

# Prevention of Hypoglycemia During Exercise in Type I Diabetes

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Insulin-dependent (type I) diabetic subjects who exercise for whatever reason do this at the risk of hypoglycemia. To enjoy physical activities without major metabolic complications, diabetic patients can take measures to prevent exercise-induced hypoglycemia. These measures basically include preventing accelerated insulin absorption, mimicking physiological insulin secretion during exercise, supplying additional carbohydrates during exercise, and providing effective diabetes education. When adapting the insulin dose, duration and intensity of the work load, time of day, prevailing insulin levels, and the state of nutrition must be considered. Additional carbohydrates can prevent hypoglycemia when exercise is spontaneous and insulin dose reduction is impossible. Prevention of exercise-induced hypoglycemia may be best achieved if patients participate in intensive and comprehensive teaching programs for self-management of diabetes.

Very much like the nondiabetic population, an ever-growing proportion of insulin-dependent (type I) diabetic patients intends to take up or intensify their leisure time physical activity for a number of motivations that are mainly not health-related. This means, like anybody else, diabetic patients exercise primarily on weekends, in the evening, and during holidays. Under these conditions, physical activity is largely spontaneous, and time, duration, and intensity of exercise are variable; thus, metabolic effects of exercise are difficult to predict. Although such factors are of no importance to the nondiabetic population, diabetic patients may abstain from participating in physical activity for fear of experiencing acute complications,

such as hypoglycemia. Because participation in exercises and games has become an important facet in the social structure of society, it is the obligation of all diabetologists to enable type I diabetic patients to perform physical activity at a minimal risk of acute complications.

Exercise may induce acute metabolic complications, such as hyper- or hypoglycemia. The latter is the more frequent and most feared acute complication of physical exercise in type I diabetic patients. It is now well established that exercise-induced hypoglycemia is mainly caused by hyperinsulinemia and the loss of physiological adaptation of the reduced insulin needs to exercise (1,2). In contrast, little is known about the incidence of hypoglycemia in association

with exercise. From a survey performed among 302 physical educators at all primary and secondary schools in Düsseldorf, Germany, the impression emerged that exercise-induced hypoglycemia is a rare incident (3). In this survey, 63 insulin-dependent (type I) diabetic patients were identified among a total of 53,609 students (0.12%). Of these diabetic students, 61 participated in physical education on a regular basis. Only 7 of the 302 physical educators reported an episode with exercise-induced hypoglycemia in their students. In a prospective study conducted over a period of 2 yr in 300 type I diabetic patients, 48 episodes of postexercise late hypoglycemia were seen (4), 32 of them severe. All of these hypoglycemias occurred after midnight when exercise was performed in the afternoon or evening. Among other causes, exercise takes a prominent role in precipitating hypoglycemia in type I diabetic patients (5).

Measures to prevent exercise-induced hypoglycemia, in principle, include the following: preventing accelerated insulin absorption, mimicking physiological insulin secretion during exercise, supplying additional carbohydrates during exercise, and providing effective diabetes education. More than a decade ago, it was shown that exercise may accelerate the absorption of regular insulin if it was injected in the thigh immediately before the onset of leg exercise in animals (6) and humans (7). Therefore, the injection of insulin into a nonmoving part of the body might prevent or at least reduce the risk of exercise-induced hypoglycemia (7). Shortly after this theory was formulated, however, it was demonstrated that this measure could not effectively prevent hypoglycemia when exercise was started  $\geq 30$  min after insulin injection (8,9). In any case, intramuscular injection of insulin should be avoided because exercise has been shown to accelerate its absorption from the muscle (10). Furthermore, warm ambient temperature has been

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shown to accelerate insulin absorption (11), which, in combination with exercise, may increase the risk of hypoglycemia (12). Thus, ambient temperature must be taken into account when adapting insulin dose in association with exercise.

From a physiological point of view, it would be logical to mimic the situation in normal subjects by reducing the insulin dose before exercise (13). However, this approach is of value only when the time, duration, and intensity of exercise can be defined. In cases when insulin already has been injected or when duration and intensity of exercise are unforeseeable, the only measure to prevent hypoglycemia is to supplement hepatic glucose production by increasing carbohydrate ingestion before, during, and after physical activity.

This principle recommendation to prevent exercise-induced hypoglycemia meets with a number of difficulties when determining the insulin dose reduction or the additional amounts of carbohydrates to be consumed. The adjustments in insulin dose and/or carbohydrate supplements certainly depend on duration and intensity of the work load, the prevailing insulin level, the level of glycemia before exercise, and the time of day exercise is performed. Thus, only general recommendations regarding the quantity of insulin dose reduction can be given. These recommendations may serve as a starting point from which each patient must find the optimal measure for his/her individual situation.

If patients plan to exercise for a longer period of time (e.g., cross-country skiing, marathon running, hiking, or bicycling), they should choose to reduce the insulin dose if possible. If such exercise is performed in the morning after a usual breakfast and normoglycemia is found before exercise, a reduction of >50% of the morning insulin dose may be necessary to prevent hypoglycemia (14,15). At blood glucose levels >11 mM, a less substantial reduction in the insulin dosage was sufficient to prevent

hypoglycemia (14). Similar results were found in patients participating in a ski race over a distance of 75 km (16). In diabetic patients participating in a marathon run (17), insulin was withheld altogether for 16–26 h before the race. Yet the patients were not deprived of insulin as documented by circulating free insulin levels, normal plasma free fatty acids, and blood ketone bodies. Only when blood glucose levels were near 300 mg/dl initially did all patients complete the race without complications, achieving normoglycemia during the final third of the race. As shown in the skiers, this type of endurance exercise increased insulin sensitivity after the race (16). This effect should be taken into consideration when endurance exercise has been performed and reduced insulin dosages may be necessary even on the day after such physical activity.

The time of day exercise is performed and the prevailing insulin levels may be of importance for consideration of the appropriate measure to prevent hypoglycemia during exercise (18). In this study, the risk of exercise-induced hypoglycemia was lowest when exercise was performed in the morning before breakfast and insulin injection when low insulin levels prevailed. However, when taking this approach, hypoglycemia may be prevented at the cost of inducing hyperglycemia. In particular, physical activity performed in the evening or afternoon carried the risk of nocturnal hypoglycemia (4,19). Because enhancement of insulin sensitivity extends beyond the exercise period (20) and muscle continues to take up substantial amounts of glucose from the circulation to replenish glycogen stores, sufficient supply to the circulation must be guaranteed. At night, the liver is the main source of glucose, and hyperinsulinemia would block this source. Insulin dose reductions of <50% of the evening dose did not effectively prevent nocturnal hypoglycemia (19). Therefore, after physical exercise in the evening, the insulin dose must be reduced more substan-

tially, and additional amounts of carbohydrates must be taken.

When exercise is spontaneous, only ingestion of extra carbohydrates can prevent hypoglycemia. No doubt exists about the efficacy of this measure, because glucose stemming from exogenous sources is oxidized almost completely by the working muscle if sufficient amounts of insulin are available (21). The choice of carbohydrate supplements should exclude bulky foods and include only rapidly absorbable carbohydrates. The additional carbohydrates should be ingested in small amounts to avoid exercising on a full stomach. Additional carbohydrates will usually be sufficient as a sole measure to maintain adequate supply of glucose to the working muscle before and/or after relatively short and mild physical exercise. However, in association with short periods of exhaustive exercise, additional carbohydrates may be disadvantageous because, under such conditions, glycemia may increase as observed in diabetic patients treated with continuous subcutaneous insulin infusion (CSII) (22) and intensified insulin treatment (23). Similar increments in glycemia were seen in cross-country skiers during the initial phase of the race (16).

CSII is now an established form of insulin therapy, and many patients use it as their preferential form of treatment. In principle, patients with CSII therapy also should follow guidelines, such as reduction of the insulin bolus, in anticipation of postprandial exercise (15) and adaptation of the insulin infusion rate (24). Patients on CSII treatment planning to perform long-term physical activity could best prevent acute exercise-induced hypoglycemia by reducing the premeal insulin bolus by 50% and stopping the basal insulin infusion rate while exercising (25). To reduce the risk of late-onset hypoglycemia, a reduction of the basal insulin infusion rate by 25% for several hours after the exercise period appeared to be the appropriate measure (25).

These rather general guidelines

can only serve as a starting point for each individual patient to discover how he/she personally reacts to the physical exercise of choice under varying conditions. Thus, to achieve any effective prevention of much feared exercise-associated hypoglycemia, insulin-treated diabetic patients who want to exercise must be offered an intensive and comprehensive teaching program for self-management of their metabolic control (26). The efficacy and long-term safety of such programs aiming at far-reaching independence of the patient from physicians and clinics has been documented even for unselected patients (27). After participating in such teaching programs, the patient must turn the newly acquired knowledge into practice. In doing so, the individual may search continuous support from his or her diabetologist and specific patient-oriented publications (28). In applying frequent blood glucose measurements, the patient will know the actual blood glucose level before starting to exercise and may discover any personal reaction to that physical exercise under various conditions. On the basis of the patient's observations and measurements, that individual must decide which preventive measure is most appropriate for the actual situation. Large variations among patients are likely to occur, underlining the absolute necessity for individual experience. As the personal experience of the patient grows and success in preventing hypoglycemia and other exercise-related complications increases, exercise can be performed safely and with optimal physical performance. The success of diabetic athletes and activities of the International Diabetic Athletes Association have impressively documented that this is very well possible.

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