Can Physical Activity Reduce the Need of Medications for Diabetes Mellitus Management?

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Abstract

Diabetes Mellitus is considered a major chronic disease and its complications have become a main cause of morbidity and mortality worldwide. The goal of treatment in type 2 diabetes is to achieve and maintain optimal blood glucose (BG), lipid, and blood pressure (BP) levels to prevent or delay chronic complications of diabetes. Many people with type 2 diabetes can achieve BG control by following a nutritious meal plan and exercise program, losing excess weight, implementing necessary self-care behaviors, and taking oral medications, although others may need supplemental insulin. Recently, studies have started to focus on the relationship between exercise and Insulin dependent Diabetes Mellitus (IDDM). Several studies have shown reduced insulin dosage with increased physical activity along with better glycemic control. In fact, moderate to vigorous activity has been associated with greater overall fitness, an increased fat free mass, and decreased glycosylated hemoglobin (HbA1c) levels in people with type 1 DM. That exercise could act by protecting islets during the onset of the disease, because in animal models of type 2 DM, long-term aerobic exercise resulted in increased islet β-cell proliferation, increased β-cell mass, and a partial sparing of the abnormal islet morphology noted in the sedentary diabetic rats. Exercise blocked the age-associated morphological changes in the pancreas, including multi lobulated, fibrotic islets. BG reductions are related to the duration and intensity of the exercise, pre exercise control, and state of physical training. Although previous PA of any intensity generally exerts its effects by enhancing uptake of BG for glycogen synthesis and by stimulating fat oxidation and storage in muscle, more prolonged or intense PA acutely enhances insulin action for longer periods. Women diagnosed with GDM are at substantially increased risk of developing type 2 diabetes; therefore, PA may be considered a tool to prevent both GDM and possibly type 2 diabetes at a later date.

Keywords: Diabetes; Type 1 Diabetes; Type 2 Diabetes; Gestational diabetes; Exercise; Physical activity

Introduction

Diabetes Mellitus is considered a major chronic disease and its complications have become a main cause of morbidity and mortality worldwide. T2DM is defined by impaired glucose tolerance, chronic hyperglycemia, altered insulin secretion, and complications that come from induction of oxidative stress [1].

The goal of treatment in type 2 diabetes is to achieve and maintain optimal blood glucose (BG), lipid, and blood pressure (BP) levels to prevent or delay chronic complications of diabetes [2]. Many people with type 2 diabetes can achieve BG control by following a nutritious meal plan and exercise program, losing excess weight, implementing necessary self-care behaviors, and taking oral medications, although others may need supplemental insulin [3]. Diet and physical activity (PA) are central to the management and prevention of type 2 diabetes because they help treat the associated glucose, lipid, BP control abnormalities, as well as aid in weight loss and maintenance. When medications are used to control type 2 diabetes, they should augment lifestyle improvements, not replace them.

Recently, studies have started to focus on the relationship between exercise and Insulin dependent Diabetes Mellitus (IDDM). In general, several studies have shown reduced insulin dosage with increased physical activity [4] along with better glycemic control [5]. In fact, moderate to vigorous activity has been associated with greater overall fitness, an increased fat free mass, and decreased glycosylated hemoglobin (HbA1c) levels in people with type 1 DM [6,7]. In a randomized study of 196 adults with type 1 DM, those that exercised moderately once to three times per week significantly reduced the HbA1c levels and insulin requirements. In another study, which was even more convincing, is a large cross-sectional study of over 19,000 children with type 1 DM, finding that the amount of physical activity was one of the strongest factors predicting lower HbA1c values [8]. However, little is known about the mechanism of action to explain the lowered the levels of blood glucose with exercise. The impact of exercise on blood glucose can be explained by the following:

- There are two general sites where exercise could directly affect blood glucose (BG) regulation:
  1. Insulin secretion of the islets.
  2. Insulin-stimulated glucose uptake in the skeletal muscle [9-11]. There are couple of papers that have directly examined the first possibility: changes in insulin levels with exercise in type 1 DM. Unfortunately, the only assay used was an immunohistochemical measurement of the number of hormone-positive cells in the islets of exercised diabetic rats [12,13]. Clearly, more must be done to begin to unravel the cellular changes occurring in islets with exercise training.

Joslin, in the 1950s first suggested that exercise should be an essential component to regulate blood glucose levels of people with type 1 DM, along with a restricted diet and insulin therapy [14]. Yet, today the mechanisms by which exercise regulates blood glucose in conditions of...
type 1 DM are not explained. In the 1980s, classic work by Reaven and Chang showed that exercised rats with T1D had lower plasma glucose and triglyceride levels than their sedentary counterparts [15].

They hypothesized that the results were due to improved peripheral insulin sensitivity; however, no direct measure of islet mass or insulin content was reported is the first to measure exercise-induced increases in insulin content and secretion in isolated islets from diabetic animals. That exercise could act by protecting islets during the onset of the disease, because in animal models of type 2 DM, long-term aerobic exercise resulted in increased islet β-cell proliferation, increased β-cell mass, and a partial sparing of the abnormal islet morphology noted in the sedentary diabetic rats [16]. Exercise blocked the age-associated morphological changes in the pancreas, including multi lobulated, fibrotic islets [17]. In addition, aerobic exercise decreased the presence of proinflammatory cytokines in islet cells [18], but did not change the islet gene expression pattern in type 2 Zucker diabetic fatty rats [19].

Morphological examination of the islets from our exercised-trained mice failed to demonstrate differences compared to the sedentary diabetic group. Our findings are similar to a previous report investigating the effect of exercise on the distribution of α-, β-, and δ-cells and pancreatic polypeptide cells in the islets of streptozotocin-induced diabetic rats [12]. Conversely, another study focused on β-cell health and exercise in type 1 DM concluded that exercise partially spared the β-cells from diabetes [13]. A difference between the exercise protocols may explain the discordant results. In our protocol and the previous paper by Howarth et al., which showed no change in β-cell numbers, the exercise protocol was initiated after the induction of diabetes [12]. In the Coskun et al. study, the aerobic exercise protocol was initiated four weeks prior to the induction of diabetes and the exercise continued for another eight weeks to the termination of the experiment [13]. Thus, exercise may be able to protect β-cells if initiated prior to the onset of the disease but has limited or no ability to rescue the β-cells once lost. In conclusion, this is the first time that insulin content and secretion -cells if initiated prior to the onset of the disease but has limited or no ability to rescue the β-cells once lost. From these findings, it appears that exercise has a protective effect on β-cell function and mass, and a partial sparing of the abnormal islet morphology noted in the sedentary diabetic rats [12].

During moderate-intensity exercise in nondiabetic persons, the rise in peripheral glucose uptake is matched by an equal rise in hepatic glucose production, the result being that BG does not change except during prolonged, glycogen-depleting exercise. In individuals with type 2 diabetes performing moderate exercise, BG utilization by muscles usually raises more than hepatic glucose production, and BG levels tend to decline [20]. Plasma insulin levels normally fall, however, making the rise of exercise-induced hypoglycemia in anyone not taking insulin or insulin secretagogues minimal, even with prolonged PA. Most benefits of PA on type 2 diabetes management and prevention are realized through acute and chronic improvements in insulin action [21-25]. The acute effects of a recent bout of exercise account for most of the improvements in insulin action, with most individuals experiencing a decrease in their BG levels during mild- and moderate-intensity exercise and for 2-72 h afterward [8,26,27].

BG reductions are related to the duration and intensity of the exercise, preexercise control, and state of physical training [8,11,20,21,28]. Although previous PA of any intensity generally exerts its effects by enhancing uptake of BG for glycogen synthesis [16,26,29] and by stimulating fat oxidation and storage in muscle [4,30,31], more prolonged or intense PA acutely enhances insulin action for longer periods [30,32-36].

During exercise, AMP is produced which stimulates AMPK enzyme. AMPK is an evolutionary conserved sensor of cellular energy status that is activated during exercise [37]. Pharmacological activation of AMPK promotes glucose uptake, fatty acid oxidation, mitochondrial biogenesis, and insulin sensitivity resulting in decrease in BG levels [32]. Exercise promotes glucose uptake by an insulin dependent mechanism involving AMPK. Exercise is important for improving insulin sensitivity; however, it is not known if AMPK is required for these improvements.

Participation in regular PA improves BG control and can prevent or delay onset of type 2 diabetes [31,38-42]. Prospective cohort and cross-sectional observational studies that assessed PA with questionnaires showed that higher PA levels are associated with reduced risk for type 2 diabetes, regardless of method of activity assessment, ranges of activity categories, and statistical methods [43-45]. Both moderate walking and vigorous activity have been associated with a decreased risk, and greater volumes of PA may provide the most prevention [46]. Observational studies have reported that greater fitness is associated with a reduced risk of developing type 2 diabetes [47,48], even if only moderate-intensity exercise is undertaken.

Women diagnosed with GDM are at substantially increased risk of developing type 2 diabetes; therefore, PA may be considered a tool to prevent both GDM and possibly type 2 diabetes at a later date [49]. Prepregnancy PA has been consistently associated with a reduced risk of GDM [50-54]. Studies during pregnancy are sparse, with only one case-control study [55], one retrospective study [56], and one study of a cohort of Hispanic women [57] observing significant protective effects of PA, while others have not [51-53,58]. Engaging in min 30 min of moderate-intensity PA (e.g., brisk walking) during most days of the week (e.g., 2.5 h/week) has been adopted as a recommendation for pregnant women without medical or obstetrical complications. However, few primary prevention studies have examined whether making a change in PA reduces risk of developing GDM [59]. Only moderate intensity and duration of activity are needed to be effective in preventing diabetes. Three to five times/week, spaced at no more than 48-hour intervals, 15-60 minutes per session, with warm up and cool down period of approximately 5 minutes. Exercises can be like brisk walking, jogging or running, swimming, bicycling, tennis, badminton, skiing, or dancing. A period of proper warm up and cool down at low intensity level for 5-10 minutes is advised [60].

Conclusion

Exercise plays a major role in the prevention and control of insulin resistance, prediabetes, GDM, type 2 diabetes, and diabetes-related health complications. Physical activity affords significant acute and chronic benefits for those with type 2 diabetes. Both aerobic and resistance training improve insulin action, at least acutely, and can assist with the management of BG levels, lipids, BP, CV risk, mortality, and QOL, but exercise must be undertaken regularly to have continued benefits and likely include regular training of varying types. Most persons with type 2 diabetes can perform exercise safely as long as certain precautions are taken. The inclusion of an exercise program or other means of increasing overall PA is critical for optimal health in individuals with type 2 diabetes. Unfortunately, physical activity is underutilized in the management of type 2 diabetes. This may be due to lack of understanding and/or motivation on the part of the person with diabetes and lack of clear recommendations, encouragement, and follow-up by health care professionals. Health care professionals must address physical activity more seriously in this patient population.
because most people with type 2 diabetes have the potential to derive benefits from regular, moderate levels of physical activity.

References


