



■ Review Article

# Exercise Strategies to Prevent Hypoglycemia in Patients with Diabetes

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The importance of adopting healthy exercise routines has been repeatedly emphasized to individuals with diabetes mellitus (DM). However, knowledge about the risk of exercise-induced hypoglycemia is limited. Regular exercise reduces and delays the onset of DM-related complications particularly in individuals who already have DM. However, an excessive exercise can lead to hypoglycemia. Excessive exercise in the evening can cause hypoglycemia while sleeping. Furthermore, if individuals with DM want to have a greater amount of exercise, the exercise duration rather than intensity must be increased. In weight resistance exercises, it is beneficial to first increase the number of repetitions, followed by the number of sets and gradually the weight of resistance. When performing intermittent high-intensity training within a short time period, hypoglycemia may develop for an extended period after exercise. In addition to adjusting exercise regimens, the medication doses must be modified accordingly. Delaying exercise, adjusting the number of snacks consumed prior to exercise, reducing insulin dose before exercise, and injecting insulin into the abdomen rather than the limbs prevent exercise-induced hypoglycemia prior to a spontaneous exercise. Ultimately, with personal knowledge on how to prevent hypoglycemia, the effects of exercise can be maximized in individuals with DM, and a healthy lifestyle can prevent future complications.

**Keywords:** Diabetes Mellitus; Hypoglycemia; Exercise; Insulin

Received: May 14, 2019, Revised: August 4, 2019, Accepted: September 5, 2019

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## INTRODUCTION

Hypoglycemia is characterized by blood glucose levels  $<70$  mg/dL<sup>1)</sup> and is one of the most common but severe complications of diabetes mellitus (DM).<sup>2)</sup> The symptoms of hypoglycemia include palpitation, sweating, dizziness, hunger, drowsiness, and anxiety. In severe cases of persistent hypoglycemia without treatment, syncope or convulsions may occur.<sup>3)</sup> Hypoglycemia has different causes, which include inadequate diet, alcohol consumption, kidney dysfunction, and administration of insulin and oral hypoglycemic agents (OHAs).<sup>4)</sup>

The most common methods used to successfully manage blood glucose levels in individuals with DM include diet control, exercise, and administration of medications, including insulin. Several studies have discussed about the prevention of hypoglycemia by adjusting OHA and insulin doses and modifying diet.<sup>5,6)</sup> However, the correlation between hypoglycemia and exercise is not fully elucidated. Although the importance of exercise itself has been repeatedly emphasized, the risk of exercise-induced hypoglycemia is not well reported to date. Thus, this study aimed to assess exercise as a risk factor for hypoglycemia in individuals with DM.

Exercise has several benefits, which include controlling blood glucose levels in individuals with DM. Therefore, it can help prevent and delay DM-related complications. Moreover, it improves cardiopulmonary endurance, physical strength, muscle mass, and bone density and can relieve stress.<sup>7-9)</sup> However, excessive exercise can cause hypoglycemia particularly in individuals with DM treated with insulin injections or OHAs. Exercise-associated hypoglycemia can lead to exercise reluctance, which can then have a negative effect on an individual's health. Thus, to prevent hypoglycemia and ensure safety during exercise, a patient's drug dose should be modified in accordance with exercise timing, intensity, and duration. In this study, the direction and recommendations of applicable exercise routines were summarized according to the records of individuals with type 2 DM (T2DM) who exercise to achieve blood glucose control. Moreover, the different clinical exercise guidelines implemented were assessed.

## EFFECTS OF EXERCISE IN INDIVIDUALS WITH DIABETES MELLITUS

In individuals with T2DM, regular exercise can reduce blood glucose levels.<sup>10)</sup> Although exercise has no direct effect on reducing blood glucose levels in individuals with type 1 DM (T1DM), it decreases the incidence of or delays the development of diabetic macrovascular complications. In addition, exercise has positive effects on both physical and mental health, which include improved cardiovascular function, increased muscle mass and strength, lower risk of coronary artery disease, weight management, improvement in blood pressure, increased self-confidence, and stress reduction.<sup>11,12)</sup> In summary, exercise can improve the quality of life of individuals with DM.

## MECHANISM BY WHICH EXERCISE INDUCES HYPOGLYCEMIA IN INDIVIDUALS WITH DIABETES MELLITUS

In general, when people exercise, blood insulin levels decrease to maintain homeostasis.<sup>13-15)</sup> In relation to this, an increase in counter-regulatory hormone levels results in gluconeogenesis and lipolysis in the liver. Via these processes, the increase in blood glucose levels and demands is balanced. Thus, the blood glucose levels will be maintained during exercise. However, in individuals with T1DM, the blood insulin levels do not decrease. Instead, blood circulation in the subcutaneous tissues increases, which then elevates insulin levels in the blood. Thus, the liver produces less glucose in T1DM individuals with high blood insulin concentrations who exercise. In addition, the glucose intake in exercised muscles increases, thereby resulting in hypoglycemia.<sup>16)</sup> Individuals with T2DM can control their blood glucose levels with dietary modification or exercise therapy alone, and the risk of exercise-induced hypoglycemia is relatively low. However, individuals with T2DM who are taking insulin or OHAs may be at moderate risk of exercise-induced hypoglycemia.<sup>17)</sup>

## PREVENTION OF HYPOGLYCEMIA BY MODIFYING EXERCISE REGIMENS

### 1. Exercise Timing

Exercise timing can have a significant effect on the risk of hypoglycemia, which may occur when an individual exercises without taking any snacks or exercises much later than usual after meals. Since exercise-induced hypoglycemia can occur during, immediately, or even 48 hours after exercise,<sup>18)</sup> exercising in the evening may cause hypoglycemia while sleeping. Therefore, exercising too late in the evening should be prevented. If an individual needs to exercise in the evening, excessive exercise must be avoided, and blood glucose levels should be closely monitored before going to sleep.

### 2. Amount of Exercise (Exercise Intensity and Exercise Time)

Sudden changes in exercise intensity or exercise time, which include starting to exercise without a plan or excessively increasing exercise intensity or exercise time, are the major causes of hypoglycemia. Therefore, individuals with DM should always be cautious when suddenly increasing the amount of their exercise. If they want to have a greater amount of exercise, their exercise time and exercise intensity must be gradually increased.<sup>19)</sup> Ideally, the exercise time should be increased first, followed by exercise intensity once an individual has adapted to a greater exercise time. For example, in the case of aerobic exercises, including walking, individuals should first increase their exercise time at 5–10-minute increments. Then, when they get used to it, their walking speed can be increased. For strength building exercises, the amount of exercise is determined according to the number of repetitions, number of sets, and resistance (weight of the equipment or tool).

If individuals want to have a greater amount of exercise, they should first increase the number of repetitions. Once they get used to it, the number of sets can be increased, followed by the weight. Thus, a gradually change in the amount of exercise should be in the following order: increasing the number of repetitions, number of sets, and then weight. In short-term, intermittent high-intensity training or sprinting, the sympathetic tone may become overly excited, and blood glucose levels may increase. This phenomenon does not increase the risk of hypoglycemia. However, caution should be observed because the risk of exercise-induced hypoglycemia may increase after the end of an intermittent high-intensity exercise.

### 3. Changes in Drug Administration

Exercising while taking insulin or OHAs at maximum doses can cause excessive blood glucose reduction due to the simultaneous blood glucose-lowering effect of insulin and exercise. If exercise is initiated within 90 minutes of insulin administration, then the drug dose must be accurately adjusted before an exercise according to the planned time and intensity of exercise (Table 1).<sup>19,20</sup> Exercise can be often performed without planning. Thus, individuals can easily adjust their insulin dose before exercising. However, caution must be observed to prevent hypoglycemia, and individuals must consult their doctors as reducing the dose of basal insulin (not premeal insulin, such as rapid or ultrarapid insulin) may only be necessary after establishing a regular physical activity plan that reduces overall insulin dose. For individuals taking OHAs, a spontaneous dose adjustment is challenging. Thus, in such cases, hypoglycemia must be prevented by eating carbohydrates between meals, and these individuals should consult their physicians prior to starting or changing exercise regimens.

### 4. Insulin Administration Site

If insulin is injected into the primary exercised muscle region, the absorption speed of insulin increases and so does the risk of hypoglycemia. If ultrarapid acting insulin is injected into the arm or leg muscles, individuals should be cautious not to exercise that muscle for 1 hour. For example, administering insulin to the thigh muscles is recommended. However, one must refrain from playing soccer or squash for 1 hour after administering the drug. In relation to these reasons, insulin should be injected into the abdomen rather than the arms or legs used during exercise.

## REGULATING THE AMOUNT AND FREQUENCY OF SNACK INTAKE PRIOR TO EXERCISE

Immediate and appropriate actions must be taken to prevent emergency situations when hypoglycemia occurs. However, preventing hypoglycemia in advance is more important. Additional carbohydrate intake can prevent exercise-induced hypoglycemia particularly in the following cases: (1) when more than 2 hours of long-term exercise is planned; (2) when an unplanned physical activity is suddenly performed; (3) when individuals exercise without adjusting the insulin dose; (4) when individuals exercise in an uncontrolled state of dose adjustment by taking OHA; and (5) when an individual is aiming to prevent prolonged hypoglycemia associated with exercise.

### 1. Exercise Planning

The most effective method to prevent hypoglycemia is to establish an exercise plan. When planning an exercise, exercising while taking insulin or OHA at maximum doses should be avoided, and the dose must be reduced.<sup>21,22</sup> Ideally, individuals who use insulin therapy should exercise daily at similar times to maintain a certain blood glucose level. If there is a sudden need to exercise, adjusting the number of snacks to prevent hypoglycemia is helpful. The intake of snacks should be adjusted according to the pre-exercise blood glucose level and exercise type, time, and intensity.

### 2. Checking Blood Glucose Levels and Snack Intake

Checking blood glucose levels before, during, and after an exercise is essential in preventing and treating hypoglycemia. The blood glucose level must be checked before exercising to ensure that it is stable. Table 2 shows the pre-exercise blood glucose levels and the recommended intake for additional snacks based on exercise intensity and exercise time.<sup>19,23</sup> Notably, the effect of exercise on reducing blood glucose levels persists even after the end of the exercise. Thus, blood glucose levels must be continually monitored after an exercise. In addition, changes in blood glucose fluctuations over time should be considered to help predict the occurrence of hypoglycemia after an exercise.

## SAFETY TIPS

### 1. Exercise Partner

Having an exercise partner can be significantly useful in taking appro-

**Table 1.** Guidelines on reducing insulin dose based on exercise intensity<sup>19,20</sup>

Variable	Reduction of rapid or ultrarapid insulin dose	
	Exercise time: 30 min	Exercise time: 60 min
Mild aerobic exercise (<25% of the maximum cardiopulmonary capacity)	Reduce by 25%	Reduce by 50%
Moderate aerobic exercise (50% of the maximum cardiopulmonary capacity)	Reduce by 50%	Reduce by 75%
Intense aerobic exercise (70%–75% of the maximum cardiopulmonary capacity)	Reduce by 75%	Not applicable*
Intense aerobic/anaerobic exercise (greater than 75% of the maximum cardiopulmonary capacity)	Do not reduce	Not applicable*

\*A high-intensity exercise lasting for ≥60 min cannot be maintained.

**Table 2.** Snack recommendations based on glucose levels before exercise<sup>19,23)</sup>

Glucose level before exercise	Recommendations
<90 mg/dL	- Depends on the exercise. An additional 10–30 g of carbohydrates can be consumed, which can be absorbed quickly before the start of the exercise. - Exercise <30 min or very high-intensity exercise, such as weight training or interval training, may not require additional carbohydrate intake. - Long-term moderate exercises require additional carbohydrate intake (0.5–1.0 g of carbohydrate intake per kilogram of body weight at 1-h intervals of exercise based on the blood glucose level).
90–150 mg/dL	- Consume carbohydrates before the start of most exercises and at 1-h intervals based on exercise type or insulin activity. (0.5–1.0 g of carbohydrate intake per kilogram of body weight at 1-h intervals of exercise).
150–250 mg/dL	- Allow blood glucose to decrease to <150 mg/dL during exercise before consuming carbohydrates.
250–350 mg/dL	- When moderate to high levels of ketones are detected in the urine ketone test, exercise may be prohibited. - Mild-to-moderate-intensity exercise can be performed; however, since high-intensity exercise may cause hyperglycemia, exercise can be postponed until the blood glucose levels decrease to <250 mg/dL.
≥350 mg/dL	- In the urine ketone test, when moderate to high levels of ketone are observed, exercise may be prohibited. - In case no urine ketone (or trace) is noted, the insulin dose can be adjusted according to insulin activity before exercise (generally 50%). - After the start of mild-to-moderate-intensity exercise, an individual must refrain from further exercise until the blood glucose levels decrease.

appropriate measures when hypoglycemia occurs during exercise. In addition, it is more fun to exercise with a partner than to exercise alone. A partner can also be a positive motivator to maintain exercise regimens.

## 2. Diabetes Tag

Individuals who exercise without a partner and experience moderate hypoglycemia or loss of consciousness may be in great danger. Therefore, a diabetes tag must be brought during exercise to help others quickly identify hypoglycemia and respond appropriately in case of an emergency.

## 3. Useful Facts

In general, insulin absorption is facilitated when exercising in warm weather compared with cold weather.<sup>24)</sup> Thus, reducing insulin doses might be required during exercise at higher temperatures. Since alcohol inhibits gluconeogenesis in the liver, exercising after drinking can also cause hypoglycemia.<sup>25)</sup> Hence, individuals should adjust their exercise regimens if there is a change in the type or dose of insulin prescribed by the doctor even though they have never experienced hypoglycemia during exercise.<sup>22)</sup> If individuals eat less than usual and skip meals or inevitably have to eat later than usual, they should postpone their exercise or take a moderate amount of snacks to prevent hypoglycemia during and after exercise or before bedtime. In addition, excessive exercise is not advised if there are modifications in the characteristics of the exercise, such as type, intensity, and time.

## CONCLUSION

Exercise is an intervention that is essential in managing DM. However, if individuals with DM exercise without proper preventive measures, they may suddenly develop exercise-induced hypoglycemia. Failure to prevent hypoglycemia can cause complications and fear of exercise. In relation these reasons, individuals with DM must discuss about insulin dose adjustments and safe exercise methods with their doctors and exercise specialists before exercising. Moreover, an individual understanding and practice of safe exercise methods and precautions for

preventing hypoglycemia can help individuals with DM achieve active and dynamic exercise routines and eventually a healthier life.

## CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

## ACKNOWLEDGMENTS

This research was supported by a grant from Korea Institute of Drug Safety and Risk Management in 2018.

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## REFERENCES

- Desouza CV, Bolli GB, Fonseca V. Hypoglycemia, diabetes, and cardiovascular events. *Diabetes Care* 2010;33:1389-94.
- ADVANCE Collaborative Group, Patel A, MacMahon S, Chalmers J, Neal B, Billot L, et al. Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes. *N Engl J Med* 2008;358:2560-72.
- Cryer PE. Death during intensive glycemic therapy of diabetes: mechanisms and implications. *Am J Med* 2011;124:993-6.
- Cryer PE. The barrier of hypoglycemia in diabetes. *Diabetes* 2008;57:3169-76.
- Palmer SC, Mavridis D, Nicolucci A, Johnson DW, Tonelli M, Craig JC, et al. Comparison of clinical outcomes and adverse events associated with glucose-lowering drugs in patients with type 2 diabetes: a meta-analysis. *JAMA* 2016;316:313-24.
- Ben-Ami H, Nagachandran P, Mendelson A, Edoute Y. Drug-induced

- hypoglycemic coma in 102 diabetic patients. *Arch Intern Med* 1999;159:281-4.
7. Kemi OJ, Haram PM, Loennechen JP, Osnes JB, Skomedal T, Wisloff U, et al. Moderate vs. high exercise intensity: differential effects on aerobic fitness, cardiomyocyte contractility, and endothelial function. *Cardiovasc Res* 2005;67:161-72.
  8. Chen CN, Chuang LM, Wu YT. Clinical measures of physical fitness predict insulin resistance in people at risk for diabetes. *Phys Ther* 2008;88:1355-64.
  9. Shahar J, Hamdy O. Medication and exercise interactions: considering and managing hypoglycemia risk. *Diabetes Spectr* 2015;28:64-7.
  10. Ibanez J, Izquierdo M, Arguelles I, Forga L, Larrion JL, Garcia-Unciti M, et al. Twice-weekly progressive resistance training decreases abdominal fat and improves insulin sensitivity in older men with type 2 diabetes. *Diabetes Care* 2005;28:662-7.
  11. Asano RY, Sales MM, Browne RA, Moraes JF, Coelho Junior HJ, Moraes MR, et al. Acute effects of physical exercise in type 2 diabetes: a review. *World J Diabetes* 2014;5:659-65.
  12. Wang Y, Simar D, Fiatarone Singh MA. Adaptations to exercise training within skeletal muscle in adults with type 2 diabetes or impaired glucose tolerance: a systematic review. *Diabetes Metab Res Rev* 2009;25:13-40.
  13. Minuk HL, Vranic M, Marliss EB, Hanna AK, Albisser AM, Zinman B. Glucoregulatory and metabolic response to exercise in obese noninsulin-dependent diabetes. *Am J Physiol* 1981;240:E458-64.
  14. Cade WT, Khoury N, Nelson S, Shackelford A, Semenkovich K, Krauss MJ, et al. Hypoglycemia during moderate intensity exercise reduces counterregulatory responses to subsequent hypoglycemia. *Physiol Rep* 2016;4:e12848.
  15. Davis SN, Tate D, Hedrington MS. Mechanisms of hypoglycemia and exercise-associated autonomic dysfunction. *Trans Am Clin Climatol Assoc* 2014;125:281-91.
  16. Younk LM, Mikeladze M, Tate D, Davis SN. Exercise-related hypoglycemia in diabetes mellitus. *Expert Rev Endocrinol Metab* 2011;6:93-108.
  17. Miller CD, Phillips LS, Ziemer DC, Gallina DL, Cook CB, El-Kebbi IM. Hypoglycemia in patients with type 2 diabetes mellitus. *Arch Intern Med* 2001;161:1653-9.
  18. Boule NG, Weisnagel SJ, Lakka TA, Tremblay A, Bergman RN, Rankinen T, et al. Effects of exercise training on glucose homeostasis: the HERITAGE Family Study. *Diabetes Care* 2005;28:108-14.
  19. Colberg SR, Sigal RJ, Yardley JE, Riddell MC, Dunstan DW, Dempsey PC, et al. Physical activity/exercise and diabetes: a position statement of the American Diabetes Association. *Diabetes Care* 2016;39:2065-79.
  20. Rabasa-Lhoret R, Bourque J, Ducros F, Chiasson JL. Guidelines for premeal insulin dose reduction for postprandial exercise of different intensities and durations in type 1 diabetic subjects treated intensively with a basal-bolus insulin regimen (ultralente-lispro). *Diabetes Care* 2001;24:625-30.
  21. Kim YS, Cho BL, Kim WS, Kim SH, Jung IH, Sin WY, et al. Frequency and severity of hypoglycemia in type 2 diabetes mellitus patients treated with a sulfonylurea-based regimen at university-affiliated hospitals in Korea: the naturalistic evaluation of hypoglycemic events in diabetic subjects study. *Korean J Fam Med* 2019;40:212-9.
  22. Yang YJ. An overview of current physical activity recommendations in primary care. *Korean J Fam Med* 2019;40:135-42.
  23. Zaharieva DP, Riddell MC. Prevention of exercise-associated dysglycemia: a case study-based approach. *Diabetes Spectr* 2015;28:55-62.
  24. Park SK, Sung KC, Shin HS, Seo HI, Hwang SJ, Kim ER, et al. Seasonal variation in insulin resistance in Koreans. *Korean Circ J* 2005;35:620-4.
  25. Yki-Jarvinen H, Nikkila EA. Ethanol decreases glucose utilization in healthy man. *J Clin Endocrinol Metab* 1985;61:941-5.