Exercise Training Improves Glycemic Control in Long-Standing Insulin-Treated Type 2 Diabetic Patients

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Regular exercise represents an effective strategy to prevent and/or treat type 2 diabetes (1,2). However, the clinical benefits of exercise intervention in a vastly expanding group of long-standing insulin-treated type 2 diabetic patients with comorbidities are less evident. As these patients generally experience muscle weakness (3–6), cardiovascular comorbidities (7–10), and/or exercise intolerance (3,11–13), it has proven difficult or even impossible for them to adhere to an intense endurance exercise training regimen (14,15). In the present study, we investigated the feasibility and benefits of a low-impact exercise intervention program, combining both endurance and resistance-type exercise, in long-standing insulin-treated type 2 diabetic patients with a high cardiovascular risk profile. We assessed the impact of 5 months of exercise training on glycemic control, body composition, workload capacity, and whole-body as well as skeletal muscle oxidative capacity.

RESEARCH DESIGN AND METHODS

— A total of 11 male type 2 diabetic patients volunteered to participate in this study. Participants (aged 59 ± 3 years, BMI 32 ± 1 kg/m^2) had been diagnosed with type 2 diabetes for 12 ± 2 years and had been on exogenous insulin treatment for 7 ± 2 years (insulin requirements 93 ± 11 units/day). All participants were sedentary and showed a high cardiovascular risk profile (with a 10-year risk for coronary heart disease of 30 ± 2% according to the UK Prospective Diabetes Study [UKPDS] [16]). Participants had been on a stable regimen of diabetes medication for at least 3 months before recruitment. Type 2 diabetic patients using thiazolidinediones and/or β-blockers <6 months and participants with impaired liver function, macroalbuminuria, severe retinopathy, or cardiovascular problems were excluded.

Before and after the 5-month exercise program, body composition (dual-energy X-ray absorptiometry), upper-leg muscle volume (magnetic resonance [MR] imaging), glycemic control, blood lipid profile, blood pressure, whole-body oxygen uptake and maximal workload capacity, intramyocellular lipid content, and skeletal muscle oxidative capacity were assessed. Plasma glucose, A1C, serum cholesterol, HDL cholesterol, nonesterified fatty acid, triacylglycerol, adiponectin, tumor necrosis factor-α, high-sensitivity C-reactive protein, and C-peptide concentrations were determined in fasting blood samples. Blood pressure was recorded during supine rest using an automatic blood pressure–measuring device. Mean arterial blood pressure was calculated from the last three stable blood pressure measurements over a 10-min period. Blood pressure–lowering medications were not changed throughout the study. Whole-body oxygen uptake capacity ($V\text{O}_{2\text{max}}$) and maximal workload capacity (W_{max}) were measured during an incremental exercise test to exhaustion. MR spectroscopy (MRS) measurements were performed using a 1.5-Tesla whole-body MR scanner. Localized ^{1}H-MRS was used to measure intramyocellular lipid content in the musculus vastus lateralis. ^{31}P-MRS was applied to measure postexercise phosphocreatine (PCr) recovery, as previously described (17). Results are expressed as the time constant of recovery for PCr and ADP, i.e., τ_{PCr} and τ_{ADP}, representing skeletal muscle oxidative capacity (18).

The backbone of the exercise program was progressive resistance training (PRT), with high-intensity interval training (HIT) as a supplement. Four bouts of resistance-type exercise targeting the upper body were performed (2 × 10 repetitions, 50% of 1 repetition max [1RM] [19]). Thereafter, resistance training was continued with horizontal leg press and leg extension (2 × 10 repetitions). Throughout the PRT, intensity was progressively increased from 50 to 80% 1RM. In each session, PRT was followed by multiple bouts of HIT to stress working leg muscle without overloading the cardiovascular system (20). Both the number of bouts and work rate for the interval modes were progressively increased. The HIT included four to eight cycling bouts of 30/60 s at 50–60% W_{max} (20). Exercise sessions required ~45 min to complete and were performed three times a week. All data are presented as means ± SE. Paired-samples t tests (two sided) were applied to evaluate changes following exercise intervention, and statistical significance was set at $P \leq 0.05$.

RESULTS

— All participants completed the exercise training program and showed an 83 ± 4% attendance rate for the supervised training sessions. Exercise

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Abbreviations: 1RM, 1 repetition max; HIT, high-intensity interval training; MR, magnetic resonance; MRS, MR spectroscopy; PCr, phosphocreatine; PRT, progressive resistance training.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

Table 1—*Body composition, muscle and whole-body oxidative capacity, functional performance, and blood plasma analyses*

	Before training	After training	*P*
Body mass (kg)	97.5 ± 4.9	97.5 ± 4.8	0.95
Waist circumference (cm)	112.6 ± 3.7	113.2 ± 4.0	0.7
Total body fat (%)	27.0 ± 0.8	25.9 ± 0.9	0.09
Truncal fat (%)	30.1 ± 1.1	28.8 ± 1.3	0.04
Total body lean mass (kg)	68.9 ± 2.9	69.6 ± 2.7	0.25
Leg lean muscle mass (kg)	20.6 ± 1.0	21.2 ± 0.9	0.03
MRI total muscle (cm^3)*	3553 ± 173	3653 ± 153	0.08
MRI musculus vastus lateralis (cm^3)†	499 ± 28	536 ± 81	0.01
Fasting plasma glucose (mmol/l)	10.4 ± 0.9	8.6 ± 0.7	0.05
A1C (%)	7.6 ± 0.3	7.2 ± 0.2	0.04
Daily insulin requirement (units)	92.5 ± 11.1	85.4 ± 12.3	0.26
$V\text{o}_{2\text{max}}$ (ml · min^{-1} · kg body mass^{-1})	24.3 ± 1.4	24.2 ± 1.5	0.87
W_{max} (W/kg body mass)‡	1.6 ± 0.1	1.9 ± 0.2	<0.01
Average 1RM§	77 ± 4	90 ± 6	<0.01
Intramyocellular lipids (percentage of water signal)	1.9 ± 0.2	2.0 ± 0.3	0.15
τ_{PCr} (s)	49.4 ± 5.5	45.6 ± 5.6	0.09
τ_{ADP} (s)	22.5 ± 2.9	21.2 ± 2.4	0.43
Mean arterial pressure (mmHg)	105.8 ± 2.3	98.1 ± 3.1	0.02
Mean systolic blood pressure (mmHg)	147.4 ± 3.7	137.9 ± 5.1	0.06
Mean diastolic blood pressure (mmHg)	82.5 ± 2.1	78.3 ± 2.4	0.13
Total cholesterol (mmol/l)	4.24 ± 0.17	4.37 ± 0.24	0.55
HDL cholesterol (mmol/l)	0.87 ± 0.07	0.91 ± 0.07	0.55
LDL cholesterol (mmol/l)	3.44 ± 0.13	3.53 ± 0.21	0.57
Triacylglycerol (mmol/l)	2.31 ± 4.26	2.26 ± 3.31	0.86
Nonesterified fatty acid (mmol/l)	0.459 ± 0.073	0.367 ± 0.044	0.07
Adiponectin (μg/l)	5.43 ± 0.78	5.47 ± 0.82	0.9
Tumor necrosis factor-α (ng/l)	7.19 ± 0.46	7.06 ± 0.47	0.74
High-sensitivity C-reactive protein (mg/l)	2.1 ± 0.6	2.08 ± 0.5	0.4
C-peptide (nmol/l)	0.94 ± 0.14	0.90 ± 0.12	0.7

Data are means ± SE. $n = 11$. *Volume measurements based on MRI data for total upper-leg muscle compartment. †Volume measurements based on MRI data for musculus vastus lateralis. ‡Maximal power output on cycle ergometer. §Average weight lifted in 1RM tests from five different resistance exercises.

training resulted in a decline in truncal fat mass and an increase in lean leg muscle mass (Table 1). Glycemic control improved, with a significant decline in both fasting blood glucose concentration and A1C (from 7.6 ± 0.3 to 7.2 ± 0.2%). Exogenous insulin requirements did not change throughout the training program. When calculating the slope of daily insulin requirement over time, it changed from on average +6.69 units per 6 months in the 3 years before intervention to −1.6 units per 6 months ($P < 0.01$) following the beginning of the program. Mean arterial blood pressure declined from 106 ± 2 to 98 ± 3 mmHg, and systolic pressure tended to decrease from 147 ± 4 to 138 ± 5 mmHg ($P = 0.06$). Both maximal power output (1.6 ± 0.1 to 1.9 ± 0.2 W/kg body mass, $P < 0.01$) and muscle strength (1RM of five exercises: 77 ± 4 to 90 ± 6 kg, $P < 0.01$) increased significantly. No changes were observed in the lipid profile or in the inflammation markers.

CONCLUSIONS— A combination of low-impact endurance and resistance-type exercise training is preferred for long-standing insulin-treated type 2 diabetic patients, as it provides a relatively low cardiovascular challenge (21) and improves functional performance (22,23). The present study shows that such an exercise regimen is well tolerated, with all patients being able to complete the program. Combined endurance and resistance-type exercise training effectively improves glycemic control, body composition, blood pressure, muscle strength, and workload capacity and attenuates the progressive increase in exogenous insulin requirements. Although selection bias and sample size should be acknowledged when generalizing the outcome of this study, we conclude that low-impact endurance and resistance-type exercise training should be prescribed in the vastly expanding population of long-standing insulin-treated type 2 diabetic patients.

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