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Mini Review

Physical exercise in type 1 diabetes: recommendations and care

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Abstract— The management of type 1 diabetes mellitus (T1DM) is based on three pillars: insulin therapy, nutrition, and regular practice of physical activity. Physical exercises are associated with metabolic demands that depend on the individual's energy stores and level of physical conditioning, and vary according to environmental conditions and intensity, duration, and type of exercise. All these factors, added to eventual distress with competitions, exert influence on glucose metabolism. The athletic career of diabetic individuals is often hindered by a risk of hypoglycemia during and after the exercise, frequent hyperglycemia before, during, and after certain physical activities, occurrence of ketoacidosis, and presence of chronic microvascular and macrovascular complications. Aerobic exercises reduce the levels of blood glucose while anaerobic exercise may promote transient hyperglycemia. Although diabetic individuals may achieve excellence in sport, their physical performance should be maximized by strict blood glucose control, adequate modifications in insulin dose on the day of the exercise, and appropriate nutritional intake. This review discusses the impact of physical exercise on glucose metabolism, as well as nutritional considerations and strategies appropriate to the practice of physical exercises by patients with T1DM.

Keywords: diabetes mellitus, type 1, exercise, physical activity, blood glucose, nutrition therapy

Introduction

Treatment of type 1 diabetes mellitus (T1DM) is comprised of medications, proper nutrition, and regular physical activity[1]. Due to its therapeutic benefits, physical exercise is widely recommended for diabetic patients. Many diabetics turn the regular practice of physical activity into a routine of training that ranges from participation in recreational activities, games, or school competitions, to even Olympic careers. Athletic activities are considered safe for patients with T1DM, provided that the athletes and the multidisciplinary team caring for them pay attention during the exercise to the particularities and requirements of the disease[2].

However, during training and competition, athletes with T1DM face some challenges and are required to deal with physiological demands associated with exercising at different intensities, such as special nutritional requirements, changes in meal schedule, and physical distress associated with competition[3].

In addition to these factors, athletes with T1DM face a substantial risk of hypoglycemia during and after exercising. There are also frequent reports of hyperglycemia before, during, and after some types of exercises, which add to the risk of ketoacidosis, and chronic microvascular and macrovascular complications may hinder the career of athletes with T1DM[4,5,6].

Despite the limited number of well-controlled studies supporting effective treatment plans for diabetic patients performing regular physical training, this review aims to discuss the current evidence regarding the impact of physical exercise on the dynamics of blood glucose control, in addition to nutritional considerations and appropriate strategies for the practice of physical exercise by patients with T1DM.

Blood glucose regulation and exercise in patients with T1DM

A routine of regular physical exercises may bring several health benefits to diabetic patients, including a decrease in cardiovascular risk, maintenance of body weight, reduction in blood pressure, and improvements in blood glucose control and well-being[6,7,8].

Guidelines of the American Diabetes Association[2] and the American College of Sports Medicine[9] recommend that diabetic individuals are prescribed individualized exercise regimens with well-defined objectives. These recommendations include participation in exercise sessions of moderate intensity for at least 150 minutes a week in the absence of contraindications such as diabetic neuropathy, proliferative diabetic retinopathy, uncontrolled hypertension, and metabolic ketoacidosis[10].

The practice of physical exercise is associated with metabolic demands that depend on the exercise type (aerobic or anaerobic, according to the predominant metabolic energy source required during exercise), form (continuous or intermittent, according to the interruption of the sets of exercise), intensity (very light, light, moderate, vigorous, near-maximal to maximal) and duration (short, moderate, long)[11,12]. These demands are also determined by ambient conditions (cold, heat, humidity, time of the day, altitude), and the individual's energy stores and level of physical fitness[13,14]. The degree of effort exerted during physical activity may be indirectly measured by the level of oxygen consumption. The maximum amount of oxygen ($VO_{2\,m}ax$) utilized by the body at each minute during the exercise measures the maximum aerobic effort capacity. During exercises of moderate intensity (40–59% of the $VO_{2\,m}ax$ or 55–69% of the maximum heart rate), the aerobic metabolism generally predominates, and carbohydrates and free fatty acids are used as energetic substrates[15]. When the oxygen requirement increases above 75% of the $VO_{2\,m}ax$, the exercise acquires anaerobic characteristics. However, low effort levels may be anaerobic at high altitudes and when performed by individuals who are sedentary, anemic, or with cardiac and pulmonary disease[16].

The transition from rest to moderate exercise is characterized by activation of sympathetic and hormonal systems that stimulate the use of the glucose stored in the muscle and liver, and the release of free fatty acids by the adipose tissue[17]. In nondiabetic individuals, a reduction of 8 mg/dL in blood glucose levels and/or blood glucose concentrations around 65–70 mg/dL leads to increases in glucagon and epinephrine levels[18,19]. Alpha-adrenergic stimulation of pancreatic islets inhibits insulin secretion and releases glucagon, leading to neoglucogenesis and glycogenolysis and increasing glucose production by about 5 mg/kg/min [19]. This process is a key factor in maintaining stable blood glucose levels (80–100 mg/dL) during exercise and preventing hypoglycemia, as the consumption of glucose by the muscle may be around 3 mg/kg/min during moderate exercise[20].

Rates of glucose oxidation during moderate intensity exercise are estimated at 2 mg/kg/min in adults with T1DM (21) and 1.5 mg/kg/min in adolescents with T1DM[22]. These rates lead to a fast decrease in serum glucose concentration due to an impairment in the glucagon counter-regulatory response. In some patients with T1DM, glucagon response to reduced blood glucose levels[23] may be impaired after a few years, although there have been reports of an appropriate release of glucagon during exercise in these patients[24]. In any case, even with a satisfactory glucagon and epinephrine response to physical exercise in T1DM, elevated levels of exogenous insulin may directly or indirectly inhibit glucagon secretion due to its antagonist effect, and reduce lipolysis and proteolysis[25-27].

Chokkalingam, Tsintzask, Norton, Jewell, Macdonald, Mansell[28] have observed that during moderate intensity exercise, fat oxidation accounts for 15% of the total energy expenditure in T1DM patients using high insulin doses and 23% in those using low insulin doses. These values are significantly lower than those in nondiabetic individuals, in whom fat oxidation accounts for about 40% of the total energy expenditure under similar conditions[29].

It is worth mentioning that in patients with T1DM, hyperglycemia itself inhibits lipid oxidation during exercise[30], and that in those with glucose levels ~97 mg/dL and insulin levels ~122 mmol/L during exercise, rates of lipid oxidation are similar to those in nondiabetics[28]. Following this line of thought, the high rate of carbohydrate oxidation during physical exercise in T1DM could be one of the factors leading to a decrease in blood glucose levels.

Several factors affect the levels of plasma glucose in diabetic athletes, and hypoglycemia may manifest immediately after the exercise or hours later. During or soon after moderate intensity exercises, it is possible that an energy balance inadequate to the demand of the exercise, added to an excessive amount of insulin administered to the subcutaneous in areas involved in the exercise, increases the rates of insulin absorption promoting hypoglycemia[31,32.] Physical exercise can also amplify the effects of insulin because it facilitates the transport of glucose through the cell membrane and increases muscle glucose absorption by up to 20 times. In fact, a single exercise session may increase the insulin sensitivity by up to 40% for 48 hours[33]. These effects promoted by physical exercises benefit the glycemic control both in nondiabetic and diabetic individuals, but in the latter they may lead to late hypoglycemia.

Studies report that the two main defenses against hypoglycemia are impaired in T1DM patients as these individuals are unable to decrease the levels of circulating insulin and have impaired glucagon response[23,25,26]. Thus, only epinephrine remains a front line counter-regulatory defense against hypoglycemia in T1DM patients. Even then, the epinephrine response may be less robust and occur only at low blood glucose levels[34,35]. Due to that, signs and symptoms of hypoglycemia related to autonomic regulation are impaired in these individuals[36,37].

Signs and symptoms of hypoglycemia due to adrenergic (sympathomimetic) stimulation include hunger, tremor, anxiety, tachycardia, and palpitation, whereas those due to neuroglycopenia (reduced availability of glucose to support cerebral functions) include weakness, fatigue, loss of coordination, disjointed speech, and blurred vision[38]. It has been postulated that repeated episodes of hypoglycemia reduce the sensitivity to epinephrine, a phenomenon known as hypoglycemia-associated autonomic failure (HAAF)[39]. Davis, Shavers, Mosqueda-Garcia, Costa[40] have reported that only two episodes of hypoglycemia at glucose levels below 70 mg/dL are sufficient to reduce 30% of the counter-regulatory response in the following episode of hypoglycemia.

Sandoval, Aftab-Guy, Richardson, Ertl, Davis[35] evaluated T1DM patients exercising at mild to moderate intensity (30% and 50% of the $VO_{2\,m}ax$, respectively) and presenting post-exercise hypoglycemia. The authors observed that these episodes of hypoglycemia reduced the response of the counter-regulatory hormones to a new episode of hypoglycemia in the following exercise session. Galassetti, Tate, Neill, Morrey, Wasserman, Davis[41] have reported that exercise sessions lasting more than 30 minutes and associated with hypoglycemia may induce HAAF in progressively lower levels of blood glucose (70, 60, and 50 mg/dL) at each new exercise session.

Hypoglycemia associated with physical exercise can occur hours after the exercise and may occasionally occur in the evening. Additionally, it has been speculated that an increased cortisol release during prolonged physical exercise may contribute to the development of HAAF[42], although a reduction in cortisol production has not been shown to improve HAAF after exercise. In contrast, the absence of hypoglycemia for a few weeks may improve the response to epinephrine by increasing the glycemic threshold for the release of counter-regulatory hormones and exacerbate the signs of hypoglycemia[37].

It is important to emphasize that sexual dimorphism seems to substantially influence the response of the counter-regulatory hormones to blood glucose levels. During prolonged exercise, women with T1DM present lower levels of epinephrine, norepinephrine, and growth hormone compared with men. Despite the low response to catecholamines, lipolytic rates have been described as significantly higher in women than men, suggesting that women have a greater beta-adrenergic sensitivity[43].

Galassetti, Tate, Neill, Morrey, Davis[43] have observed that males, when compared with females, present an attenuated decrease in glucagon, fat oxidation, and endogenous glucose production after physical exercise at 50% of the $VO_{2\,m}$ax. There is also an apparent sexual dimorphism in glucagon/insulin rate in favor of women, resulting in a better endogenous glucose production. In a way, the fact that women preserve fat oxidation after exercise-induced hypoglycemia confers a protective benefit, and therefore, lower susceptibility to HAAF.

Hypoglycemia is a common and dreaded complication in athletes with T1DM[42,44]. Levels of blood glucose in athletes or individuals with T1DM who perform routine training should be maintained between 120 and 180 mg/dL, although patients often become aware of their ideal levels of blood glucose for each particular exercise.

The best approach to hypoglycemia associated with exercise is to prevent its occurrence. Athletes with T1DM, and those professionals and friends close to them, must be alert to signs and symptoms of hypoglycemia, which should be treated with ingestion of carbohydrates, preferably with glucose. If the patient is unconscious and unable to ingest food or fluids orally, they must receive a glucagon injection[45].

Generally, youths with T1DM seem to have a 20% lower aerobic capacity than healthy youths. However, physically active individuals with well-controlled T1DM often have an aerobic capacity within the normal age range[46,47]. Several cardiovascular, metabolic, and muscular impairments in patients with T1DM help explain the decrease in aerobic and anaerobic performances[23,36,46,48]. In a recent study, Rissanen, Tikkanen, Koponen, Aho, Peltonen[49] observed that physically active adults with T1DM present a lower cardiovascular response to exercise at peak working rate, in addition to a lower systolic volume, systemic vascular resistance, $VO_{2\,m}$ax, and blood flow. These observations reflect central and peripheral limitations in diabetic individuals when compared with nondiabetic ones. In contrast, studies have not found significant differences in aerobic capacity in diabetic adults who are long distance runners or very active when compared with nondiabetics[50,51]. Therefore, it is still uncertain whether the reduced aerobic capacity in T1DM is due to poor muscular oxygenation or to the amount of muscle capillaries[52].

Anaerobic exercises, such as sprints, short-distance races, or even collective sports, generally do not cause significant changes in blood glucose, but when this occurs it is often associated with an increase in blood glucose levels in individuals with T1DM due to an increase in catecholamines and production of lactate[53,54]. The increase in levels of lactate and catecholamines during anaerobic exercise is known to reduce the consumption of glucose and free fatty acids by the muscle[55] and increase the hepatic production of glucose via blood lactate[56].

Exercise-induced hyperglycemia may last for hours after the end of an activity and somehow interfere with the glycemic control and later performance in sport[44]. Studies suggest that high-intensity intermittent exercises attenuate the decrease in blood glucose levels that are frequently observed in moderate intensity exercises[4,57-59].

Harmer et al.[60] have reported that high-intensity exercises lasting 30 seconds result in an increase in blood glucose levels during and after the exercise in patients with T1DM. Such an increase may be related to plasma levels of lactate, as lactate may induce insulin resistance during high-intensity exercise[27,61]. This phenomenon explains the increase in blood glucose levels even in the presence of increased insulin levels.

The changes in blood glucose levels observed after high-intensity anaerobic training suggest that this type of training is associated with better insulin clearance, reduced catecholamine stimulation, and increased cellular content of glucose transporter type 4 (GLUT4)[60]. The transport of blood glucose to the myocyte is mainly performed by GLUT4. In response to insulin (post-exercise) or muscle contraction and stimulated by the increase in calcium concentration during exercise, GLUT4 translocates both to the cellular membrane and to the T-tubules[62].

Interestingly, studies indicate that only 10 seconds of high-intensity aerobic exercise are required to prevent post-exercise hypoglycemia in patients with T1DM[57,63]. Similarly, the practice of exercising with weights before aerobic exercises attenuates the decrease in blood glucose[64].

Another study attempted to mimic sports games using high-intensity stimuli with 4-second shots followed by 2 minutes of active recovery for 20 minutes. The authors observed that the association of anaerobic and aerobic exercises did not increase the risk of hypoglycemia[4]. Thus, the increase in catecholamines and growth hormone levels during high-intensity exercise may prevent hypoglycemia, as after exercise these hormones increase the hepatic production of glucose and inhibit the uptake of glucose in response to insulin stimulation[56,65].

Although most studies related to the prescribing of anaerobic exercises to T1DM patients have shown positive results regarding the reduction of cases of hypoglycemia associated with acute exercise, the risk may increase hours later[66]. Still, more studies are required to provide a scientific basis for the development of guidelines in this setting.

Nutritional recommendations: schedules, type of nutrients, and hydration

Carbohydrates must comprise 50–60% of the daily diet of diabetic athletes performing regular exercises[67], which should be coordinated with the time of the exercise and the dose of insulin. This approach is fundamental to an ideal glycemic control, maintenance of muscle mass, and storage of hepatic and muscular glycogen, optimizing the exercise performance, reducing fatigue, and preventing complications[3].

Before performing exercises, T1DM patients should follow a diet based on the following recommendations:

A) Ingestion of 200–350 g (4g/kg) of carbohydrates, 3–6 hours before the exercise. This recommendation has proven effective in improving physical performance[68]. Although patients with T1DM should ingest 60–90 g of carbohydrates per meal, diabetic patients undergoing training are required to increase their glycogen stores before competitions and athletic activities by increasing the amount of carbohydrates in their meals, monitoring the blood glucose levels, and if necessary, adjusting the dose of insulin accordingly[69].

B) Ingestion of an additional amount of 1g of carbohydrate per kg of weight is recommended 1 hour before the exercise. Preference should be given to low-fat food or fluids[12].

C) If the exercise lasts for less than 45 minutes, a snack with 15g of carbohydrates ingested 15–30 minutes before the activity has been reported to be sufficient[70].

During physical exercises lasting more than 45 minutes, or even after their end, strategies may be used to maintain carbohydrate oxidation and prevent a reduction in glycogen stores (Table 1).

Table 1. Nutritional recommendations for T1DM patients involved in physical activities.

During the activity
Ingestion of 0.5–0.6g of carbohydrates per kg of body weight for every hour of activity.
In activities lasting more than 2 hours, ingestion of a larger amount of carbohydrates (0.8 g/kg) may be necessary.
During prolonged and high-intensity (>70% $VO_{2\,m}$ax) training or competitions, ingestion of 15g of carbohydrates at each 30–45-minute interval.
This amount of carbohydrates may increase blood glucose levels by 30–50 mg/dL, 15–30 minutes after their ingestion (Gonder-Frederick, 2001).
Food rich in solid or liquid carbohydrate may be ingested. Liquid foods help with hydration, while solid foods may prevent hunger. However, liquid foods are more widely recommended (Coyle & Montain, 1992).
After the activity
Ingestion of 1.5g of carbohydrate per kg of body weight after the end of prolonged exercises (>90 minutes).
Ingestion of carbohydrates immediately after the exercise helps to replenish glucose stores in the muscle and liver (Ivy, Katz & Cutler, 1988).
An additional amount of 1.5g of carbohydrate per kg of body weight may be required 1–2 hours after the exercise to reduce the risk of post-exercise hypoglycemia.
Blood glucose monitoring is required immediately after the exercise and 1–2 hours later to adjust the caloric intake and insulin dose.

As for hydration, the body may eliminate up to 2.5 liters of fluids daily, depending on environmental and individual conditions. During rest, an individual weighing 70 kg produces 60W of heat, whereas they may produce up to 1kW of heat during intense exercise. To counterbalance the production of heat, the body must produce 1.5–2 liters of sweat[71]. Thus, to prevent the complications associated with dehydration during physical activities, individuals with T1DM must ingest fluids before, during, and after the exercise. Adequate hydration helps control the body temperature and reduce the overload to the cardiovascular system. Ingestion of water and isotonic drinks is, therefore, a very important strategy[3] (Table 2).

Table 2. Recommendations regarding fluid ingestion before, during, and after physical activities for patients with T1DM.

Recommendations for ingestion of fluids
Drink 3–4 cups of water approximately 2 hours before the activity.
Drink 1–2 cups of water between 10–15 minutes before the exercise.
Drink half a glass of water at intervals of 10–20 minutes during the exercise, mainly in prolonged activities.
In prolonged activities, isotonic drinks containing at least 8% of carbohydrates (50% dilution in natural fruit juices and/or isotonic fluids) are generally the best options to replenish fluids and calories.
After the end of the exercise, drink 1–2 cups of water for each kilogram of weight lost during the exercise.

Studies demonstrated the importance in blood glucose control and caloric ingestion even when the values are higher than 100 mg/dL[27,72,47,64]. Due to biological individualities, metabolic responses to physical training, and environmental variations in temperature, trainers, nutritionists, and physiologists must guide the diabetic patients to determine the best strategy for fluid ingestion and adjustment of carbohydrate content in the diet for adequate hydration and maintenance of normal blood glucose levels.

Strategies and care for the practice of physical exercises regarding insulin

As insulin has been used illicitly by some athletes (especially weightlifters and fighters), it has been listed as a banned substance since 2005. Any athlete with T1DM who wants to compete in national or international sports events following international antidoping regulations, is required to have an appropriate documentation provided by a physician about the diagnosis and treatment of the disease[13].

In addition to determining the levels of capillary blood glucose as part of the routine in T1DM, glucose levels should also be determined 1–2 hours and, again, moments before the exercise, so that the glucose trend can be determined and appropriate procedures adopted. If the glucose levels show a trend toward a decrease (values that are lower just moments before the exercise than 2 hours before), carbohydrates may be ingested as a preventive strategy. In contrast, if the trend points toward an increase (a higher glucose level before the beginning of the exercise) this strategy may not be necessary[73].

In addition to measuring the glucose levels before the exercise, they should also be monitored at the end of the exercise and 1–2 hours later. In this situation, if the level is too low, the patient should ingest carbohydrates to reduce the risk of hypoglycemia. In the case of anaerobic exercises in which hyperglycemia may occur due to the intensity of the exercise, insulin adjustments should be avoided or conducted in small doses[74]. Another aspect to be observed is the possibility that the athlete may be using anabolic agents, as these agents may induce or worsen hyperglycemia.

Regarding the type of insulin, the absorption of mealtime and basal insulin can change with exercise. In the case of NPH insulin, the absorption doubles with increased temperature at the injection site. This occurs primarily due to increased subcutaneous blood flow, which improves the absorption of free insulin, regardless of the type of insulin, although it may also increase the dissociation of complex insulin in the case of NPH insulin, or microprecipitates with insulin glargine. With insulin detemir, however, more insulin is also expected to enter the circulation with the increased absorption of free insulin detemir; however, once in circulation, insulin detemir enters into a large pool of bound albumin, so the effect on absorption changes is blunted, and insulin detemir appears to promote less hypoglycemia after exercise in individuals with relatively well-controlled T1DM[75].

Another important factor regarding the insulin type is that lispro insulin has faster absorption than regular insulin; this improves the early postprandial glycemic increase, reducing the risk of late postprandial hypoglycemia[76].

Exercises below 70% of the $VO_{2\,m}$ax and lasting less than 30 minutes require only minimum adjustments in insulin therapy[74]. A 30–50% reduction in rapid-acting insulin after exercise has been reported as effective in reducing the risk of hypoglycemia. Another important step is to reduce 10–30% of the total daily insulin[67,74].

Individuals with T1DM performing physical activities at moderate intensity for 45 minutes during the afternoon or early evening have a 30–40% increased risk of nocturnal hypoglycemia[77,78]. This may be problematic because patients may be unaware of hypoglycemia during sleep. Therefore, a 20–50% reduction in the dose of basal insulin or a snack with complex carbohydrates and proteins is advisable in this situation[74,76,79].

Final considerations

In summary, a large number of neuroendocrine disorders may influence the regulation of blood glucose during exercise. Glycemic control during the practice of physical activities then becomes challenging for professionals working with T1DM patients. Studies indicate that aerobic exercises promote reductions in blood glucose levels, whereas anaerobic exercises may promote transient hyperglycemia. Although diabetic individuals may achieve excellence in sport, rigorous blood glucose control and appropriate insulin modifications on the day of the exercise, in addition to appropriate nutritional intake, are fundamental to maximize their physical performance. The fitness improvement associated with regular physical exercise in T1DM patients clearly demonstrates the importance of physical activities in these patients' health and quality of life.

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