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Clinical aspects of physical exercise for diabetes/metabolic syndrome

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Abstract

Evidence-based medicine (EBM) has come to be regarded as essential in all fields of medical sciences and practical medicine. In the field of diabetes and exercise, among the epidemiological studies of physical exercise, recent mega-trials such as the Diabetes Prevention Program (DPP) in the U.S. have shown that lifestyle intervention programs involving diet and/or exercise reduce the progression of impaired glucose tolerance (IGT) to type 2 diabetes. In studies examining the endocrinological and metabolic effects of exercise, it has been demonstrated that physical exercise promotes the utilization of blood glucose and free fatty acids in muscles and lowers blood glucose levels in well-controlled diabetic patients. Long-term, mild, regular jogging increases the action of insulin in both carbohydrate and lipid metabolism without influencing body mass index or maximal oxygen uptake. A significant correlation has been observed between delta MCR (Δinsulin sensitivity) and the average number of steps performed in a day. Our recent data suggested that the improved effectiveness of insulin that occurs as a result of physical exercise is attributable, at least in part, to increases in GLUT4 protein, IRS1 and PI3-kinase protein in skeletal muscle. As a prescription for exercise, aerobic exercise of mild to moderate intensity, including walking and jogging, 10–30 min a day, 3–5 days a week, is recommended. Resistance training of mild intensity with the use of light dumbbells and stretch cords should be combined in elderly individuals who have decreased muscle strength. An active lifestyle is essential in the management of diabetes, which is one of typical lifestyle-related diseases.

Keywords: Diabetes; Metabolic syndrome; Physical exercise; Euglycemic clamp; Insulin resistance

1. Introduction

Evidence-based medicine (EBM) is an important component of medical care and research. In the field of exercise therapy for diabetes and obesity/metabolic syndrome, the results of a number of large-scale epidemiological follow-up studies have demonstrated that weight loss resulting from lifestyle modification, including physical exercise, is useful for decreasing the development of type 2 diabetes among obese people with impaired glucose tolerance (IGT). The mechanisms of the effects of physical exercise in muscles and adipose tissues after physical training have been elucidated by molecular biological approaches.

These and other studies have accumulated evidences that suggest the usefulness of physical exercise for the prevention and the treatment of diabetes and obesity/metabolic syndrome.

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The Japanese Ministry of Health, Labor and Welfare has emphasized the concept of lifestyle-related diseases, including type 2 diabetes, obesity, hypertension, etc. In addition, Health Japan 21, a large-scale project limed at decreasing diabetes and other lifestyle-related diseases has been enacted. This project aims to prolong active lifespan by reducing obesity and other risk factors through physical activity/exercise and modification of nutrition/eating habits, and other component of lifestyles. As a legal basis for this program, the Health Promotion Law was enacted in May 2003 [1,2].

2. Physical activity and diabetes/metabolic syndrome: results of epidemiological studies

2.1. Increased insulin resistance caused by lack of exercise

In Japan and Korea, most diabetic patients are type 2 (non-insulin dependent). Decreased insulin secretion and insulin resistance play important roles in occurrence and progression of type 2 diabetes. Insulin resistance is exacerbated by aspects of modern westernized lifestyle such as overeating (high fat diet), sedentary state and stressful daily life.

Lack of physical exercise induces insulin resistance results in compensatory hyperinsulinemia, leading to type 2 diabetes, hypertension, hyperlipidemia, and atherosclerosis, as well as obesity, playing an important role in the development and progression of pathological conditions known as syndrome X, multiple-risk-factor syndrome, the deadly qualtet, the insulin-resistance syndrome and the visceral-fat syndrome [1,2]. Recently, notion of metabolic syndrome has been introduced by WHO and Japanese Society of Internal Medicine [3].

2.2. Prevention of type 2 diabetes and the role of physical exercise

The results of various follow-up studies have revealed that the proper diet combined with physical exercise is not only useful in preventing type 2 diabetes and improving disease status but is also effective in the prevention and treatment of all other insulin-resistance-related diseases (lifestyle-related diseases/metabolic syndrome), by improving in vivo sensitivity to insulin [1].

(1) The incidence of diabetes decreases by 6% with every 500 kcal/week increase in energy consumption in leisure-time physical exercise (Paffenbarger Study, USA, 1994).
(2) Although patients with impaired glucose tolerance are at high risk for type 2 diabetes and death from coronary disease, the implementation of dietary counseling and physical exercise lead to the decrease in the mortality of IGT patients to the level of individuals with normal glucose tolerance (Malmö Study, Sweden 1998) [4].
(3) The incidence of diabetes mellitus in IGT patients decreased by 31% during a 6-year period when diet therapy alone was prescribed, by 46% when exercise therapy alone was prescribed, and by 42% when a combination of diet and exercise therapy was prescribed (Da Qing Study, China, 1997) [5].
(4) Positive modification of lifestyle habits concerning diet and exercise has a greater suppressive effect on the development of diabetes than that of the oral antihyperglycemic agent metformin (58% versus 31%) (Diabetes Prevention Program, DPP; USA, 2002) [6].

Although the results of intervention trials have been reported from various countries, few studies of this kind have been carried out in the field of diabetes prevention in Japan. Data from the JDPP (Director: Dr. Kuzuya H., National Kyoto Hospital) have been awaited.

3. Metabolic and endocrinological effects of physical exercise

3.1. Acute metabolic effect

(1) In patients in whom metabolic regulation is well maintained, exercise promotes the use of glucose and free fatty acids (FFA) in muscles. Therefore, physical exercise combined with dietary restriction has beneficial effects for prevention and treatment of metabolic syndrome/obesity. And exercise after meals by diabetic patients with relatively good glucose control may lead to better control of diabetes by suppressing the rapid postprandial elevation of blood glucose [2].
(2) High-intensity exercise may aggravate abnormal carbohydrate metabolism through increased secretion of insulin-counter regulatory hormones such as glucagon and catecholamine. When diabetes is poorly controlled, secretion of these counter regulatory hormones is further increased. If diabetic control is extremely poor, physical exercise is contraindicated.
(3) The implementation of moderate-intensity exercise [relative intensity up to about 50% of maximum oxygen uptake ($V_{O_{2max}}$)] for several minutes causes increased utilization of carbohydrate and FFA as

muscle energy sources. However, as exercise intensity increases above the lactate threshold (LT), the ratio of carbohydrate utilization increases, and maximal exercise (anaerobic exercise) depends on the glycolytic pathway, using only glucose, not lipid, as the source of energy [2].

In physical exercise therapy for diabetes and metabolic syndrome/obesity, it is necessary to elevate the rate of utilization of fat stored in adipose tissue, in addition to muscle training. Therefore, exercise of moderate or lower intensity (LT level) is preferable [1].

3.2. Training effect

3.2.1. Physical exercise and insulin sensitivity

(1) Even mild physical exercise that does not affects $V_{O_{2max}}$ can cause improvement in the in vivo insulin sensitivity if continued for a prolonged period of time (Fig. 1). The implementation of dietary restriction and physical exercise in obese people and obese patients with type 2 diabetes will result in a elective decrease of body fat, leading to weight loss, while causing no changes in lean body mass (LBM). Thus, dietary restriction combined with physical exercise is more useful for improving insulin sensitivity than dietary restriction alone (Fig. 2). In addition, increase in glucose metabolic clearance rate (ΔMCR) shows a positive correlation with the number of steps performed per day determined by a pedometer [7].

(2) Aerobic exercise such as jogging is more useful in improving in vivo insulin sensitivity than anaerobic exercise like weightlifting [2]. However, mild resistance training, if carry out in an aerobic manner, is also useful for elderly patients who have decreased muscular strength and mass [8,9].

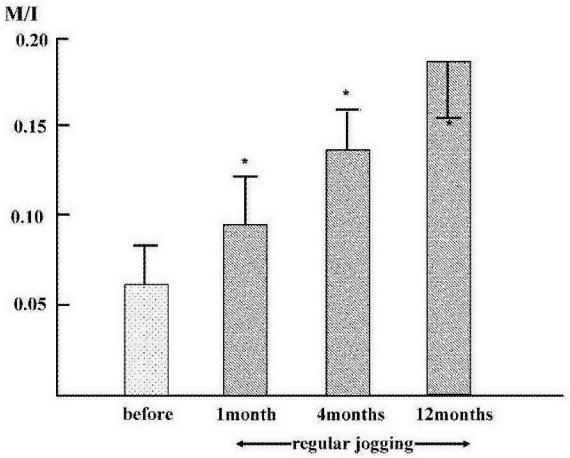

Fig. 1. Changes in ratio of glucose metabolism (M) to steady-state insulin levels (I) during euglycemic clamp before and after long-term regular jogging. Values before and after regular jogging were compared using a one-way analysis of variance and were significantly different. $^{*}P < 0.05$ [15].

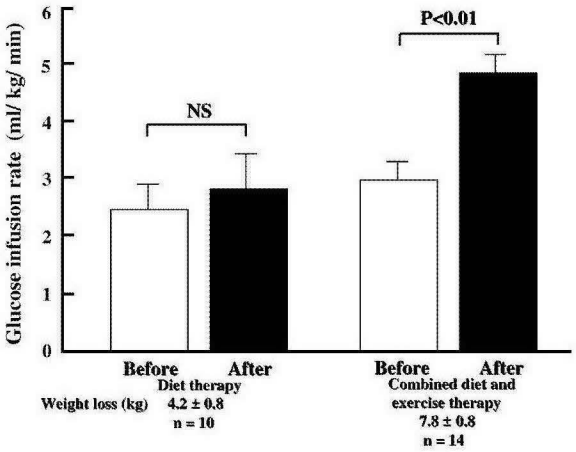

Fig. 2. Changes in insulin sensitivity (glucose infusion rate) in patients on diet therapy alone and on combined diet and exercise therapy (Yamanouchi et al., 1995).

(3) Low intensity exercise using the horseback riding therapeutic equipment (Joba®) might be useful as an auxiliary therapy for the treatment of insulin resistance in type 2 diabetes and obesity [10].

(4) Visceral fat, rather than subcutaneous fat, promotes the formation of insulin-resistance-related atherosclerosis. Physical exercise combined with dietary restriction decreases visceral fat [1]. On the other hand, absence of an effect of liposuction from abdominal subcutaneous adipose tissue on insulin action and risk factors for coronary heart disease was reported [11].

(5) The implementation of exercise brings about a decrease in plasma triglyceride level, an increase in high-density lipoprotein (HDL) cholesterol, and improvement of mild hypertension. Thus, physical exercise exerts an inhibitory effect on the development and progression of atherosclerosis through a number of mechanisms [1].

(6) Continued physical exercise increases basal metabolic ratio (BMR), which tends to decrease with dietary restriction, and diet-induced thermogenesis (DIT) in obese individuals [1].

(7) Implementation of physical exercise improves physical fitness.

(8) Physical exercise can improve blood glucose control in patients with type 2 diabetes, as mentioned above. However, since metabolic status can vary on a daily basis in patients with type 1 diabetes mellitus, the effect of physical exercise is not necessary constant.

3.2.2. Mechanisms of training effects

(1) Improved insulin sensitivity is the major beneficial effect of exercise. Muscular factors including postreceptor steps, such as muscle weight gain, glycolytic pathway in muscle, increase in enzyme activity in the tricarboxylic acid (TCA) cycle, and increase in glucose signal transductions (Fig. 3), play major roles in its manifestation [2,12].
(2) Adipose tissue factors such as decreases in body fat and the size of fat tissue decreases, plasma TNF-α levels secreted from adipose tissue may decrease and secretion of adiponection increase, resulting in improved in vivo insulin sensitivity [1,13].

4. Practical aspects of prescribed exercise

4.1. Indications of physical exercise and medical check-up

Before patients undertake programs of physical exercise, various medical examinations are needed to determine that diabetes is in the good controlled condition and diabetic patients do not have progressive severe complications.

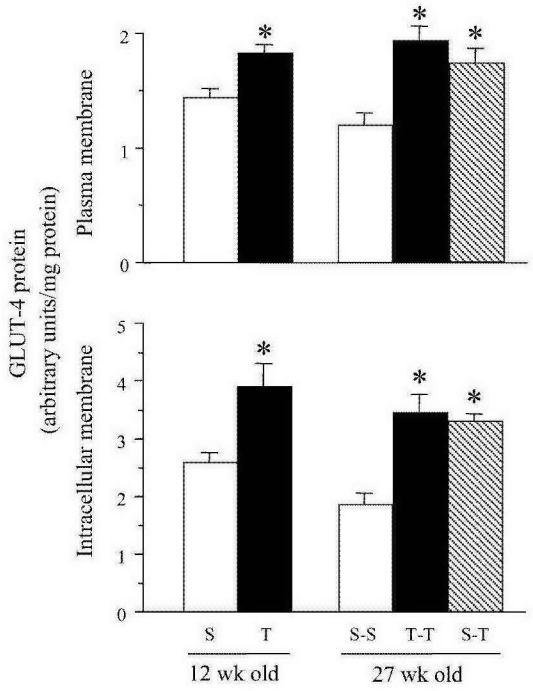

Fig. 3. Concentration of GLUT-4 protein in skeletal muscle plasma membrane (top) and intracellular membrane (bottom) for 12-week-old sedentary (S) and exercise-trained (T) rats; and for 27-week-old sedentary rats (S-S) and rats allowed to exercise before maturation (T-T) and after maturation (S-T). Signals of immunoreactive GLUT-4 were measured with a Bio Imaging analyzer. Values are means ± S.E. for six rats. *Significant difference from sedentary rats at same age. $^{*}P < 0.05$ (Nakai et al., 1996).

4.2. Type and intensity of exercise

The effect of exercise that manifests in improved insulin sensitivity decreases within 3 days after exercise, and is no longer apparent after 1 week [14]. Free fatty acids produced from lipolysis through physical exercise are converted to acetyl coenzyme A (CoA) via β-oxidation, and are metabolized in the tricarboxylic acid cycle. Therefore, it is easy to understand why the exercises prescribed for exercise therapy are restricted to those of an aerobic nature.

Specifically, moderate-intensity exercise that results in $V_{O_{2max}}$ of about 50% (pulse rate of about 120 min^{-1} for those in their 50 s or younger and about 100 min^{-1} for those in their 60 and 70 s, LT level) should be performed for 10–30 min at a time (2–3 times a day, preferably after meals), at least 3–5 days a week. Recommended types of exercise are aerobic exercise that use muscles throughout the body, such as walking, jogging, radio gymnastic exercises, stationary bicycle exercise, and swimming. For the elder diabetic patients with tendency of muscle atrophy, mild resistance training such as light dumbbells exercise and half squat should be performed in addition to aerobic exercise. The horseback riding equipment (Joba®) is also useful for aged patients and patients with knee or foot disorders [10].

Type 2 diabetes is a typical lifestyle-related disease. It is necessary to instruct patients to incorporate some exercise into their daily life, e.g., getting off the bus at a stop before the destination and walking the rest of the way. The use of a pedometer and the Lifecorder® are useful for motivating patients and for determining how much exercise has been performed. The recorded figures should be checked during regular inpatient rounds or in the outpatient clinic, with the goal set at 10,000 steps (or at least 7500 steps) per day [2].

4.3. Precautions in implementing physical exercise

(1) If diet therapy is not followed, good controlled condition of blood glucose will not be achieved. Dietary restriction should be instructed.
(2) Usually, exercise should be performed after meals.
(3) In patients on insulin therapy, the insulin dose should be reduced prior to physical exercise. If exercise extends over a prolonged period of time, dietary supplementation is necessary before, during, and after exercise. If hypoglycemia occurs during exercise, a cola drink or glucose (pet sugar)

Table 1
Yardsticks of energy consumption during exercise

Intensity of exercise	Times required per unit exercise	Type of exercise (energy consumption, kcal/kg/min)
Very low	Exercise continued for about 30 min to achieve 1 unit	A stroll (0.0464), on a vehicle: standing in a train or bus (0.0375), cooking (0.0481), housework: laundry, cleaning (0.0471–0.0499), general clerical work (0.0304), shopping (0.0481), gymnastic exercise: low intensity (0.0552)
Low	Exercise continued for about 20 min to achieve 1 unit	Walking: 70 m/min (0.0623), bathing (0.0606), stairs: descending (0.0658), radio gymnastic exercise (0.0552–0.1083), bicycle: level ground (0.0658), and golf [males (0.0640), females (0.0500)]
Moderate	Exercise continued for about 10 min to achieve 1 unit	Jogging: mild (0.1384), stairs: ascending (0.1349), bicycle: slope (0.1472), cross-country skiing (0.0782–0.1348), skating (0.1437), volleyball (0.1437), mountain climbing (0.1048–0.1508), tennis: practice (0.1437)
High	Exercise continued for about 5 min to achieve 1 unit	Marathon running (0.2959), rope skipping (0.2667), basketball (0.2588), rugby: forward (0.2234), swimming: breaststroke (0.1968), kendo (0.2125)

Note: A single unit corresponds to about 80 kcal. It should be used as a yardstick for supplementary feeding in diabetic patients on insulin therapy.

dissolved in lukewarm water should be taken. Cookies, cheese, and milk are suitable before and after exercise to prevent hypoglycemia. Table 1 provides a guide to food intake.

(4) General precautions including the use of sports shoes and incorporation of warm-up and cool-down exercises should be given.

5. Conclusion

Evidences for the usefulness of physical exercise for diabetes and obesity/metabolic syndrome have been described, with an outline of the practical aspects of exercise prescription. Higher quality guidance in physical exercise should be expected, particularly in term of EBM, i.e., based on the rationale derived from recent experimental and clinical studies.

Acknowledgments

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