Role of Physical Exercise in Children and Adolescents with Diabetes Mellitus

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ABSTRACT

During the past 50 years several studies have underlined the central role of physical exercise in the management of patients with both type 1 and type 2 diabetes mellitus. The numerous benefits described in normal individuals who practise regular exercise have also been demonstrated in patients with diabetes who obtained significant physical and psychological advantages for the care of the underlying disease. Despite physical and psychological benefits, the occurrence of acute complications and some important effects on diabetes-related vascular complications may often discourage patients from participation in sports activities. However, even though adverse events may occur, exercise is still judged one of the most important components in the treatment of patients with diabetes. Thus, children, adolescents and young adults with diabetes must be educated on the metabolic changes occurring during physical activity in order to be able to acquire the ability to individually modulate their diet and insulin therapy before and after exercise. Appropriate education may allow a proper and correct approach to physical exercise.

KEY WORDS

type 1 diabetes mellitus, hypoglycaemia, hyperglycaemia, diabetes complications

INTRODUCTION

Active life and physical fitness may represent the most effective strategies to prevent chronic diseases and to improve growth and development for children. During the past 50 years, clear evidence of the tight correlation between lifestyle and prevention of chronic diseases has been reported in numerous longitudinal studies in both adult and paediatric populations. Furthermore, these studies have clearly demonstrated significant prevention and reduction of mortality and morbidity for vascular disease by regular physical exercise. All these positive effects appear to be due to the important influences of regular exercise on metabolic and cardiovascular functions. Being able to decrease fat mass, to normalize lipid profile and to increase insulin sensitivity, exercise has critical influences on metabolic status. Moreover, adequate and constant physical exercise improves cardiovascular fitness and regulates blood pressure within the normal range. In addition, all these metabolic changes positively affect the prevention of the development of metabolic syndrome even in childhood.

The exercise-related benefits reported in normal individuals are described even in patients with type 1 and type 2 diabetes mellitus (DM1, DM2). Physical exercise, diet and adequate insulin therapy still represent the basis for the management of patients with diabetes. Several lines of evidence have shown that physical activity improves insulin sensitivity, reduces insulin dosage and increases muscular glucose uptake, exercising a positive effect on blood glucose control. Furthermore, regular exercise prevents obesity and reduces cardiovascular and metabolic diseases, even in patients with DM1. Despite the benefits, adverse acute events (hypoglycaemia, hyperglycaemia and ketosis) and some important effects on diabetes-related vascular complications may often occur,

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thus discouraging patients from participation in sports activities. However, some simple behaviour related to blood glucose monitoring, modulation of both insulin dose and site of injection and, even more, appropriate dietary supplementation, will significantly reduce the risk of exercise-induced complications, which in turn allows patients with DM1, parents and paediatricians to have a positive attitude about physical activity for its protective and constructive effects.

Recent randomized clinical trials on the prevention of diabetes among adults have demonstrated the positive benefits of lifestyle intervention on the progression from impaired glucose tolerance to DM2. It has been established that in patients with impaired glucose tolerance a combination of a reduced fat diet and physical exercise is associated with a reduction of body weight of 5-7% and of the risk of developing DM2 by 58%§. Other studies have shown that less time spent watching television and playing video games together with an increase of aerobic exercise is significantly correlated with a decline in both BMI and in fatness parameters, and is associated with improved glucose tolerance. Furthermore, in children with impaired glucose tolerance, diet plus exercise programs reduce the risk of developing DM2 by 60%, while in adolescents with overt DM2, diet and exercise together produce a greater reduction in need for pharmacological drugs than diet alone. Exercise can diminish the impairment of glucose metabolism in insulin resistant patients, and can retard the use of hypoglycaemic medications in patients with DM2. This evidence should encourage patients with DM2 to engage in physical exercise as a first therapeutic approach to this metabolic disease. Furthermore, there are data that in patients with diabetes, modest physical activity reduces the risk of overall mortality two-fold; thus the institution of physical activity programs should be encouraged in the care of patients with TDM2.

FUEL METABOLISM DURING EXERCISE IN NON-DIABETIC CHILDREN AND ADOLESCENTS

Fats, carbohydrates and proteins represent the three major fuels of tissue and circulating energy content. Among them, glucose represents the most important caloric source directly able to modulate blood glucose control, although its caloric support is lower than that of fat. During glucose load, the increased blood glucose levels stimulate the pancreatic release of insulin which in turn promotes the peripheral disposal of glucose, especially in skeletal muscle by promoting GLUT-4 receptor mediated uptake. During exercise, the increased glucose demand activates complex hormonal responses which modulate insulin and other counter-regulatory hormone (glucagon, catecholamines, growth hormone [GH] and cortisol) concentrations. These hormones operate in two main different pathways: during the early phase there is first a decrease of insulin levels and an increase of epinephrine and glucagon, associated with a local relative increase in insulin levels related to increased blood supply to the working muscle; while, during prolonged physical activity, there is an increase of glucagon, cortisol and GH, which promote metabolic changes occurring later in time (Table 1). During the different phases of exercise, these hormones modulate fuel metabolism mainly by activating hepatic gluconeogenesis and glycogenolysis, as well as muscle glycogenolysis, improving adipose tissue lipolysis, and even more stimulating muscle glucose uptake through the recruitment of the insulin-independent GLUT transporters in muscle.

At rest, free fatty acids (FFAs) are the main fuel utilized by muscle basal metabolism. During sports activities, energy supply to the muscles is guaranteed by circulating FFAs, muscle triglycerides, muscle glycogen and blood glucose derived liver glycogen. The proportions of each substrate burned are adjusted according to physical demands, i.e. to the intensity and the duration of the activity. During low/moderate activity, plasma-derived FFAs predominate, while plasma glucose and muscle glycogen make up the majority of fuel as the exercise intensifies. During severe and prolonged physical activity, there is a greater reliance on fuels from outside the muscle, including plasma FFAs and blood glucose, while the shorter the exercise the greater the utilization of muscular glycogen stores.

An age-dependent ability to utilize certain substrates represents an additional important difference.
rence in fuel utilization during exercise. Compared to adults, children and adolescents use less carbohydrate and more fat during exercise related to the same relative intensity. This appears to be due to the lower endogenous carbohydrate stores detected in children. Furthermore, hypo- and hyperglycaemia are unusual in non-diabetic children because insulin secretion is suppressed within normal physiological low levels and the counter-regulatory hormones are released, thereby causing glucose production by the liver in order to match fuel utilization by the working muscle. All these changes maintain glycaemia in the normal range in non-diabetic individuals during exercise.

FUEL AND METABOLIC RESPONSE DURING EXERCISE IN CHILDREN AND ADOLESCENTS WITH TYPE 1 DIABETES MELLITUS

During exercise in children with DM1 there is an increase in blood flow to working muscles to improve oxygen delivery, carbon dioxide disposal and supply of energy substrates. Furthermore, the increased muscle energy requirements allow a quick fall in blood glucose concentrations. However, the regulation of glycaemia is not as well controlled as in normal individuals. The lack of endogenous insulin secretion makes patients with diabetes totally different in comparison to non-diabetic individuals. The pancreas is not able to control insulin levels, making normal fuel regulation nearly impossible. Thus, peripheral insulin concentrations are tightly related by the injective therapy as well as to the site of injection and the time elapsed since the last administration. Thus, physiologically suppressed insulin levels may not be achieved in diabetic patients, leading to higher or lower insulin levels during sports activities. All these alterations promote inadequate glucose uptake by the muscle, inadequate glucose production by the liver, and inadequate FFA production by adipose tissue, resulting in impaired metabolic control during and after muscular activity.

The mix of fuel utilization during exercise in youths with DM1 appears to be similar to that of non-diabetics, except that those with diabetes may rely even more on fat and less on carbohydrates. As well as fuel utilization not being quite the same, the counter-regulatory response during exercise appears to be blunted in patients with DM1. Several studies have clearly reported an impaired released of epinephrine and glucagon that during physiological conditions help glucose production and release by the liver in order to maintain blood glucose within the normal range. In patients with DM1, both inadequate peripheral insulin concentrations and the blunted counter-regulatory response, often detected during
and after exercise, are directly responsible for either increase (hyperglycaemia) or decrease (hypoglycaemia) in blood glucose concentrations.

**FUEL AND METABOLIC RESPONSE DURING EXERCISE IN PATIENTS WITH TYPE 2 DIABETES MELLITUS**

During exercise in children with DM2, there is also an increase in blood flow to working muscles to improve oxygen delivery, disposal of carbon dioxide and supply of energy substrates. However, the efficacy of glucose oxidation is not as well controlled as in normal individuals. Several studies have demonstrated that non-oxidative glucose utilization is impaired in the families of patients with DM2 and appears to be 25% lower in the children of patients with DM2 compared to normal individuals. This may result in impaired glucose utilization during sports activities compared to normal individuals.

Physical exercise induces an increase of insulin-dependent and -independent glucose transport to working muscle. Physical exercise promotes the translocation of glucose transporter 4 (GLUT-4) to the surface of muscle cells, resulting in increased intracellular glucose transport in response to insulin. Moreover, muscle contractions increase both AMP/ATP and creatinine/phosphocreatinine ratios, activating the adenosine monophosphate kinase (AMPK) which is an important mediator of fatty acid oxidation and glucose transport. In addition, AMPK seems to increase the translocation by GLUT-4 of both insulin-dependent and -independent glucose pools. Physical exercise improves the activity of glycogen synthase and thus increases non-oxidative glucose metabolism and the rate of intramuscular glycogen synthesis. Exercise may also increase the density of the muscular capillary supply, thus increasing overall blood flow. Furthermore, regular activity promotes an increase of muscle fibres type 1 or 2 which are characterized by insulin sensitivity. In addition, physical exercise can decrease body fat and increase muscle mass which in turn decreases FFAs and insulin resistance. These data show that insulin resistance is compensated by exercise, supporting the idea that regular exercise may help to prevent diabetes in patients at high risk.

**RISKS OF PHYSICAL EXERCISE IN CHILDREN AND ADOLESCENTS WITH DIABETES MELLITUS**

The hormonal and metabolic differences in patients with diabetes should be taken into account when considering the risk of adverse events during and following exercise. The influences of exercise on glucose metabolism and the subverted physiological regulation, both of insulin secretion during and following exercise and of counter-regulatory response to muscular activity, appear to be the first determinant in exercise-associated complications. All these factors may influence the occurrence of adverse acute or late events (hypoglycaemia, hyperglycaemia and ketosis) and may determine important consequences for diabetes-related vascular complications (Table 2).

**Exercise hypoglycaemia**

Hypoglycaemia, defined as glucose levels lower than 60 mg/dl, represents the most important and recurrent complication in patients with DM1 who practise sports. Due to the inadequate balance between peripheral glucose uptake and hepatic glucose production, exercise hypoglycaemia may occur in the setting of physical exercise or even several hours following exercise in patients with DM1. The physiological hormonal modulation activated during muscle exercise, characterized by insulin suppression associated with an increase of counter-regulatory hormones, represents the key factor responsible for exercise hypoglycaemia in patients with DM1. In a status of increased glucose requirement and amplified peripheral glucose uptake, documented during both exercise and the restorative phase, the occurrence of elevated absolute or relative plasma insulin concentrations, which may easily happen in patients with DM1, results in poor blood glucose modulation. In the setting of a fixed dose of insulin given before starting exercise, increased insulin concentrations might easily develop in patients with DM1. Furthermore, peripheral insulin release from the site of injection cannot be physiologically suppressed during muscular activity, allowing prolonged insulin plasma emission and consequently often to exaggerated concentrations. Increased insulin concentration leading to continuous glucose
uptake in peripheral tissues associated with increased utilization in working muscles is directly responsible for the rapid decrease of blood glucose concentrations.\textsuperscript{33}

Several factors related to insulin treatment may contribute to the over-insulinization related hypoglycaemia during exercise. Among them, the most relevant is increased absorption from the injection site. A rise in body temperature and increased blood flow in subcutaneous tissue and skeletal muscle have been demonstrated to be casually related to the increased insulin concentrations during sports.\textsuperscript{37} These effects are drastically enhanced by injection into the working muscle and by injecting insulin just before starting exercise. These factors may drastically increase the risk of hypoglycaemia. Furthermore, when exercise is performed before insulin administration in the morning, the risk of hypoglycaemia is reduced, because circulating insulin is low, and liver and muscle glycogen stores are full.\textsuperscript{38} The use of insulin analogues, in both a multiple injection basal bolus regimen and subcutaneous infusion by pump, has been demonstrated to offer significant advantages in reduction of hypoglycaemic episodes.\textsuperscript{39-41} Even with appropriate reduction in the pre-exercise insulin dose, over-insulinization can still occur during or shortly after exercise, because contractions make the muscle more sensitive to insulin. Late onset hypoglycaemia can still occur despite appropriate insulin reduction,
insulin sensitivity and to repletion of muscle glycogen stores. Although hypoglycaemia often occurs during exercise, a number of patients experience late-onset episodes, which may occur even 5-24 hours following the exercise. Exercise dramatically improves insulin sensitivity in the working muscles, which in turn increases glucose uptake both during and especially following muscular activity. Thus, an inadequately elevated amount of insulin may directly cause a rapid fall of blood glucose concentrations both in the setting of exercise and especially several hours after exercise. All these effects may be amplified by depletion of glycogen stores as insulin sensitivity is dramatically increased.

Beside the lack of physiologically regulated insulin concentrations, the inadequate increase of counter-regulatory hormones represents a further factor responsible for exercise-induced hypoglycaemia in patients with DM. Several studies have clearly demonstrated a blunted counter-regulatory hormonal response to exercise in patients with DM. As the level of glycaemia is the result of the balance between glucose utilization by working muscle and glucose production by glycolysis, glucogenogenesis and lipolysis, an inadequate increase of the counter-regulatory hormones drastically increases the risk of exercise-induced hypoglycaemia. Several studies have demonstrated an increased risk of hypoglycaemia in patients with DM who develop abnormalities in the counter-regulatory hormone system. In addition, in patients with DM, the blunted neuro-hormonal response to exercise appears to be exponentially increased by previous exercise performance or by antecedent hypoglycaemic episodes.

Several characteristics of exercise may strongly influence the development of exercise hypoglycaemia in patients with DM. Among them, duration and intensity of the exercise, physical training, and diet prior to the exercise have been especially documented to be major determinants. Sports characterized by alternations in intensity result in a continuous release of catecholamines and GH induced by the intermittent high-intensity exercise, which might facilitate the development of hypoglycaemia. The longer the duration and the lower the intensity of the exercise, the less is the influence on glucose metabolism, as fatty acid oxidation is dramatically increased. The clear shift from glucose to lipid metabolism by reducing the intensity and prolonging the duration of exercise explains the lower risk of exercise-induced hypoglycaemia associated with sports with these characteristics. Similar effects have been demonstrated in trained individuals. Fat utilization, insulin sensitivity and skeletal muscle glycogen synthetic activity are significantly improved by physical training which in turn determines a better utilization of fuel sources; in particular, there is an increase of lipid utilization in trained athletes compared to untrained individuals. All these effects lower the chance of drastic changes in blood glucose concentrations during exercise.

**Exercise hyperglycaemia and ketosis**

In patients with DM increased blood glucose levels might occur during and after physical exercise, especially in poorly controlled patients. An inadequate metabolic balance, characterized by increased peripheral glucose uptake and excessively low insulin level, might easily develop in patients with DM, enhancing the risk of hyperglycaemic episodes during and after exercise, especially during high intensity sports.

Glycaemic levels before exercise represent one of the most important factors influencing the risk of sports hyperglycaemia. If exercise is started when blood glucose is higher than 250 mg/dl and ketones
are detected, the state of impaired metabolic control may be worse. Thus, if urinary ketones are present in urine, exercise must be delayed until they disappear and insulin supplementation is needed, while if a ketone test is negative, exercise should be started, providing that blood glucose does not exceed 300 mg/dl and insulin supplementation is administrated\textsuperscript{46}. The excessive increase of blood glucose concentrations may be worse after counter-regulatory hormone activation. It has been clearly demonstrated in patients with DM that, even during intensive insulin therapy, an inadequate blood insulinization status may induce an increase in blood glucose levels during and after high intensity exercise, probably due to failure of insulin release, resulting in inadequate counterbalancing of the increase of the counter-regulatory hormones. During and after high intensity exercise, catecholamines increase significantly and promote the release of hepatic glucose and FFAs, the production of ketones, and the impairment of glucose utilization by skeletal muscle\textsuperscript{45,47}.

A number of risk factors, such as the time between the last insulin injection and starting exercise, and/or duration and type of sports and/or hydrated status, are directly involved in the occurrence of hyperglycaemic episodes during sports\textsuperscript{45}. The later the exercise is started in relation to the last insulin injection, the higher the risk of hyperglycaemia, due to the lower insulin levels; while the higher the intensity and the lower the duration of the activity, the higher the prevalence of hyperglycaemia due to the state of impaired activation of the counter-regulatory hormones which promote gluconeogenesis and hepatic glycolysis\textsuperscript{48}.

Exercise and chronic complications

Exogenous insulin administration in patients with DM1 represents the key factor in the pathologically decreased or increased blood glucose concentrations associated with physical exercise. Although abnormalities in glucose metabolism represent the main adverse effects during sports, exercise may also negatively influence some of the diabetes-related complications (nephropathy, retinopathy, autonomic neuropathy, neuropathy)\textsuperscript{3}.

Several observational studies have clearly demonstrated that blood pressure significantly increases during exercise, especially during vigorous sport. This excessive increase in blood pressure might have important influence on the progression of retinopathy, increasing the risk of both retinal and vitreal haemorrhage and retinal detachment in patients with overt diabetic retinopathy\textsuperscript{3}. The association between continuous and severe physical activities and degeneration of renal functions has not been clearly shown in diabetic patients. In patients with proteinuria, a significant correlation between increased urinary protein excretion and physical exercise has been demonstrated\textsuperscript{49,50}. In contrast, it is well known that exercise reduces blood pressure chronically. According to these opposite effects, benefits are not yet clear, and so far no international guidelines have established the benefits or risks related to physical exercise in nephrotic patients with DM1. Furthermore, in patients with diabetic neuropathy, both unnoticed foot ulcers and articular and/or tissue injury may be worsened by the underlying lack of sensation. In addition, physical exercise may exacerbate abnormalities detected in patients with diabetic neuropathy, such as maximal cardiac capacity and output, decreased cardiovascular rate to response to physical exercise, orthostatic hypotension, impaired sweating, and impaired gastrointestinal function\textsuperscript{51-53}. In adult patients with DM1, exercise can induce episodes of angina\textsuperscript{54}.

PRACTICAL APPROACHES TO CHILDREN AND ADOLESCENTS WITH DIABETES MELLITUS DURING PHYSICAL EXERCISE

Knowledge about the several changes and modulating factors occurring both during and after physical exercise in patients with DM represents the starting point to prevent and to reduce the incidence of adverse events. In well-controlled patients with DM, no drastic changes in therapy or diet are needed during physical activity, as the status of insulinization in these patients is able to provide adequate metabolic balance\textsuperscript{3}.

Diet and insulin therapy management represent the two main important strategies possible in patients with DM practising sports in order to
minimize the occurrence of sports-related adverse events. It is now universally accepted that these interventions should be made on an individualized basis, depending on the inter-individual specific response to a particular activity. As insulin demands are substantially different during exercise, overall individual experience must be collected in order to determine individual glycaemic variation. The American Diabetes Association recommends keeping blood sugar above 100 mg/dl and under 250-300 mg/dl for people with DM who decide to practise physical activities. Furthermore, before starting physical exercise, the guidelines suggest delaying exercise if blood sugar is above 300 mg/dl whether or not ketones are present. Because the pre-exercise blood glucose level might change radically during exercise, especially depending on the intensity and duration of physical activity, blood glucose levels above 150 mg/dl are recommended in order to prevent hypoglycaemia in patients who programme heavy aerobic activity. During prolonged and moderate intensive exercise, blood glucose levels should be checked every 30 minutes.

It is advisable to check blood sugar 1 hour before and 30 minutes before any activity, in order to identify a trend of blood sugar going down (150-90 mg/dl) or possibly up (150-260 mg/dl), and to adjust insulin and/or diet before or after exercise properly. These practical approaches to diet and insulin therapy modulation may reduce the risk of sports-related complication. Furthermore, parents, the coach, metabolic fitness operator and friends should be able to evaluate hypoglycaemic symptoms and to be quickly able to offer snacks with a high concentration of sugar, or hypotonic sweet drinks during acute episodes. Adequate education of the team which follows children and adolescents with DM1 during exercise represents an important step to guarantee a safe approach to sports activities in these children.

**DIET MANAGEMENT DURING EXERCISE IN CHILDREN WITH DIABETES MELLITUS**

The diet of children and adolescents with DM who practice sports is not substantially different from the diet of healthy people. These children need an adequate quantity of fats, proteins and carbohydrates to support muscular exercise, as well as micronutrients. A diet consisting of 55-60% carbohydrate, 25-30% lipid and 10-15% protein is recommended for patients with DM. Carbohydrate consumption depends on the sport practiced; it must not be lower than 60%, and should reach 70% if long-lasting aerobic exercise is programmed, preferably complex carbohydrates. Studies have demonstrated that a diet characterized by specific amounts and types of carbohydrate may help patients with DM to achieve good metabolic control during sports. Before physical activity, diets containing smaller carbohydrate molecules which are broken down and absorbed more quickly than the longer chains are preferable. In patients with DM who exercise regularly it has been shown that a diet containing complex carbohydrates can reduce the risk of hypoglycaemia because it guarantees the formation of muscle and hepatic glycogen stores. In the hours immediately before exercising it has been shown that sugary drinks containing about 15 g of simple chain molecules could be used in order to facilitate a good glucose level during exercise. Animal and vegetable proteins should be in a 1:1 ratio, and 60% of vegetable lipids are needed with a mono/polyunsaturated ratio of 1:1. Moreover, fats are critically important in the diets of athletes because they provide energy, fat-soluble vitamins, and essential fatty acids necessary for daily activity and health (Table 3).

The intensity and type of sport practiced play an important role in the choice of diet. Carbohydrates are the main substrates consumed during moderate physical activity, so that depleted muscle and liver
glycogen stores can be replaced after exercise. Because lipids, FFAs and triglycerides are utilized during low intensity and prolonged exercise at a rate of 40% during the first hour and 70% in the next hours, adequate lipid support is needed in the diet.\textsuperscript{58}

Some children may wrongly interpret hypoglycaemic symptoms as exercise fatigue, thus easily experiencing severe hypoglycaemic attacks immediately after exercise. In contrast, due to the fear of hypoglycaemia, some other children eat an excessive amount of food as snacks, or even refrain from exercising altogether. Children with DM1 during prolonged activity might develop frequent hypoglycaemic episodes which are often refractory to the oral glucose supply of 15 g which is supposed to be useful in adults. In such a case, a dosage of 35-45 g of oral glucose could be adequate to treat hypoglycaemia efficiently.

**INSULIN THERAPY MODULATION DURING EXERCISE IN CHILDREN AND ADOLESCENTS WITH DIABETES MELLITUS DURING PHYSICAL EXERCISE**

The insulin level is the foremost determinant of the metabolic response to exercise in patients with DM1. Being exogenously administered, insulin concentrations are not physiologically suppressed during physical activity in patients with DM1 as occurs in normal individuals. To the contrary, an absolute or relative increase of insulin concentrations may develop, first due to the enhanced absorption of injected insulin, especially if exercise is undertaken shortly after administration of a ‘rapid’ insulin analogue, and secondly due to the increase in insulin sensitivity.\textsuperscript{59} Patients with DM1 must be taught about these effects and the importance of adequate insulin concentrations in the setting of physical exercise in order to try to program insulin therapy according to the exercise.\textsuperscript{3}

In patients who programme exercise, modulation of the injected dose of insulin is needed both before and following the exercise session. However, the insulin level is strongly influenced by several factors, including the duration and intensity of the physical activity, blood glucose levels before and during exercise, emotional stress, training status and environmental factors. As insulin modulation is dependent on multiple factors, no universal programme can be applied to daily diabetes management.\textsuperscript{60} However, some general advice should help in the individual case.

If activity is performed in the fasted state (>3 hours after insulin analogue administration and meal) and normal glycaemia is measured, moderate and middle duration exercise may be performed with no reduction in bolus insulin, except for taking care to avoid injection into a site next to the working muscles to minimize the risk of hypoglycaemia due to accelerated absorption.\textsuperscript{39-41} As plasma insulin levels are elevated 2-3 fold immediately after a meal, if exercise is programmed, the pre-meal insulin might be reduced by 30-50%, according to the intensity and extent of the exercise, and if possible delaying the activity by at least 2 hours. For more prolonged exercise, the insulin dose might be reduced by up to 60-90%. In addition, reduced doses of insulin would be useful even before the next meal and the evening injection of intermediate or long-acting insulin by 20-50%, according to the intensity of the exercise.\textsuperscript{38,61,62}

In patients with an insulin pump, administration of insulin can easily be stopped by simply disconnecting the device before and during exercise if necessary. For exercise performed in the postprandial state, 50% reduction of basal rate and lower pre-meal bolus should be planned, according to the duration of the exercise. As the basal rate infusion effects are delayed by 2-3 hours during
pump administration, it may be useful to start the basal rate reduction 60 minutes before the programmed exercise. Furthermore, 10-30% reduction of overnight infusion might be necessary in order to prevent late onset hypoglycaemia, especially after prolonged exercise. Modulation of insulin dosage is not only useful to prevent hypoglycaemia but also to minimize the risk of hyperglycaemia. Both poor metabolic control and the effect of catecholamines and/or sympathetic nervous system activation of hepatic glucose production promote the development of hyperglycaemic episodes in diabetic patients. Therefore, when the glucose level is higher than 250 mg/dl and ketones are present, insulin supplementation is needed, and exercise should be postponed until the urinary ketones disappear. If the ketone test is negative, exercise can be started, providing that blood glucose does not exceed 300 mg/dl and insulin supplementation is undertaken. High adrenergic output could induce an increase of glucose level after competitions or intensive exercise bouts. In these circumstances, the absence of urinary ketones is an index of a sufficient insulin/glucose ratio, and hyperglycaemia can be prevented by a significant reduction of pre-exercise snacks. Moreover, new knowledge about insulin pharmacokinetics and pharmacodynamics suggests that during physical activity, hyperglycaemia will be avoided if the exercise session is about 2-3 hours after regular insulin administration, about 6-8 hours after intermediate insulin administration, and 90-180 min after ultra-rapid analogues. Insulin therapy characterized by administration of slow-acting or even ultra-lente insulin is not safe during physical exercise in children.

CONCLUSIONS

Recent studies have shown a positive association between glycaemic control, HbA1c, aerobic fitness and DM1 also in younger patients with diabetes. In patients with diabetes and their parents, adequate instruction about self-monitoring diet and insulin adjustments that must be undertaken during physical exercise represents a pivotal moment in order to assure good glucose control and to prevent hypo- or hyperglycaemia. Children and young adults with diabetes must be accurately educated on the metabolic changes occurring during sports activities in order to be able to acquire the ability to individually modulate their diet and insulin therapy before and after exercise. Furthermore, the coach and other participants should be informed and instructed in order to be able to recognize adverse events and to provide adequate therapeutic correction. Only appropriate education will allow a proper and correct approach to physical exercise in patients with diabetes in order to fully appreciate exercise-related benefits.

REFERENCES


### TABLE 1

Metabolic and hormonal changes during physical activity

<table>
<thead>
<tr>
<th>Physical activity</th>
<th>Hormonal response</th>
<th>Energy source</th>
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<tr>
<td><strong>Starting exercise</strong></td>
<td>↓ insulin</td>
<td>ATP</td>
</tr>
<tr>
<td></td>
<td>↑ insulin (in muscle)</td>
<td>creatine phosphate</td>
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<td></td>
<td>↑ epinephrine</td>
<td></td>
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<tr>
<td><strong>Minutes/first hour</strong></td>
<td>↑ insulin (in muscle)</td>
<td>glycolysis in muscle</td>
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<tr>
<td></td>
<td>↑ epinephrine</td>
<td>gluconeogenesis</td>
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<td></td>
<td>↑ glucagon</td>
<td></td>
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<tr>
<td><strong>Prolonged activity and intensive exercise</strong></td>
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<td>gluconeogenesis</td>
</tr>
<tr>
<td></td>
<td>↑ cortisol</td>
<td>free fatty acids</td>
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<tr>
<td></td>
<td>↑ growth hormone</td>
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### TABLE 2

Benefits and risks of physical exercise in patients with type 1 diabetes mellitus

<table>
<thead>
<tr>
<th>Benefits of exercise</th>
<th>Risks of exercise</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Decreases blood glucose level before and after exercise</td>
<td>• Hypoglycaemia</td>
</tr>
<tr>
<td>• Reduces insulin dosage</td>
<td>• Hyperglycaemia and ketosis</td>
</tr>
<tr>
<td>• Increases insulin sensitivity</td>
<td>• Deterioration of microvascular complications (retinopathy, nephropathy, neuropathy, autonomic neuropathy)</td>
</tr>
<tr>
<td>• Controls blood pressure</td>
<td></td>
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<tr>
<td>• Increases cardiovascular function</td>
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<td>• Improves lipid profile</td>
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TABLE 3
Diet before, during and after physical exercise

| Balanced diet: | Carbohydrate 55-60% |
|               | Lipids 25-30% (mono/polyunsaturated ratio 1:1) |
|               | Protein 10-15% (1:1 between vegetable and animal protein) |

**Before and after long-lasting activity:** Complex carbohydrates 70% to increase muscle and hepatic glycogen store

No increased fat intake to prevent ketosis

**During moderate physical activity:** Smaller carbohydrate molecules to be broken down and absorbed more quickly