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Randomized control trials

Effect of different exercise modalities plus a hypocaloric diet on inflammation markers in overweight patients: A randomised trial

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SUMMARY

Background & aims: Inflammation markers (IM) have been associated with the development of chronic diseases. This study compares the effects on IM of three exercise programs combined with a hypocaloric diet.
Methods: 119 overweight participants (73 women, 46 men) aged 18–50 years were randomised into four treatment groups: strength training (S; $n = 30$), endurance training (E; $n = 30$), combined S + E (SE; $n = 30$), and a diet and physical activity recommendations group (D; $n = 29$). Energy intake, anthropometric variables (AV), training variables (VO_{2peak}, strength index, dynamometric strength index [DSI]) and plasma IM were recorded at baseline and after 22 weeks of treatment.
Results: 84 participants completed the study. At 22 weeks, all groups showed a significantly reduced energy intake ($P < 0.001$) and improved AV ($P < 0.001$). VO_{2peak} significantly increased in all groups ($P < 0.01$). DSI increased in the exercise groups only ($P < 0.05$). Plasma leptin fell significantly ($P < 0.001$) in the S and E groups, but not significantly in the SE group ($P = 0.029$) (no significant differences between these groups). Tumour necrosis factor-α (TNF-α), and C-reactive protein (CRP) concentrations decreased in all groups when examined together, but not when examined separately. No significant differences were seen in interleukin-6 (IL-6).
Conclusions: Combining strength or endurance training with a hypocaloric diet improved AV and reduced plasma leptin concentrations. No differences were seen between groups in terms of TNF-α, IL-6 or CRP reduction. This trial was registered at clinical trials.gov as NCT01116856. http://clinicaltrials.gov/.

1. Introduction

The majority of epidemiological studies indicate excess body weight during midlife, including overweight, to be associated with an increased risk of death.[1–3] For example, people with a BMI of 25–28.9 have a relative risk of developing cardiovascular disease twice that of people with a BMI of <21,[4] while those with a BMI of ≥29 are at almost three times the risk. Further, the results of the Framingham Heart Study show that being overweight at age 40 reduces life expectancy by three years.[5] Given the increasing prevalence of obesity, finding more efficient treatments for overweight should be seen as a public health priority.

Low-grade chronic inflammation is one of the key metabolic alterations linked to excessive energy intake, physical inactivity and adiposity, and the markers of this inflammation – tumour necrosis factor-α (TNF-α), interleukin-6 (IL-6) and C-reactive protein (CRP) – have all been associated with the development of atherosclerosis and insulin resistance.[6,7] Several studies have shown that inflammation markers (IM) are reduced following weight loss.[8–10] Physical exercise may therefore be effective in reducing inflammation. Indeed, data from observational and intervention studies show that greater physical activity is associated with lower plasma IM

Non-standard abbreviations: S, strength training group; E, endurance training group; SE, strength + endurance combined training group; D, diet and physical activity recommendations group; VO_{2peak}, peak oxygen uptake; DSI, dynamometric strength index; SI, strength index; AV, anthropometric variables; TFM, total fat mass; AF, android fat; AF/GF, android/gynoid fat ratio; LM, lean mass.

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concentrations,[10–13] and regular exercise and an appropriate diet are reported to protect against all-cause mortality. This is achieved primarily through protection against atherosclerosis, type 2 diabetes, colon cancer and breast cancer.[14–16]

The mechanism that underlies the anti-inflammatory response associated with acute exercise might, surprisingly, involve an *increase* in the circulating concentration of IL-6. Under exercise conditions, this cytokine appears to induce an anti-inflammatory environment by promoting the production of IL-1ra and IL-10, and by inhibiting TNF-α production.[14–16] Exercise also increases the release of epinephrine, cortisol, growth hormone, prolactin and other factors that have immunomodulatory effects.[16]

A few studies have tried to determine the types of exercise intervention that produce the greatest changes in IM concentrations,[13,17–20] but the results have been controversial. A recent review indicates that increasing aerobic physical activity may be effective for reducing chronic inflammation especially in individuals with chronic diseases associated with a state of elevated inflammation (Beavers et al., 2010). The aim of the present study was to compare the effects on plasma IM concentrations of three different exercise programs – strength, endurance, and combined strength + endurance training – all in conjunction with a hypocaloric diet, and the normal clinical practice of achieving weight loss using the same hypocaloric diet as above, plus the provision of recommendations regarding physical activity.

2. Materials and methods

2.1. Study subjects

This study was performed as part of the larger study *Nutrition and Physical Activity for Obesity* (the PRONAF study according to its Spanish initials), the aim of which was to assess the usefulness of different types of physical activity and nutrition programs for the treatment of obesity. Participants were sought via advertisements posted in newspapers and announced on the radio, the internet and TV. The eligible sample population consisted of 119 overweight subjects (73 women and 46 men; age range 18–50 years; body mass index [BMI] $\geq$25–<30 kg/m^2) living in the Region of Madrid, Spain. Eighty four participants completed the study (50 women and 34 men) (Fig. 1). All subjects were healthy adults with no history of relevant concomitant illness, such as heart, lung or liver disease, or neoplasia. All were normoglycaemic non-smokers and took no medications or drugs, but led sedentary lifestyles. All female subjects had regular menstrual cycles. The exclusion criteria covered all physical and psychological diseases that may have precluded the performance of the requested strength or endurance training, along with the taking of any medication known to influence physical performance or that might interfere with the interpretation of the results. Subjects with a background of systematic strength or endurance training (moderate to high intensity training more than once a week) in the year before the study started were also excluded. In agreement with the guidelines of the Declaration of Helsinki regarding research on human subjects, all participants signed an institutionally approved document of informed consent. All subjects were carefully informed about the possible risks and benefits of the study, which was approved by the Human Research Review Committee of the La Paz University Hospital (PI-643).

2.2. Study design

Subjects who fulfilled the inclusion criteria and passed a baseline physical examination were stratified by age and sex and assigned (using a randomisation table) to a strength training group (S), endurance training group (E), combined strength + endurance training group (SE), or diet and physical activity recommendations group (D).

This study design was that of an intervention trial of 22 weeks duration. Baseline measurements for all subjects were made before starting the intervention period. The final measurements were taken once the intervention period was over (within 48–72 h of the last training session for the exercise groups).

2.2.1. Exercise training programs

The different exercise groups followed their corresponding training programs, which in all cases involved training 3 times/week for 22 weeks. All training sessions were carefully supervised by certified personal trainers. An adherence to training of 90% was demanded.

The S group followed a circuit involving the following eight exercises: shoulder press, squat, barbell row, lateral split, bench press, front split, biceps curl, and French press for triceps. E group training involved the use of an exercise bike or cross trainer. The SE group performed a combination of cycle ergometry, treadmill or cross trainer work, plus weight training with the following exercises intercalated between lift sets (15 lifts per set): squat, rowing machine, bench press and front split. The D group subjects followed the hospital's habitual clinical practice for achieving weight loss, i.e., the same dietary intervention as the training groups plus being made aware of the general recommendations of the American College of Sports Medicine (ACSM) regarding physical activity.[22]

All subjects were instructed to keep their daily physical activity habits unchanged. These habits were carefully checked with a dairy registry by personal trainers in all training sessions to the groups S, E and SE. Group D subjects were not supervised, although they were subjected to activity monitoring using an armband accelerometer, just as they would be in normal practice.

The exercise programs were designed taking into account each subject's muscular strength (MS) and heart rate reserve (HRR). MS was measured in the strength program subjects (S, SE) using the 15-repetition maximum (15 RM) testing method[21] every other day during the week before the intervention period. The intraclass correlation coefficient of reliability for all exercises was ICCr = 0.995 for the men and ICCr = 0.994 for the women (groups S and SE subjects together). The HRR was calculated to set the exercise intensity ([maximum heart rate-resting heart rate] × 50%–60%) and resting heart rate for the E and SE programs.

The intensity of exercise was increased over the study period. In weeks 2–5, exercise was at an intensity of 50% of the 15RM and HRR, and lasted an overall 51 min and 15 s (twice around the circuit, lasting 7 min 45 s each lap). In weeks 6–14, exercise was performed at an intensity of 60% of 15RM and HRR, again with a duration of 51 min and 15 s (again, twice around the circuit). Finally, in weeks 15–23, exercise was performed at an intensity of 60% of 15RM and HRR, with a duration of 64 min (three times around the circuit). The recovery period between circuits was set at 5 min. Participants performed 15 repetitions (45 s) of each exercise with a rest period of 15 s between them. Each training session for the S, E and SE subjects commenced with a 5 min aerobic warm-up, followed by the main session exercises, and concluded with 5 min of cooling down and stretching exercises. In all sessions the exercise rhythm was controlled by instructions recorded on a compact disk. The cadence for the resistance exercises was fixed at 1:2 (concentric-eccentric phase).

2.2.2. Hypocaloric diet program

Hypocaloric diets (between 5028 and 12,570 kJ) were prescribed individually for all participants by expert dieticians at the Department of Nutrition, La Paz University Hospital, Madrid. The diet was designed to provide 25% less energy than the baseline daily energy