5 min for cool-down.

The resistance training sessions were started with warm-up exercises including cycling or rowing with ergometer for 5 min and the stretching of the main muscle groups. After that the main part of the program was performed by using regular resistance equipment with the training focus on strength and power exercises of the lower extremities and trunk; but also the muscles in the upper extremities were trained. Muscle contractions were performed with high or maximal velocity and external loads started from 50% of exercise specific maximal strength at the beginning of the training program and reached to 85% by week 9, which were sustained till the end of 12 weeks. Exercise specific maximal strength was determined during