Physical exercise for the prevention and treatment of type 2 diabetes

C. Sanz\textsuperscript{a,b,c,*}, J.-F. Gautier\textsuperscript{d,e,f}, H. Hanaire\textsuperscript{a,b}

\textsuperscript{a} Department of Diabetology, Metabolic Diseases and Nutrition, CHU de Toulouse, 31073 Toulouse, France
\textsuperscript{b} University Toulouse III, 31073 Toulouse, France
\textsuperscript{c} Inserm unit U558, 37, allées Jules-Guesdes, 31073 Toulouse, France
\textsuperscript{d} Department of Diabetes and Endocrinology, hôpital Saint-Louis, Assistance Publique–Hôpitaux de Paris, Paris, France
\textsuperscript{e} University Paris-Diderot Paris 7, Paris, France
\textsuperscript{f} UMR-S Inserm 872, centre de recherche des Cordeliers, University Pierre-et-Marie-Curie, Paris 6, Paris, France

Received 9 June 2010; accepted 14 June 2010
Available online 1 August 2010

Abstract

The prevalence of type 2 diabetes is rapidly increasing worldwide, yet its primary prevention and treatment are still a challenge. The objectives of this review are to assess the effects of exercise on the prevention of type 2 diabetes in high-risk individuals and on glycaemic control in type 2 diabetic patients. Considering the available reports, there is unequivocal and strong evidence that physical exercise can prevent or delay progression to type 2 diabetes in subjects with impaired glucose tolerance. Also, lifestyle interventions, including diet and physical exercise, can result in a reduction of around 50% in diabetes incidence that persists even after the individual lifestyle counselling has stopped. In addition, short-term randomized studies have confirmed that physical training based on endurance and/or resistance exercises can also improve blood glucose control in type 2 diabetics with a mean glycated haemoglobin decrease of 0.6%. Thus, physical exercise should be part of any therapeutic strategy to slow the development of type 2 diabetes in high-risk individuals and to improve glucose control in type 2 diabetes.

Keywords: Diabetes; Exercise; Primary prevention; Glycaemic control; Review

1. Introduction

The prevalence of type 2 diabetes is rapidly increasing worldwide, and the risk of complications begins as early as in the prediabetic phase [1]. Type 2 diabetes is an expensive disease, representing 10–15% of the total health costs in the developed countries [2]. This means that the primary prevention of type 2 diabetes and its early treatment are necessary to avoid the later complications of type 2 diabetes and their related costs. Exercise, in addition to diet modification and medication, has been recommended as one of the three main components of diabetic therapy [3]. The present review aims to assess the effects of exercise in the prevention and treatment of type 2 diabetes.
2. Exercise and the prevention of type 2 diabetes

Both genetic and environmental backgrounds are involved in the development of type 2 diabetes [4]. Although genetic factors are important in the development of type 2 diabetes, it is not possible to modify them to prevent the disease. In the US, the Nurses’ Health Study prospectively examined the separate and combined associations of obesity and physical activity with the development of type 2 diabetes in 68,907 female nurses who had no history of diabetes [5]. Obesity and physical inactivity independently were found to contribute to the development of type 2 diabetes. Using women of a healthy weight (body mass index [BMI] < 25 kg/m²) who were also physically active as the reference group, the relative risks of type 2 diabetes were 16.75 (95% CI: 13.99–20.04) in women who were obese (BMI > 30 kg/m²) and inactive [exercise < 2.1 metabolic equivalent (MET) h/week], and 2.08 (95% CI: 1.66–2.61) in women who were lean, but inactive.

To identify the nature and contribution of environmental influences on type 2 diabetes, Schulz et al. [6] studied two groups of Pima Indians in Mexico and in the US. The two Pima groups shared considerable genetic similarities with each other and with other Native Americans. The age- and gender-adjusted prevalence of type 2 diabetes in the Mexican Pima Indians (6.9%) was less than one-fifth that of the US Pima Indians (38%). Levels of physical activity were considerably higher in the Mexican Pima Indians than in those in the US. Thus, even in populations genetically prone to type 2 diabetes, its development is determined mostly by environmental circumstances, thereby suggesting that type 2 diabetes is largely preventable.

The efficacy of diabetes primary prevention in subjects with impaired glucose tolerance (IGT) has also been tested and there is unequivocal and strong evidence that the progression to type 2 diabetes can be delayed or prevented. This suggests that early lifestyle modifications aimed at diabetes primary prevention may be the best way to avoid later diabetes and its complications.

2.1. Main lifestyle trials of diabetes prevention in high-risk subjects

In lifestyle trials, diabetes primary prevention has been based on lifestyle modifications including exercise and diet. One of the first randomized, controlled, lifestyle trials was conducted in the city of Da Qing in China [7]. In 1986, 577 adults with IGT at 33 clinics in Da Qing were recruited and randomized by clinic into either a control group or one of three lifestyle intervention groups involving diet, exercise and diet plus exercise. The goal of the dietary intervention was to increase the participants’ vegetable intake, and lower their alcohol and sugar intakes. Those who were overweight or obese were also encouraged to lose weight by reducing their total calorie intakes. The goal of the exercise intervention was to increase leisure-time physical activity. The effect of the intervention was assessed every 2 years. The cumulative incidence of diabetes at 6 years was 67.7% (95% CI: 59.8–75.2) in the controls compared with 43.8% (95% CI: 35.5–52.3) in the diet group, 41.1% (95% CI: 33.4–49.4) in the exercise group and 46.0% (95% CI: 37.3–54.7) in the diet-plus-exercise group (P < 0.05). The relative decrease in the progression rate to diabetes in the active-treatment groups was similar when the participants were classified into lean and overweight groups according to BMI (< 25 kg/m² and ≥ 25 kg/m², respectively). Diet and/or exercise interventions led to a significant decrease in the incidence of diabetes over a 6-year period among those with IGT.

The Finnish Diabetes Prevention Study (FDPS) found similar results [8]. The investigators randomly assigned 522 middle-aged overweight subjects (172 men and 350 women; mean age, 55 years; mean BMI, 31 kg/m²) with IGT to either the intervention group or the control group. Each subject in the intervention group received individualized counselling aimed at reducing weight (≥ 5% of body weight), total fat intake (< 30% of energy) and intake of saturated fats (< 10% of energy), while increasing levels of fibre (≥ 15 g/1000 kcal) and physical activity (moderate exercise for ≥ 30 min/day). An oral glucose tolerance test (OGTT) was performed each year, the diagnosis of diabetes was confirmed by a second test and the mean duration of follow-up was 3.2 years. The net weight loss by the end of year 2 was 3.5 ± 5.5 kg in the intervention group and 0.8 ± 4.4 kg in the control group (P < 0.001). The cumulative incidence of diabetes after 4 years was 11% (95% CI: 6–15%) in the intervention group and 23% (95% CI: 17–29%) in the controls. During the trial, the risk of diabetes was reduced by 58% (P < 0.001) in the intervention group.

The US Diabetes Prevention Program (DPP) [9] included a comparison of lifestyle changes with pharmacological intervention by metformin. The investigators randomly assigned 3234 non-diabetics who had raised fasting and postload plasma glucose concentrations to receive either placebo, metformin (850 mg twice daily) or a lifestyle-modification programme aiming to lose at least 7% of body weight and to achieve at least 150 min/week of physical activity. The average follow-up was 2.8 years. The incidence of diabetes was 11.0, 7.8 and 4.8 cases per 100 person-years in the placebo, metformin and lifestyle groups, respectively. The lifestyle intervention reduced disease incidence by 58% (95% CI: 48–66%) and metformin by 31% (95% CI: 17–43) compared with the placebo. Thus, the lifestyle intervention was significantly more effective than drug treatment by metformin.

The Indian Diabetes Prevention Program [10] explored the effect of metformin plus lifestyle interventions on diabetes incidence. This programme recruited 531 subjects with IGT who were randomly assigned to one of four groups: controls; lifestyle modification; treatment with metformin; and a combination of lifestyle modification and metformin. The lifestyle intervention was less intensive than in the DPP or FDPS. Subjects who engaged in physical labour, or walked or cycled for > 30 min/day, or exercised regularly were asked to continue with their usual activities. Subjects who were sedentary or performed only light physical activity were advised and regularly motivated to walk briskly for at least 30 min/day. The dietary intervention consisted of reductions in total calories, refined carbohydrates and fats, with avoidance of sugar and an increase in fibre-rich foods. The relative risk reduction was 28.5% with lifestyle modification (95% CI: 20.5–37.3; P = 0.018), 26.4% with metformin alone.
any of those who achieved four or five of the study goals. Among those who met the success score and incidence of diabetes. Diabetes had not developed in the 10th percentile of weight loss showed a 96% risk reduction in the former. This suggests that those who lose even more weight than the DPP average (5–7%), and who meet physical activity and dietary fat goals, could reduce their diabetes risk by more than 90%. A smaller proportion of fat calo-
ries and increased physical activity was predictive of weight loss, and increased physical activity was important in helping to sustain such weight loss. Among the 495 participants not meeting the weight loss goal at 1 year, those who achieved the physical-activity goal still managed to have a 44% lower diabetes incidence.

Similar results were found in the FDPS [8]. Study subjects were ranked according to their success in achieving intervention goals using a success score ranging from 0 to 5 at the 1-year examination, with higher scores indicating more goals met. There was a strong inverse correlation between the success score and incidence of diabetes. Diabetes had not developed in any of those who achieved four or five of the study goals. Among those in the intervention group who failed to reach the goal of losing 5% of their initial weight, the odds ratio for diabetes in those who at least achieved the exercise goal (> 4 h/week) during year 1 was 0.2 (95% CI: 0.1–0.6) compared with those who maintained a sedentary lifestyle. Consequently, weight reduction appears to be an important component, but exercise itself leads to a reduction in type 2 diabetes risk. Similarly, in the Indian Diabetes Prevention Program [10] and Chinese Diabetes Prevention Study [7] the participants were relatively lean, and no large changes in body weight were seen, there was nevertheless a remarkable reduction in diabetes risk.

In the Chinese Prevention Study [7], exercise alone was compared with exercise plus diet. In the proportional-hazards analysis adjusted for differences in baseline BMI and fasting glucose, the exercise and diet-plus-exercise interventions were associated with similar reductions in the risk of developing diabetes (46 and 42%, respectively).

Despite the need for more studies exploring the effect of exercise alone, physical exercise is one of the best ways to prevent type 2 diabetes in high-risk populations. However, in most of these trials, exercise coaching was important. In the DPP [8], a 16-lesson curriculum covering diet, exercise and behavioural modification was designed to help the participants achieve these goals during the first 24 weeks after enrolment. After this time, substantial individual sessions (usually monthly) and group sessions with case managers were designed to reinforce the behavioural changes. The need for strong coaching to make people changing their lifestyles appears to be the main limitation to implementation of prevention trials in the general population.
of active intervention persisted for two decades. The Chinese participants with IGT randomized to the lifestyle-intervention groups had a 43% lower diabetes incidence (age- and clinic-adjusted) for up to 14 years after the active intervention had ceased, and diabetes onset was delayed by an average of 3.6 years. In the FDPS [15], the beneficial lifestyle changes achieved by participants in the intervention group were maintained after discontinuation of the intervention, and the corresponding incidence rates during the postintervention follow-up were 4.6 and 7.2 (P = 0.0401), indicating a 36% reduction in relative risk.

Lifestyle interventions in those at high risk for type 2 diabetes resulted in sustained lifestyle changes and a reduction in diabetes incidence that persisted even after individual lifestyle counselling had stopped. It is worth noting that in most of the studies, the participants who initially lost weight gradually regained it, although they still weighed less than they did at the time of study randomization.

3. Exercise for the treatment of type 2 diabetes

3.1. Main effects of exercise

Exercise, in addition to diet modification and medication, has been recommended as one of the three main components of diabetic therapy [3]. In spite of its recommendation, the effects of exercise in type 2 diabetics are not well documented, and there have been no large-scale studies with adequate statistical power to determine the effects of exercise on blood sugar control in type 2 diabetes. However, a meta-analysis was conducted on behalf of the Cochrane Collaboration [16] to assess the effects of exercise in type 2 diabetes. The studies selected for the meta-analysis were all randomized controlled trials with a duration of intervention of >8 weeks, and the only difference between the intervention and comparison groups was a well-documented exercise programme (aerobic fitness or progressive resistance-training exercise). Fourteen randomized controlled trials were included, involving 377 participants and lasting for eight weeks to 12 months. The duration of the individual exercise sessions varied from at least 30 min for resistance training to 120 min for a Qi Gong programme. Most interventions involved at least three sessions per week with exercise on non-consecutive days. Compared with the controls, the exercise interventions significantly improved glycaemic control, as indicated by a decrease in glycated haemoglobin levels of 0.6% (95% CI: −0.9 to −0.3; P < 0.05). This result was both statistically and clinically significant. The decrease of 0.6% HbA1c was achieved over relatively short periods of time, as the shortest studies in the review lasted only 8 weeks, and only two studies with interventions continued for 6 months or more. Analyses of subgroups showed a trend towards a slightly more pronounced effect on glycaemic control in the shorter-duration trials, which was probably a reflection of the higher intensity of exercise in some of the shorter trials, as well as the difficulty of maintaining compliance with exercise regimens in longer-term studies. However, there was no significant difference between groups in whole body mass. Visceral adipose tissue decreased with exercise (−45.5 cm²; 95% CI: −63.8 to −27.3), and subcutaneous adipose tissue was also reduced, and participants in the exercise groups were likely to have developed muscle, which is heavier than adipose tissue. Nevertheless, no study reported adverse effects or any diabetic complications in the exercise group. Thus, exercise interventions significantly increased insulin response (area under the curve [AUC]: 131; 95% CI: 20–242). Table 2 summarizes the main results of the meta-analysis.

3.2. Effects of exercise on cardiovascular risk factors

In the Cochrane Collaboration meta-analysis [16], there was also a significant reduction in plasma triglycerides (−0.25 mmol/L; 95% CI: −0.48 to −0.02) in the exercise group compared with the controls, but no significant differences between groups in either total cholesterol or blood pressure. Physical activity appears to be a protective factor against cardiovascular disease in the general population. INTERHEART [17], a large-scale international, standardized, case-control study, was designed as an initial step in the worldwide assessment of the importance of risk factors for coronary heart disease. This study showed that nine easily measured and potentially modifiable risk factors account for a large (>90%) proportion of the risk for an initial acute myocardial infarction (MI). Smoking, a raised ApoB-to-ApoA1 ratio, a history of hypertension, diabetes, abdominal obesity and psychosocial factors were all found to be related to an increased risk of MI. On the other hand, daily consumption of fruit and vegetables, regular alco-
hol consumption and regular physical activity were all related to a decreased risk of MI. Individuals were considered to be physically active if they were regularly involved in moderate or strenuous exercise for 4 h or more a week, and such regular physical activity decreased the odds ratio for acute MI to 0.86 (95% CI: 0.76–0.97) after adjusting for other cardiovascular risk factors.

3.3. What kind of exercise is to be recommended?

The American Diabetes Association provides standards of medical care for diabetes and recommends physical exercise in the treatment of type 2 diabetes [3]. People with diabetes are advised to perform at least 150 min/week of moderate-intensity aerobic physical activity (at 50–70% of maximum heart rate). In the absence of contraindications, those with type 2 diabetes are also encouraged to perform resistance training three times a week. Resistance exercise improves insulin sensitivity to about the same extent as does aerobic exercise [18]. Dunstan et al. [19] assessed the effects of resistance training in older patients with type 2 diabetes in a 6-month randomized controlled clinical trial, with repeated measurements at 3-month intervals. Twenty-nine subjects were randomly assigned to a programme of either high-intensity progressive resistance training plus moderate weight loss or moderate weight loss plus flexibility exercise (controls). During the intervention period, all subjects attended the exercise laboratory on 3 non-consecutive days per week. Resistance training consisted of a 5-min warm-up before and a 5-min cool-down after low-intensity stationary cycling and 45 min of high-intensity resistance training (dynamic exercise involving concentric and eccentric contractions). HbA1c fell significantly more in the resistance-training group than in the control group at 3 months (0.6 ± 0.7% vs 0.07 ± 0.8%; P < 0.05) and at 6 months (1.2 ± 1.0% vs 0.4 ± 0.8%; P < 0.05). Similar reductions in body weight (on average, 2.5 kg) were observed after 6 months. In contrast, lean body mass increased in the resistance-training group (0.5 ± 1.1 kg) and decreased in the control group (0.4 ± 1.0 kg) after 6 months.

Another study aimed to determine the effects of aerobic training alone, resistance training alone and combined aerobic–resistance training on HbA1c values in patients with type 2 diabetes [20]. The study included 251 participants randomly allocated to the aerobic training, resistance training, combined training and control groups. Exercise-group participants exercised three times a week for 22 weeks. The aerobic-training group used treadmills or bicycle ergometers, and the resistance-training group performed seven different exercises on weight machines at each session, progressing to two to three sets of each exercise at the maximum weight that could be lifted seven to nine times. The absolute changes in HbA1c values compared with the controls were −0.51% (95% CI: −0.87 to −0.14) in the aerobic-training group and −0.38% (95% CI: −0.72 to −0.22) in the resistance-training group. The combined exercise training resulted in an additional change in HbA1c of −0.46% (95% CI: −0.83 to −0.09) compared with aerobic training alone, and of −0.59% (95% CI: −0.95 to −0.23) compared with resistance training alone.

Thus, these clinical trials provide strong evidence for the HbA1c-lowering effect of resistance training in older adults with type 2 diabetes [19], as well as for the additional benefits of combined aerobic and resistance exercise in adults with type 2 diabetes [20]. However, patients in the combined exercise group also had twice as many sessions of exercise as did the other exercise groups. Thus, the study does not permit definitive conclusions about whether the benefits were due to longer exercise duration or to the combined exercise training.

4. Conclusion

Physical exercise is an efficient tool for the prevention and treatment of type 2 diabetes and should, therefore, be part of any therapeutic strategies for such patients. In those at high risk of developing type 2 diabetes, lifestyle interventions, including diet and physical exercise, results in a 50% reduction in diabetes incidence that persists for several years after the supervised lifestyle intervention has stopped. Because of the growing prevalence of high-risk patients worldwide and the need for strong coaching to make people to change their lifestyles, the implementation of prevention trials in the general population clearly requires the involvement of the entire public-health system. Several studies have demonstrated both the efficacy of physical exercise in achieving a significant decrease in HbA1c and the clinically relevant improvement of glycaemic control in those with type 2 diabetes. Interventions in which the exercise prescription involved a variety of activities were as effective as those based on a single mode of exercise. However, using different

Table 2
Main results of a meta-analysis [16] assessing the effects of exercise in type 2 diabetes.

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Studies (n)</th>
<th>Participants (n)</th>
<th>Mean difference [95% CI]</th>
<th>Significance (P&lt;0.05)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glycated haemoglobin (%)</td>
<td>13</td>
<td>361</td>
<td>−0.62 [−0.91, −0.33]</td>
<td>Yes</td>
</tr>
<tr>
<td>Visceral adipose tissue (cm²)</td>
<td>2</td>
<td>40</td>
<td>−45.5 [−63.7, −27.3]</td>
<td>Yes</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>10</td>
<td>248</td>
<td>−0.04 [−3.83, 3.76]</td>
<td>No</td>
</tr>
<tr>
<td>VO₂max [mL/(kg × min)]</td>
<td>3</td>
<td>95</td>
<td>4.84 [2.55, 7.12]</td>
<td>Yes</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>4</td>
<td>127</td>
<td>−4.16 [−9.46, 1.14]</td>
<td>No</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>3</td>
<td>78</td>
<td>−0.13 [−3.70, 3.45]</td>
<td>No</td>
</tr>
<tr>
<td>Triglycerides (mmol/L)</td>
<td>5</td>
<td>139</td>
<td>−0.25 [−0.48, −0.02]</td>
<td>Yes</td>
</tr>
<tr>
<td>HDL cholesterol (mmol/L)</td>
<td>5</td>
<td>139</td>
<td>−0.02 [−0.10, 0.06]</td>
<td>No</td>
</tr>
<tr>
<td>LDL cholesterol (mmol/L)</td>
<td>5</td>
<td>139</td>
<td>0.12 [−0.29, 0.53]</td>
<td>No</td>
</tr>
</tbody>
</table>

HDL: high-density lipoprotein; LDL: low-density lipoprotein.
kinds of physical training may be the key to making the exercise more acceptable to people, thereby increasing the sustainability of the exercise required to achieve and maintain longer-term health benefits.

Conflict of interest statement

The authors have not declared any conflicts of interest.

References