

Revisión

## Physical exercises on glycemic control in type 1 diabetes mellitus

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**Abstract**

Type 1 diabetes is a metabolic diseases characterized by hyperglycemia, results from the destruction of insulin-producing pancreatic beta cells. Diabetes management usually by insulin, dietary and physical activity.

**Aim:** Assess the relationship between physical activity and glycemic control in type 1 diabetes subjects.

**Methods:** The literature search conducted in Pubmed and ScienceDirect databases and was initially identified 24 articles and we applied the inclusion criteria that considered original, full-text, remaining thirteen articles published between 1992 and 2009.

**Results and discussion:** Two studies found a positive association between physical exercises and adequacy of glycemic control on long-term, determining by glycated hemoglobin (HbA1c) and increase the insulin sensitivity, whereas three articles didn't found relations between exercises and glucose, insulin sensitivity and formation of ketone bodies.

**Conclusion:** There are positive influences of exercise of long-term glycemic control in type 1 diabetes, however results are contradictory with respect to insulin sensitivity and fasting glucose. Glycemic control in diabetes should be based on HbA1c values, self-monitoring of blood glucose and reduction of insulin requirement, such as have been demonstrated in several studies. Thus physical exercise, along with dietary therapy and medication, are important to control diabetes.

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Key words: *Diabetes mellitus. Physical exercises. Glucose. Insulin resistance.*

### EJERCICIOS FÍSICOS SOBRE EL CONTROL GLUCÉMICO EN LA DIABETES MELLITUS TIPO 1

**Resumen**

La diabetes tipo 1 es una enfermedad metabólica caracterizada por hiperglucemia, resultante de la destrucción autoinmune de las células beta productoras de insulina del páncreas. El tratamiento de la diabetes se basa en la insulina, dieta y actividad física.

**Métodos:** La búsqueda bibliográfica se realizó sobre la base de Pubmed y ScienceDirect, que se identificaron inicialmente 24 artículos y aplicarse teniendo en cuenta los criterios de inclusión artículos originales en texto completo, la obtención de trece artículos publicados entre 1992 y 2009.

**Resultados:** Dos estudios encontraron una asociación positiva entre el ejercicio y la adecuación de control de la glucemia en el largo plazo, para la determinación de la hemoglobina glucosilada (HbA1c) y mayor sensibilidad a la insulina, mientras que tres artículos no encontraron ninguna relación entre el ejercicio, la glucosa sanguínea, la sensibilidad a la insulina y la formación de cuerpos cetona.

**Conclusión:** Hay influencia positiva del ejercicio sobre el control glucémico en DM1 a largo plazo, sin embargo los resultados son contradictorios con respecto a la sensibilidad a la insulina y la glucosa en ayunas. El control glucémico de la diabetes debe basarse en los valores de HbA1c, autocontrol de la glucosa en la sangre y disminución de las necesidades de insulina, como se ha demostrado en varios estudios. Así, el ejercicio físico, junto con la terapia nutricional y la medicación son importantes para controlar la diabetes.

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Palabras clave: *Diabetes mellitus. Ejercicios físicos. Glucosa. Resistencia a la insulina.*

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## Abbreviations

EGP: endogenous glucose production.

HbA1c: glycated; hemoglobin.

VO<sub>2</sub>max: maximum volume of oxygen.

## Introduction

Diabetes mellitus as a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Type 1 diabetes results from the destruction of insulin-producing pancreatic beta cells. Diabetes management usually by insulin, dietary and physical activity.<sup>1</sup>

Exercises can be classified as aerobic or anaerobic. The definition of aerobic exercise as any activity that uses large muscle groups and can be maintained continuously. During anaerobic exercise, muscle fibers have to derive their contractile energy from stored substrates (glycogen, adenosine tri-phosphate and creatine phosphate).<sup>2</sup> The distinction between the two types of exercise is important because of their different effects on blood glucose concentration.

Elevated skeletal muscle blood flow and increased body temperature because of exercise can increase the rate of insulin absorption, for several hours to replenish glycogen stores.<sup>3,4</sup> As a result, an episodes of hypoglycemia can occur not only during periods of activity but up to 24 hours later.<sup>5</sup>

A high-intensity anaerobic exercise can cause excessive levels of catecholamines, nonesterified fatty acids and ketone bodies, inhibit glucose utilization in skeletal muscle, causing transient hyperglycemia (30 to 60 minutes), probably due to development of substantial counterregulatory hormone secretion.<sup>6</sup>

The aim of this systematic review was to assess the relationship between physical activity and glycemic control in type 1 diabetes subject.

## Methods

The review focused on language literature in English. The literature search was conducted in the following databases: Pubmed and ScienceDirect. The keywords used were selected from the following terms: "type 1 diabetes"; physical exercises and "glucose".

Were initially identified 24 articles and we applied the inclusion criteria that considered original, full-text, in humans articles. Were excluded two studies with animals; one article with type 2 diabetes subjects; and eight review articles, remaining thirteen articles published between 1992 and 2009.

## Results

Screening criteria previously explained resulted in fifteen studies (table I). Two studies found a positive association between physical exercises and adequacy of glycemic control on long-term, determining by glycated hemoglobin (HbA1c)<sup>7,8</sup> and increase the insulin sensitivity,<sup>9,10</sup> whereas three articles didn't found relations between exercises and glucose,<sup>7,11</sup> insulin sensitivity<sup>8</sup> and formation of ketone bodies.<sup>11</sup>

## Discussion

### *Contributions of physical exercises for reducing glycated hemoglobin*

Although physical exercises are recommended since 1990s, Salvatoni et al.<sup>8</sup> evaluated the influence of exercise to improve long-term glycemic control in 69 in type 1 diabetes subject, were divided into groups according hours per week spent on exercises: sedentary (less than 2 hours); irregularly active (2 to 4 hours); active (4 to 6 hours); or very active (more than 6 hours). As a result, lower levels of HbA1c are shown of most active group ( $p < 0.05$ ), however no significant difference was observed in need of insulin.

Assessing 19,143 type 1 diabetes adolescents, stratified according frequency refers to exercise per week and HbA1C is inversely correlated with physical exercises for both sexes ( $p < 0.001$ ), while only more-active men had significantly lower insulin doses ( $p < 0.01$ ).<sup>10</sup>

Also monitoring type 1 diabetes adolescents. Faulkner et al.,<sup>12</sup> related maximum volume of oxygen (VO<sub>2</sub>max), heart rate variability, cardiovascular endurance and HbA1c variables in 105 type 1 and 27 type 2 diabetes subjects. All volunteers reported hours of sleep per night and answered a 7-day recall activity questionnaire, being classified as sleep, light, moderate, hard and very hard according to a report of the American College of Sport Medicine.<sup>13</sup> The findings of this investigation revealed that regardless of gender or type of diabetes, the group with higher body mass index had higher levels of HbA1c and lower cardiovascular endurance. When compared the types of diabetes, were observed lower VO<sub>2</sub>max and cardiovascular endurance in type 2 diabetes subjects.

Boehncke et al.,<sup>14</sup> followed, for three years, ten type 1 diabetes subjects and five health subjects in triathlon competitions and all subjects presented hyperglycemia in beginning and glucose reduction concentration during cycling step. In conclusion, the authors suggests that diabetic subjects can practice extreme endurance exercises and physiological change affected by diabetes can be easily compensated for adjust insulin doses and nutritional modifications.

Another study assessing ten adolescents with type 1 diabetes subjects, related parameters of cardiovascular endurance, muscular strength and glycemic control.

**Table I**  
*Studies evaluating the influence of physical exercises on glycemic control in healthy and diabetes mellitus subjects*

| <i>Reference</i> | <i>Subjects</i>   | <i>Study design</i>   | <i>Significant results</i>   |
|------------------|---|---|--|
| 8                | 69 children with type 1 diabetes subjects (8,98 ± 3,90 years old)   | Subjects were classified according type and hour a day of physical exercise   | Lower levels of HbA1c in most active group (p < 0.05);<br>No difference in dosage of insulin   |
| 7                | 10 adolescents with type 1 diabetes subjects (17,2 ± 1,2 years old)                                       | Subjects were submitted an aerobic exercises for 12 weeks.  | Reduction in HbA1c of 0.96% (p < 0.05%);<br>No difference in fasting glucose   |
| 9                | 8 subjects with type 1 diabetes subjects (33 ± 3,1 years old)   | Subjects received 100%, 50% or 25% of lispro insulin dose usually used and different exercise intensities.                  | Hypoglycemia was observed in all exercise intensity after 100% of insulin dose;<br>Necessary 75% reduction in insulin for euglycemia at 75% of VO2max.   |
| 10               | 19,143 adolescents with type 1 diabetes subjects (3 to 20 years old)                                      | Subjects were classified according type and hour a day of physical exercise   | HbA1c is inversely correlated with physical exercises for both sexes (p < 0.001);<br>More-active men had significantly lower insulin doses (p < 0.01)  |
| 11               | 15 subjects with type 1 diabetes subjects (7 females e 8 males)   | Subjects were submitted an aerobic exercise (80% of anaerobic threshold and 50% of VO2max) during 90 minutes                | Higher EGP in men (p < 0.05);<br>Glycerol levels were higher in women (p < 0.05);<br>No difference in glucose or insulin   |
| 12               | 105 adolescents with type 1 diabetes subjects and 27 adolescents with T2DM                                | Subjects were classified according hour a day of physical exercise  | BMI was positively related with HbA1c and inversely related with cardiovascular endurance, regardless of type of diabetes;<br>Subjects with type 2 diabetes subjects showed lower VO2max and cardiovascular endurance  |
| 14               | 10 subjects with type 1 diabetes subjects and 5 health subjects   | All subjects were triathletes   | All presented hyperglycemia in beginning and lower glucose concentration during cycling  |
| 15               | 18 subjects with type 1 diabetes subjects (42 ± 10 years old)   | Subjects were classified according type and hour a day of physical exercise   | No difference in HbA1c and fasting glucose   |
| 16               | 5 subjects with type 1 diabetes subjects and 6 health subjects  | Subjects were submitted a rest, moderate and vigorous physical  | Type 1 diabetes subjects showed 60% higher EGP during rest than health subjects (p < 0.0001);<br>EGP during moderate and vigorous physical were lower than rest in type 1 diabetes subjects (p < 0.006)  |
| 17               | 8 subjects with type 1 diabetes subjects, 2 subjects with type 2 diabetes subjects and 15 health subjects | All subjects began to practice aerobic exercise for one hour a day  | Type 1 diabetes subjects showed higher postmeal glucose and EGP (p < 0.001);<br>Fasting adiponectin concentration was lower in type 2 diabetes subjects (p < 0.01) and health subjects (p < 0.05)  |
| 18               | 16 subjects with type 1 diabetes subjects   | Subjects were submitted a submaximal exercise after 100% or 1/3 of usual fast insulin dose                                  | BPM was positively related with VO2max (p = 0.002);<br>No difference in dosage of insulin;<br>Hypoglycemic episodes occurred when insulin wasn't reduced   |
| 19               | 20 subjects with type 1 diabetes subjects   | Subjects were submitted a resistance exercises for 3 months   | Increased insulin sensitivity, heart ratio and VO2max;<br>Reduction in severe hypoglycemic episodes  |
| 20               | 44 subjects with type 1 diabetes subjects and 44 health subjects  | Subjects were assessed by neuropsychological test   | Muscle strength was lower in type 1 diabetes subjects, compared to healthy volunteers (p < 0.01).<br>Muscle strength was not related to neuropathy or glycemic control for any muscle groups   |
| 21               | 23 subjects with type 1 diabetes subjects and 21 health subjects  | Subjects ingested dextrosol solutions (1 g/kg) or placebo (saccharin) 30 minutes before aerobic exercises until exhaustion. | Ingestion of dextrose increased muscle strength in health (p < 0.05) and subjects with type 1 diabetes subjects who had hypoglycemia during exercise (p < 0.05);<br>Hyperglycemia induced by dextrose was normalized after fifteen minutes of exercise in health subjects and after sixty minutes in type 1 diabetes subjects. |

*Note:* BMI: body mass index; BPM: beats per minute; EGP: endogenous glucose production; HbA1c: glycated hemoglobin; T12M: type 2 diabetes mellitus; T1DM: type 1 diabetes mellitus; VO2max: maximum volume of oxygen.

After twelve weeks in anaerobic exercise program, observed reduction in HbA1c of 0.96% ( $p < 0.05\%$ ), however was no change in fasting glucose.<sup>7</sup>

In contrast to previous works, longitudinal study conducted by Haider et al.,<sup>15</sup> didn't observe changes in HbA1c and fasting glucose in eighteen type 1 diabetes subjects who practice aerobic exercise for one hour a day.

#### *Stimulation of glucose production during exercise*

Galassetti et al.<sup>11</sup> investigated the effects of glycemic control and gender on neuroendocrine and metabolic variables in fifteen type 1 diabetes subjects (7 females and 8 males), matched for age, duration of diabetes and physical exercises. The clinical trial consisted of 90-minute in cycle ergometer (considering 80% of anaerobic threshold and 50% of VO<sub>2</sub>max for each individual). Results showed higher endogenous glucose production (EGP) in men ( $p < 0.05$ ) and glycerol levels were higher in women ( $p < 0.05$ ). Other variables measured did not differ in both sexes. In conclusion, there are sex differences also in type 1 diabetes subjects in response to exercise and EGP is the main determinant of sexual dimorphism.

Were also evaluated contribution of glycogenolysis and gluconeogenesis to hepatic glucose production during rest, moderate and vigorous physical exercises in five type 1 diabetes subjects and six health subjects matched for age, weight and VO<sub>2</sub>max. The experimental consisted of 200 minutes of rest, 50 minutes treadmill measuring 35% of VO<sub>2</sub>max (moderate physical) and 50 minutes treadmill measuring 70% of VO<sub>2</sub>max (vigorous physical). After the tests, type 1 diabetes subjects showed 60% higher EGP during rest than health subjects ( $p < 0.0001$ ), however EGP during moderate and vigorous physical were lower than rest in type 1 diabetes subjects ( $p < 0.006$ ).<sup>16</sup>

Perseghin et al.<sup>17</sup> compared concentrations of insulin, glucose, HbA1c and adiponectin and physical exercises between forty subjects (eight with type 1 diabetes subjects, two with type 2 diabetes subjects, fifteen prediabetic and fifteen health subjects). As a result, type 1 diabetes subjects showed higher postmeal glucose and EGP ( $p < 0.001$ ), however fasting serum adiponectin concentration was lower in type 2 diabetes subjects ( $p < 0.01$ ) and health subjects ( $p < 0.05$ ), proving a relationship between adiponectin and insulin resistance.

#### *Adjusting insulin dose before, during and after physical exercises*

A randomized crossover study was conducted in eight twentieth type 1 diabetes subjects in the presence of good glycemic control (HbA1c =  $6 \pm 0.002\%$ ) assessed the requirements insulin dose reduction after exercise at different intensities and durations, to mini-

mize the risk of severe hypoglycaemic episodes. Each volunteer served as his own control, with changes in insulin lispro dosage (100%, 50% or 25% of insulin dose usually used) and different VO<sub>2</sub>max (determined by indirect calorimetry). After tests, 100% of insulin dose was associated with an increased risk of hypoglycemia for all exercise intensity and 75% reduction of the insulin dose was required for adequate glucose concentration at 75% of VO<sub>2</sub>max. Thus, the authors suggested insulin dose adjustment to minimizing hypoglycemia.<sup>9</sup>

Another crossover study related the aerobic capacity with insulin dose in sixteen subjects with type 1 diabetes subjects submitted to exhaustion during submaximal exercise (170 beats per minute) after usual dose or one-third usual fast insulin dose. As a result, beats per minute was correlated positively with VO<sub>2</sub>max ( $p = 0.002$ ) and aerobic fitness no changes with the dosage of insulin, however hypoglycemic episodes occurred when insulin wasn't reduced.<sup>18</sup>

Confirming that regular exercise promotes long-term benefits, twenty type 1 diabetes subjects were followed by three months and submitted to resistance training for 135 minutes per week. Results showed increased insulin sensitivity, heart ratio and VO<sub>2</sub>max, besides a reduction in severe hypoglycemic episodes.<sup>19</sup>

#### *Influence of exercises on resistance and muscular strength in diabetics*

Anderson em 1998,<sup>20</sup> conducted a study comparing muscle strength with neuropathic complications and glycemic control in forty four subjects with type 1 diabetes subjects and forty four health subjects. All participants were assessment of muscle strength, neuropsychological test (including nerve conduction and sensory nerve conduction tests) and blood samples were collected for glucose, HbA1c and creatine analysis. Results show that the muscle strength was lower in type 1 diabetes subjects, compared to healthy volunteers ( $p < 0.01$ ) and muscle strength was not related to neuropathy or glycemic control for any muscle groups.

Ramires et al.,<sup>21</sup> conducted a double-blind, controlled, crossover study also assessing the influence of resistance exercise and glucose ingestion in twenty one type 1 diabetes and twenty three health subjects, using each subject as his own control. All ingested dextrosol solutions (1 g/kg) and placebo (saccharin) thirty minutes before exercises on ergometer (55 to 60% of VO<sub>2</sub>max) until exhaustion. End of tests, performed on different days, ingestion of dextrose increased muscle strength in health subjects ( $p < 0.05$ ) and subjects with type 1 diabetes subjects who had hypoglycemia during exercise ( $p < 0.05$ ). Another important fact is hyperglycemia induced by dextrose was normalized after fifteen minutes of exercise in health subjects and after sixty minutes in type 1 diabetes subjects.

## Conclusion

This systematic review concluded that there are positive influences of exercise of long-term glycemic control in type 1 diabetes, however results are contradictory with respect to insulin sensitivity and fasting glucose.

Glycemic control in diabetes should be based on HbA2c values, self-monitoring of blood glucose and reduction of insulin requirement, such as have been demonstrated in several studies. Thus physical exercise, along with dietary therapy and medication, are important to control diabetes.

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