Regular Aerobic Exercise Training Improves Endothelium-Dependent Arterial Dilation in Patients With Impaired Fasting Glucose

XIANG GUANG-DA, MD[1]
WANG YUN-LIN, MD[2]

Vehkavaara et al. (1) demonstrated that impaired endothelium-dependent arterial dilation characterizes patients with impaired fasting glucose (IFG). The purpose of the study was to investigate the effects of exercise training on endothelium-dependent arterial dilation in subjects with IFG using noninvasive measurement of flow-mediated, endothelium-dependent dilation of the brachial artery.

RESEARCH DESIGN AND METHODS

— The study group included 30 sedentary Chinese Han men with IFG between 48 and 74 years of age, mean age 63 ± 12 years. The diagnosis of IFG fulfilled the diagnostic criteria proposed by the American Diabetes Association. The subjects participated in a 6-month exercise training program. Of them, eight discontinued the study after 1 month of training. Additionally, 30 sedentary healthy men aged 46–76 years, mean age 65 ± 11 years, were selected as control subjects.

Subjects with IFG underwent a supervised orientation and thereafter performed exercise on their own. Initially, subjects walked 25–30 min a day 3–4 days a week at a relatively low intensity (~60% of maximal heart rate). As their exercise tolerance improved, the intensity and duration of walking were increased to 40–45 min per day 4–6 days per week at an intensity of 70–75% of maximal heart rate. The vascular studies of the brachial artery were performed as previously described (2) 1–3 days before and 6 months after the initiation of exercise training program.

RESULTS

— At baseline, the fasting serum glucose, LDL cholesterol, and C-reactive protein concentrations and positive family history were higher in patients with IFG than in control subjects ($P < 0.05$). HDL cholesterol was lower in patients with IFG than in control subjects ($P < 0.05$). The flow-mediated arterial dilation among subjects with IFG was lower than in control subjects ($P < 0.05$). After 6 months of exercise training, there was a remarkable increase in the flow-mediated arterial dilation in subjects with IFG (22.7%) ($P < 0.05$). The significant decreases in fasting plasma glucose (17.3%), LDL cholesterol (17.7%), and C-reactive protein (30.8%) and significant increases in HDL cholesterol (21.6%) as well as $V_{O_{2max}}$ (19.7%) were observed over the exercise training period ($P < 0.05$) (Table 1). The absolute changes in the flow-mediated arterial dilation showed significant linear correlation with the changes in fasting plasma glucose ($r = -0.69$, $P < 0.01$), LDL cholesterol ($r = -0.62$, $P < 0.05$), and HDL cholesterol ($r = +0.88$, $P < 0.001$).

CONCLUSIONS

— Endothelial dysfunction is an important early event in atherogenesis. Impairment of endothelial function in early life could result in abnormal reactions between the vessel wall and platelets, neutrophils, and macrophages, and thus could contribute to the initial stages of atherogenesis (3). The present study showed that the endothelium-dependent arterial dilation in sedentary patients with IFG decreased significantly, and the impaired endothelium-dependent arterial dilation in sedentary patients with IFG was significantly improved over the 6-month exercise training period. Our results are in agreement with other training studies in different patient cohorts (4). As far as we know, this is the first report of an IFG patient cohort.

There is no direct evidence of which mechanisms contribute to the functional improvement of the vasculature in patients with IFG in our study. Most authors have discussed the role of increased shear stress, which affects the vascular nitric oxide (NO) system in many ways (5). Endothelial L-arginine uptake, the substrate of NO production, is increased (6); furthermore, NO synthase gene expression in endothelial cells (7) and NO release of endothelial cells are increased (8). In animals, enhanced NO synthase gene expression, higher NO production, and increased endothelium-dependent dilation of the coronary artery are associated with training (9). Training could have increased the antioxidative capacity by increased expression of the potent antioxidative extracellular enzyme superoxide dismutase, as shown in animal studies, or indirectly by enhanced NO formation (10).

In summary, these results showed that regular aerobic exercise training can improve endothelium-dependent arterial dilation in patients with IFG, although the mechanism for the improvement of endothelium-dependent arterial dilation has not been completely explained.

From the [1]Department of Endocrinology, Guangzhou Command Wuhan General Hospital of the People's Liberation Army, Wuluo Road 627, Wuhan 430070, Hubei Province, China; and the [2]Department of Gerontism, Tongji Hospital, Tongji Medical College, Huazhong Scientific University, Jiefang Road, Wuhan 430030, Hubei Province, China.

Address correspondence and reprint requests to Dr. Xiang Guang-da, Department of Endocrinology, Wuluo Rd. 627, Wuchang 430070, Wuhan, Hubei 430070, China. E-mail: guangda64@163.net.

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Abbreviations: IFG, impaired fasting glucose.

Table 1—*Clinical, biochemical characteristics, and results of brachial artery studies in both control subjects and patients with IFG before and 6 months after exercise training*

	IFG before intervention	IFG after intervention	Control subjects
n	30	22	30
Age (years)	63.0 ± 12	63.6 ± 10	65 ± 11
BMI (kg/m^2)	25.65 ± 1.25	25.07 ± 0.94	25.23 ± 1.12
Fasting plasma glucose (mg/dl)	123.7 ± 1.14*	102.3 ± 1.26†	92.67 ± 1.31
HbA_{1c} (%)	5.74 ± 0.16	5.68 ± 0.14	5.51 ± 0.25
Fasting serum insulin (mU/l)	8.83 ± 1.25	7.92 ± 1.64	7.42 ± 1.59
Mean arterial pressure (mmHg)	104 ± 6	101 ± 8	106 ± 5
Family history (positive/negative)	10/20*	8/14*	2/28
Total cholesterol (mmol/l)	5.44 ± 0.31	5.25 ± 0.33	5.12 ± 0.26
LDL cholesterol (mmol/l)	3.33 ± 0.21*	2.74 ± 0.26†	2.46 ± 0.20
HDL cholesterol (mmol/l)	1.21 ± 0.14*	1.52 ± 0.16†	1.62 ± 0.14
Triglycerides (mmol/l)	1.78 ± 0.80	1.53 ± 0.61	1.42 ± 0.64
Apolipoprotein A1 (g/l)	1.20 ± 0.21	1.22 ± 0.22	1.35 ± 0.31
Apolipoprotein B (g/l)	1.35 ± 0.17	1.28 ± 0.19	1.13 ± 0.14
Lipoprotein (a) (mg/l)	164 ± 62	157 ± 60	147 ± 56
C-reactive protein (mg/l)	0.26 ± 0.14*	0.17 ± 0.15†	0.15 ± 0.13
$V_{O_{2max}}$ (ml · kg^{-1} · min^{-1})	27.4 ± 2.3	32.8 ± 2.5†	29.3 ± 2.1
Baseline vessel (mm)	3.76 ± 0.61	3.73 ± 0.52	3.75 ± 0.46
Baseline flow (ml/min)	84.55 ± 34.71	85.12 ± 32.85	83.79 ± 40.13
Flow-mediated dilation (%)	3.96 ± 0.27	4.86 ± 0.24†	4.72 ± 0.20†
GNT-induced dilation (%)	20.34 ± 1.72	21.38 ± 1.36	21.85 ± 1.18

Data are means ± SD. *$P < 0.05$ compared with control group; †$P < 0.05$ compared with IFG before exercise training. GNT, glyceryltrinitrate.

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