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Review

Insulin Management Strategies for Exercise in Diabetes

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ABSTRACT

There is no question that regular exercise can be beneficial and lead to improvements in overall cardiovascular health. However, for patients with diabetes, exercise can also lead to challenges in maintaining blood glucose balance, particularly if patients are prescribed insulin or certain oral hypoglycemic agents. Hypoglycemia is the most common adverse event associated with exercise and insulin therapy, and the fear of hypoglycemia is also the greatest barrier to exercise for many patients. With the appropriate insulin dose adjustments and, in some cases, carbohydrate supplementation, blood glucose levels can be better managed during exercise and in recovery. In general, insulin strategies that help facilitate weight loss with regular exercise and recommendations around exercise adjustments to prevent hypoglycemia and hyperglycemia are often not discussed with patients because the recommendations can be complex and may differ from one individual to the next. This is a review of the current published literature on insulin dose adjustments and starting-point strategies for patients with diabetes in preparation for safe exercise.

Mots clés :
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RÉSUMÉ

Il ne fait aucun doute que l'exercice pratiqué de façon régulière peut être bénéfique et entraîner une amélioration de la santé cardiovasculaire dans son ensemble. Toutefois, l'exercice chez les patients diabétiques peut également rendre le maintien de l'équilibre glycémique difficile, particulièrement si les patients reçoivent de l'insuline ou certains agents hypoglycémiants par voie orale. L'hypoglycémie qui est l'événement indésirable le plus fréquent est associée à l'exercice et à l'insulinothérapie. De plus, la crainte de l'hypoglycémie constitue le principal obstacle à l'exercice chez de nombreux patients. Par l'ajustement approprié des doses d'insuline, et dans certains cas, par la prise d'une supplémentation en glucides, il est possible de mieux prendre en charge les concentrations de la glycémie durant l'exercice et lors de la récupération. En général, les stratégies d'insulinothérapie qui contribuent à favoriser la perte de poids en association avec l'exercice pratiqué de façon régulière et les recommandations en matière d'ajustement de l'exercice pour prévenir l'hypoglycémie et l'hyperglycémie ne sont pas souvent abordées avec les patients puisque les recommandations peuvent être complexes et varier d'un individu à l'autre. Cette revue récente de la littérature porte sur l'ajustement des doses d'insuline et les stratégies de départ destinées aux patients en vue de les préparer à faire de l'exercice de façon sécuritaire.

Introduction

Maintaining blood glucose (BG) concentrations in a targeted range is a challenge for individuals with diabetes receiving insulin therapy. For people living with either type 1 or type 2 diabetes, insulin management for exercise is a somewhat imprecise science that can often frustrate the patient and caregiver. For individuals who perform varying types of physical activity (i.e. sometimes mild, sometimes intense) at varying times of day, insulin management is an even greater challenge. This is because most forms of exercise increase insulin sensitivity not only at the time of the activity but also for hours into recovery as energy stores are replenished (1). On the other hand, some patients may experience hyperglycemia after intense exercise, possibly because of an acute stress response that blunts insulin sensitivity, which can require a corrective insulin bolus (2). This insulin correction after exercise can further increase the risk for late-onset hypoglycemia. Patients with diabetes receiving multiple daily injections (MDIs) or a continuous subcutaneous insulin infusion (CSII), must consider a number of factors before

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they can safely engage in physical activity. The insulin management strategy (i.e. MDIs vs. CSII) will affect the type of insulin dose adjustments (i.e. rapid-acting meal-time insulin vs. long-acting basal insulin) needed for activity. At the core of decision-making, it is important to understand the patient's goals for exercise (e.g. weight loss, fitness, performance and competition, social activity) and the patient's capacity to evaluate all of the factors that might affect their BG concentrations. These factors include duration and intensity of the activity, the glucose concentration at the start of exercise, circulating insulin levels, insulin sensitivity, time of day, prior hypoglycemia, recent exercise, ambient temperature, competition stress, electrolyte balance and perhaps menstrual cycle for females (3).

Primarily, aerobic exercise (e.g. walking, jogging, gardening, cycling) increases hypoglycemia risk during the activity and, therefore, specific insulin dose reductions are required (i.e. bolus and/or basal insulin) to better manage BG levels in these conditions. These exercise-specific insulin dose reductions are often implemented well before exercise start time to allow for circulating insulin levels to drop by the start of exercise. In recovery, insulin dose reductions (basal and/or bolus insulin) are also often needed to allow for the increase in insulin sensitivity that can last for up to 48 hours after the end of exercise (4). For patients living with type 1 diabetes, a single bout of exercise typically lowers insulin needs over the next 12 to 24 hours (5,6). Surprisingly, very long activities such as marathon running, may not be associated with enhanced insulin sensitivity in recovery in patients with type 1 diabetes (7), and some forms of intermittent high-intensity exercise (HIE) may promote elevations in BG for up to several hours in recovery (8). Vigilance around BG monitoring becomes even more important after exercise.

Although most active individuals with type 1 diabetes make some form of adjustments in insulin dosing and/or carbohydrate intake around exercise, the majority still report experiencing hypoglycemia after exercise (9). Therefore, irrespective of the current strategies used to manage BG levels during exercise and in recovery, it is essential that individuals increase the frequency of capillary BG monitoring by using a reliable glucose monitor, and they should use real-time continuous glucose monitoring (CGM), if it is available. These tools will provide individuals with the ability to titrate recommendations accordingly with altered carbohydrate intake and/or insulin dose adjustments. Although exercise itself might affect CGM sensor accuracy to some degree (10–12), having glucose trend lines and reasonable estimations of BG concentrations during most forms of exercise (13) will markedly help with fine-tuning initial adjustments to insulin and/or nutrient intake.

It is important to mention here that the evidence for current guidelines in insulin dose adjustments for exercise are generally based on small-scale studies (typically <20 subjects) conducted on relatively physically active patients with type 1 diabetes in strictly controlled laboratory settings (Table 1). Because of the great interindividual variability in glycemic responses to exercise and limited reproducibility within individuals, at least in the postprandial state (14), the recommendations that follow are only suggested starting points.

Importance of regular physical activity

Health-care practitioners (e.g. physicians, nurses, certified diabetes educators) should strongly promote regular physical activity for individuals with diabetes. The American Diabetes Association Physical Activity Guidelines suggest that regular aerobic exercise can increase insulin sensitivity, improve lung function and cardiac output and markedly lower the risk of cardiovascular disease (3). In addition, these guidelines have established that the addition of regular resistance training (2–3 times per week) to regular aerobic activity (150 or more minutes per week) significantly improves body composition, bone mineral density, blood lipid profiles and overall cardiovascular health (15). This volume of physical activity includes routine activities of daily living. Even simple low-grade physical activity (e.g. walking) has been shown to have beneficial effects on BG concentrations in people living with diabetes (16,17). Walking is particularly effective in reducing postprandial BG concentrations in patients with type 2 diabetes (18). Emerging evidence suggests that less activity time can be associated with significant improvements in cardiometabolic health in diabetes if HIE training is performed (3). Although insulin dose adjustments and other precautions are normally required to maintain BG levels in a targeted range for various types of exercise performed, regular physical activity should continue to be prescribed and promoted for all individuals with diabetes.

Types of adjustments for exercise

Depending on the type of intensive insulin therapy used to manage BG concentrations, different adjustments may be necessary for exercise. Individuals may be using MDIs (basal insulin only, intermediate-acting insulin with regular insulin or an insulin analog) or CSII to manage their diabetes. Patients receiving MDIs typically require both a long-acting insulin analog (e.g. insulin glargine, detemir, or degludec) and a rapid-acting insulin analog (e.g. insulin aspart, glulisine, or lispro), whereas patients receiving a CSII use only a rapid-acting analog in "basal" and "bolus" regimens. Some insulin therapy strategies are less adaptable for exercise (e.g. regular insulin, neutral protamine Hagedorn [NPH] insulin, insulin degludec) but can still be titrated appropriately for planned exercise.

MDI

For patients receiving MDIs, adjustments for exercise are slightly more restricted, mainly because basal insulin adjustments tend to have significant effects on BG concentration for much of the day, not just for the planned period of exercise. In general, long-acting insulin analogs are taken either 1 or 2 times daily for basal insulin coverage (19). In 1 study, insulin detemir use was associated with less hypoglycemia risk than NPH or insulin glargine in patients with type 1 diabetes performing 30 minutes of aerobic exercise 5 hours after mealtime (20). However, with all 3 basal insulin types unadjusted for activity, mild hypoglycemia was relatively common either during the 30 minutes of exercise or soon after exercise was finished (21%–57% of patients, depending on the basal insulin used) (20).

Those individuals who choose to split their long-acting insulin into a morning dose and an evening dose have more flexibility to reduce the morning dose before exercise, leaving the evening dose the day before unchanged. Moreover, those taking a split dose can also lower the evening dose after a day of vigorous exercise, if desired, to protect against postexercise late-onset hypoglycemia. In general, long-acting insulin analogs (i.e. detemir, glargine) can be reduced by 20% to 30% (21) in anticipation of an unusually physically active day (e.g. sports camps, tournaments, hiking/trekking, a long-distance run, or a cycling event) (22). If long-acting insulin is given at bedtime, these basal insulin adjustments should be made the evening before an unusually active day. If long-acting insulin is given in the morning, these adjustments should be made that same morning. In cases of prolonged aerobic activity, an additional reduction in bedtime basal insulin by 10% to 20% after exercise, when possible, should be implemented to protect against postexercise nocturnal hypoglycemia (21,23). In situations in which planned exercise occurs 1 to 3 hours after a meal, bolus insulin adjustments are preferred for those receiving MDIs, since the impact on 24-hour BG levels will be minimal.

Table 1
Summaries of relevant published research studies

Author	Journal	Insulin regimen	Exercise type and intensity	Insulin adjustments	Main findings
Campbell et al (28)	*Diabetes Care*	MDIs	45 min treadmill running (72.5±0.9% VO_2peak)	25% of usual rapid-acting insulin dose taken 1 h before exercise and consumed breakfast 1 h post-exercise, randomization: • Full bolus injection • 75% bolus injection • 50% bolus injection	25% pre-exercise and 50% postexercise insulin reduction protects against early-onset hypoglycemia (≤8 h), but not late-onset postexercise hypoglycemia
Campbell et al (21)	*BMJ Open Diabetes Res Care*	MDIs	45 min treadmill running (~70% of VO_2peak)	TDD basal insulin randomization: • Unchanged (100%) • Reduced by 20% (80%) 75% reduced rapid-acting insulin 1 h before exercise 50% reduced rapid-acting insulin with LGI meal 1 h after exercise	100% vs. 20% basal insulin reduction leads to similar BG change with no hypoglycemia until 6 h after exercise After 6 h, BG levels fall in unchanged (100%) conditions, and most subjects experience nocturnal hypoglycemia A combination of reducing basal insulin, prandial bolus insulin, and LGI feeding protects against hypoglycemia for 24 h in recovery without causing hyperglycemia
Taplin et al (45)	*J Pediatr*	CSII	60 min aerobic exercise (heart rate achieved at 55% of VO_2max)	Randomization (overnight after exercise): • 2.5 mg oral terbutaline • 20% basal rate reduction for 6 h • No reduction	20% basal insulin reduction after exercise is safe and effective in raising BG and reducing hypoglycemia after exercise and overnight Terbutaline prevents hypoglycemia but promotes hyperglycemia overnight
McAuley et al (43)	*Diabetologia*	CSII	30 min aerobic exercise (65%–70% of age-predicted maximum heart rate)	50% basal rate reduction 1 h before exercise after single insulin basal rate overnight	While helpful, 50% basal insulin reductions 1 h before exercise do not fully prevent hypoglycemia when BG is in low-normal range When BG<7.0 mmol/L (126 mg/dL) before exercise, consider carbohydrate snack and basal reduction >50%
Franc et al (35)	*Diabetes Oboes Metab*	CSII	30 min aerobic cycling (50% of VO_2max) 30 min intense cycling (75% of VO_2max)	Moderate-intensity exercise: • 50% basal rate reduction at start of exercise (+2 h in recovery) • 80% basal rate reduction at start of exercise (+2 h in recovery) Intense exercise: • Pump suspended during exercise • 80% basal rate reduction	Options to limit hypoglycemia risk 3 h after meal with 30 min of exercise include a reduction in basal insulin delivery by 80%–100% at exercise start For moderate exercise within 90 min of a meal, reduce the prandial bolus insulin by ~50% rather than lower basal insulin
Rabasa-Lhoret et al (31)	*Diabetes Care*	MDIs	30 min or 60 min cycling at 25%, 50%, or 75% of VO_2max	Randomization crossover: • Postprandial rest after full dose (100%) of LP preprandial insulin • Postprandial exercise after 100% of LP • Postprandial exercise after 50% of LP • Postprandial exercise after 25% of LP	Intensity and duration are important factors in bolus reductions (within 90 min of meal). Reduce prandial insulin by 50% for shorter- duration, moderate-intensity activities. Preprandial reductions: • Mild aerobic exercise (30 min=25% bolus reduction vs. 60 min=50% bolus reduction) • Moderate aerobic exercise (30 min=50% bolus reduction vs. 60 min=75% bolus reduction) • Heavy aerobic exercise (30 min or more=75% bolus reduction
Zaharieva et al (37)	*Diabetes Tech Their*	CSII	40 min aerobic exercise (~50% of VO_2 max) 40 min circuit exercise (mean intensity ~55% of VO_2 max)	Suspended basal insulin (100% reduction) at onset of both types of exercise; resumed to regular rate immediately after exercise	With basal insulin suspension, aerobic exercise is associated with a greater drop in BG compared with circuit-based exercise
Turner et al (66)	*Scans J Med*	MDIs	RE: • 1 set, 2 sets, 3 sets • 8 exercises×10 reps (60%–70% of 1 RM)	Participants took usual basal insulin but omitted morning rapid-acting insulin	1–2 sets of RE after overnight fast may lead to hyperglycemia lasting at least 1 h after exercise 3 sets of RE are associated with less hyperglycemia
Turner et al (38)	*Diabet Med*	MDIs	RE: • 6 exercises for 2 sets×10 reps (60% of 1 RM)	Algorithm included individualized dose of rapid-acting insulin administered immediately after RE (i.e. 50% of usual bolus correction based on postexercise BG; ranging from 0–4 units)	Individualized dose of rapid-acting insulin reduces early postexercise hyperglycemia without causing hyperglycemia 2 h after exercise
Yardley et al (67)	*Diabetes Care*	MDIs & CSII	45 min treadmill running (60% VO_2peak) before 45 min RE (7 exercises, 3 sets×8 reps) Vice versa (i.e. RE before aerobic)	For patients receiving MDIs: • 10% decrease in long- or intermediate-acting insulin For patients receiving CSII: • 50% decrease in basal insulin 1 h before exercise • Further 25% basal insulin decrease if BG<5.0 mmol/L (90 mg/dL)	RE before aerobic exercise improves glycemic stability throughout exercise and reduces duration and severity of postexercise hypoglycemia Trained individuals with type 1 diabetes should consider RE before aerobic exercise if they usually develop exercise-associated hypoglycemia

(*continued on next page*)

Table 1 (*continued*)

Author	Journal	Insulin regimen	Exercise type and intensity	Insulin adjustments	Main findings
Yardley et al (44)	*Diabetes Care*	MDIs & CSII	Randomization: • 45 min RE (7 exercises, 3 sets×8 reps) • 45 min treadmill running (60% of VO2peak) • No exercise	For patients receiving MDIs: • 10% reduction in long-acting insulin For patients receiving CSII: • 50% basal rate reduction 1h before RE until the end of exercise	RE causes less initial BG decline than aerobic exercise but is associated with more prolonged reductions in postexercise BG vs. aerobic exercise
Bussau et al (47)	*Diabetologia*	MDIs	Randomization: • 10-sec sprint before 20 min cycling (40% of VO_2peak) • Rest	Usual morning insulin dose and breakfast When BG fell to ~11 mmol/L (198 mg/dL), began exercise or rest	10-sec sprint before aerobic cycling limits the fall in BG in early recovery
Mauvais-Jarvis et al (68)	*Diabetes Care*	MDIs	60 min intense cycling (70% of VO_2max)	Those receiving 3 daily injections: • 90% bolus insulin reduction 90 min before exercise Those receiving 2 daily injections: • 50% bolus insulin reduction 90 min before exercise	50%–90% reduction of insulin dose before intense exercise maintains BG in a near normal range When insulin is not reduced, two-thirds of subjects develop hypoglycemia
Moser et al (33)	*PloS One*	MDIs	30 min HIE 30 min aerobic exercise 3 different mean target workloads	Subjects had adjustments made to ultra-long-acting insulin. Short-acting insulin reductions, depending on mean intensity: • 25% bolus reduction • 50% bolus reduction • 75% bolus reduction All insulin reductions made 4 h before exercise with meal and repeated immediately after exercise with meal	Drop in BG with HIE is significantly smaller vs. drop with aerobic exercise Hypoglycemia less likely during or after HIE compared with aerobic exercise Bolus dose reductions of 25%–75% further reduce hypoglycemia risk during aerobic exercise
Guelfi, Jones and Fournier (46)	*Diabetes Care*	MDIs	30 min HIE cycling (40% VO_2peak and 4-sec sprints every 2 min) 30 min aerobic cycling (40% VO_2peak)	Regular morning short- or rapid-acting insulin and long-acting insulin taken (same for both trials)	Decline in BG is less with HIE compared with aerobic exercise during exercise and early recovery Risk of hypoglycemia is increased with aerobic exercise compared with HIE
Miller et al (23)	*Diabet Med*	MDIs & CSII	Week-long summer camp (observational study): • Wide range of activities (e.g. arts & crafts, swimming and high ropes) • Intensity varied by activity and child	For patients receiving CSII: • ~10% reduction in basal insulin on day 1 (11.3%±6.3% less basal insulin than home doses) For patients receiving MDIs: • Decreased intermediate / long-acting insulin by 8.2%±12.8% on day 1 Children did not have further significant reductions in TDD by last day of camp	On last day of camp, fewer episodes of hypoglycemia occurred compared with the first day Empiric 10% reduction in basal insulin appears reasonable; however, hypoglycemia is still common in all age groups

The table summarizes the relevant published exercise studies with insulin dose adjustments and their main outcomes.
BG, blood glucose; CSII, continuous subcutaneous insulin infusion, IHE, intermittent high-intensity exercise; LGI, low glycemic index; LP, insulin lispro; MDIs, multiple daily injections; RE, resistance exercise; RM, repetitions maximum; TDD, total daily dose; VO_2max, maximum volume of oxygen utilization; VO_2peak, peak volume of oxygen utilization.

CSII

For patients receiving a CSII, common strategies for exercise include changing basal insulin rates (i.e. temporary basal rates) before, during and/or after exercise. With a CSII, individuals can also perform a combined reduction in basal and bolus insulin in preparation for exercise. The primary determinant of what type of insulin to alter (basal or bolus) for the planned activity is the timing of exercise relative to mealtime. For example, if postprandial activity is planned, then mealtime bolus insulin adjustments can be targeted, whereas if the activity will occur 3 or more hours after a meal (i.e. postabsorptive), then basal insulin reductions should be performed instead (Figure 1). With basal adjustments, even with the ability to make adjustments at the start of (or during) exercise, the impact on BG levels will be delayed because of the current pharmacokinetics of rapid-acting insulin analogs and the associated lag time in the hormone entering the circulation (24). Therefore basal insulin reductions for exercise are best implemented in specific situations when the exercise is more prolonged (i.e. >30 minutes of aerobic exercise) and planned well in advance (i.e. 60–90 minutes after the reduction in basal insulin delivery). It is worth noting that exercise increases the absorption rate of basal insulin from the subcutaneous tissue, even in individuals receiving CSII therapy. It is also important to note that aggressively reducing insulin delivery for too long (i.e. >2 hours) may lead to hyperglycemia, particularly in early recovery (25).

Bolus insulin adjustments

As mentioned previously, bolus insulin reductions should be made when aerobic exercise is performed soon after a meal (i.e. within 3 hours) (Figure 2). This strategy requires some planning and knowledge about the timing, duration and intensity of the exercise. The longer the delay before exercise start time and the more aggressive the bolus insulin reduction, the greater will be the rise in BG concentration before exercise begins (26–28). Compared with regular human insulin, insulin lispro is associated with greater hypoglycemia risk if the activity takes place soon after a meal (29). Table 2 shows different bolus insulin adjustment strategies used for exercise based on published studies and breaks down exercise into aerobic (moderate-to-heavy intensity), resistance, anaerobic and mixed (both aerobic and anaerobic components) intensities.

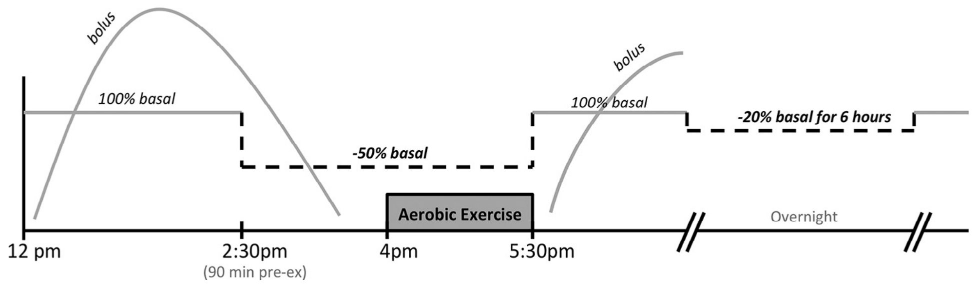

Figure 1. Basal rate insulin reductions for patients receiving a continuous subcutaneous insulin infusion. Basal rate reductions should be done well in advance of the planned exercise (~90 minutes before exercise) and generally last until the end of exercise. After aerobic exercise,~20% basal insulin reductions are recommended for 6 hours overnight (starting at bedtime) to help protect against nocturnal hypoglycemia.

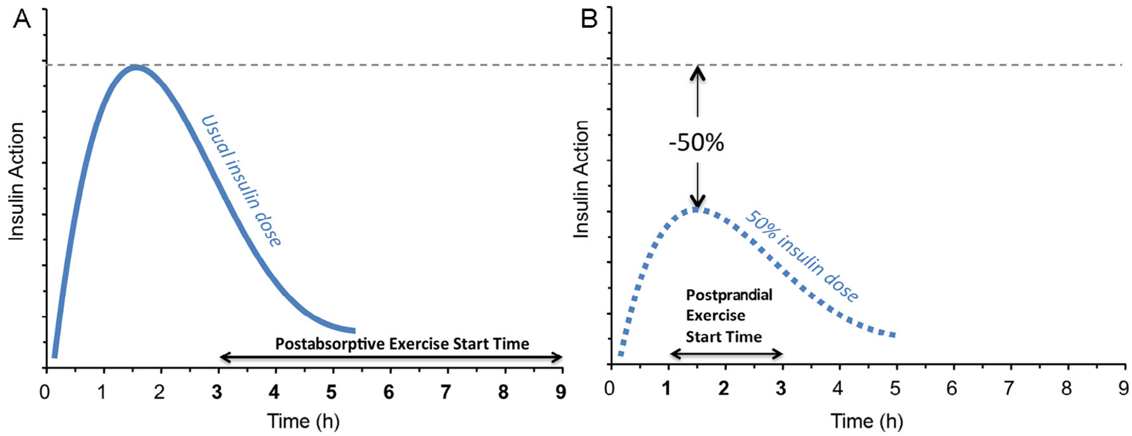

Figure 2. Bolus insulin adjustments based on the timing of exercise relative to mealtime. A, If the onset of exercise occurs 3 or more hours after a meal, generally, no bolus adjustments are made. B, If the start of exercise occurs 1 to 3 hours after a meal, generally, a 50% reduction in bolus insulin is required with the meal before exercise. These recommendations are applicable for aerobic exercise lasting >30 minutes.

Table 2
Bolus insulin adjustments for postprandial exercise

	Meal before exercise		Meal after exercise
	Exercise (~30 min)	Exercise (~60 min)	
Aerobic: moderate-to vigorous intensity continuous exercise	25%–50% bolus reduction	50%–75% bolus reduction	Up to 50% bolus reduction
Resistance: weight lifting	No reduction typically performed	25%–50% bolus reduction	No change in bolus
Brief intense anaerobic (sprinting, powerlifting)	Not applicable: Exercise typically lasts only a few minutes		Small (~50%) bolus correction if hyperglycemic*
Mixed: intermittent aerobic and anaerobic	~ 25% bolus reduction	~ 50% bolus reduction	Up to 50% bolus reduction

Suggested starting points for bolus insulin reductions for various types and durations of exercise (not all recommendations have been formally tested). These suggestions are for rapid-acting insulin only. Bolus insulin adjustments are typically made when the exercise is performed within 1 to 3 hours after a meal. Knowing the type of activity that is being performed will guide the bolus insulin adjustments, as described previously. This summary table is based on studies conducted in patients with type 1 diabetes who received prandial (bolus) insulin adjustments (2, 21, 28, 31–33, 38).
* Requires continued monitoring to help protect against postexercise hypoglycemia, particularly overnight.

In addition to the type of exercise being performed, the duration of the activity is also an important variable that may affect the bolus insulin adjustment necessary to maintain BG control. Prolonged aerobic activities require a greater reduction in the mealtime bolus insulin than HIE (15). This is because with aerobic exercise, glucose uptake by muscle exceeds glucose production by the liver if the insulin levels do not drop during the activity (30). In general, moderate-intensity aerobic exercise that lasts approximately 30 minutes requires a 25% to 50% meal bolus insulin reduction, whereas more prolonged activity (~60–90 minutes) requires a 50% to –75% meal bolus insulin reduction (see Table 2) (28,31–33). HIE is associated with less risk for hypoglycemia because of the elevations in glucose counterregulatory hormones (32,34) and therefore typically requires a smaller bolus insulin dose reduction. Sprinting and weight training may not require any insulin dose reduction, since the energy systems used are primarily anaerobic in nature.

Ideally, bolus insulin reductions are to be made when exercise is initiated within 90 minutes of insulin administration and meal consumption (35). Some carbohydrate feeding (~15–30 g/hr) may be required if BG levels continue to drop with these initial insulin dose reductions (15). An aggressive bolus insulin reduction before exercise (e.g. a reduction of 75% or more) may promote some level of hyperglycemia (26,31), but ketone production does not appear to be significantly affected as long as some insulin is administered (26). With intensive HIE, ketone levels may rise in exercise recovery if insulin delivery is reduced (34).

To date, much of the research focus related to bolus insulin adjustments is on aerobic exercise (Table 2), as this particular type of exercise increases hypoglycemia risk. For activities that are mixed in nature, which include some component of aerobic activity and some anaerobic bursts, hypoglycemia risk is less apparent and therefore may not require such an aggressive insulin dose reduction with the meal preceding exercise (36,37). For brief, anaerobic activity (e.g. sprinting or powerlifting), Turner et al (38) have demonstrated that the delivery of an individualized dose of rapid-acting insulin, based on the patient's own insulin sensitivity index (i.e. a 50% correction factor), after morning resistance exercise could counter post–exercise hyperglycemia. Further investigation is required for the delivery of rapid-acting insulin after resistance exercise; however, this study is a good starting point for determining ways to help reduce hyperglycemia after more intense anaerobic activity.

Basal Insulin Adjustments

Basal insulin dose adjustments can be made when the exercise occurs well after (3 or more hours) a meal or in the fasted state. For patients receiving a CSII, the basal insulin reduction should ideally be done well in advance of the planned activity (60–90 minutes, Table 3) so that insulin levels have time to drop in the circulation by exercise start time (39). As mentioned previously, patients receiving MDIs should lower the dose of long-acting insulin for unusually active days either the evening before or the morning of the active day. Those on a split-dose basal regimen can lower the basal insulin dose on the morning of the active day.

Aerobic exercise often leads to a rapid drop in BG levels in patients with type 1 diabetes because of the body's inability to decrease portal insulin concentrations rapidly at the start of exercise. This may or may not occur as dramatically in individuals with type 2 diabetes, since these patients tend to have some capacity to lower endogenous insulin secretion at the time of exercise. Basal insulin adjustments should be made well in advance of aerobic exercise to be effective, since exercise itself increases subcutaneous insulin absorption rates (40–43). For individuals engaging in moderate-intensity aerobic exercise, the duration of exercise and starting BG concentration will affect the timing and amount of basal insulin adjustment recommended to help maintain euglycemia. For example, if aerobic exercise lasts longer than 30 minutes and BG concentrations are near a normal range (~5.0–8.0 mmol/L, 90–144 mg/dL), a reduction of 50% to 80% in basal insulin is suggested 90 minutes before the start of exercise (35). For mixed aerobic and anaerobic activities and for predominantly aerobic exercise lasting ~40 minutes, full basal insulin suspension at the start of exercise has been shown to reduce the likelihood of hypoglycemia during activity (35), although BG values may still drop ~4.0 mmol/L (~72 mg/dL), on average (37). Although aggressive basal insulin reductions at exercise start (pump suspension or 80% reduction) may offer some protection against hypoglycemia, BG levels will typically drop to some degree (35). For resistance exercise (e.g. weight lifting), Yardley et al (44) implemented a 50% basal insulin reduction 60 minutes before exercise and an additional 25% basal insulin reduction if BG levels were <5.0 mmol/L (90 mg/dL). Although BG levels generally remained more stable in recovery as compared with aerobic exercise, resistance exercise had a tendency to cause more frequent hypoglycemia early the next morning. After prolonged resistance training, postexercise hypoglycemia may be ameliorated overnight by reducing basal insulin by 20% for 6 hours (Figure 1), similar to the reduction recommended after aerobic exercise (45).

In addition to manipulating insulin levels before exercise start time, some consideration of the warm-up and order of exercise is warranted. For example, studies have shown that with no adjustments in insulin levels, brief intense anaerobic exercise (e.g. 4- to 10-second sprints) before moderate-intensity aerobic exercise may reduce the likelihood of exercise-induced hypoglycemia (46,47). These HIE sprints often contribute to an increase in catecholamines and growth hormone that may play a role in the prevention of hypoglycemia during exercise and in early recovery. It should also be noted that if a sprint is done without any aerobic activity, it tends to increase the BG concentration for at least 3 hours (48).

For patients receiving MDI therapy, Campbell et al (21) demonstrated that reducing total long-acting basal insulin (insulin glargine or detemir) by 20%, in addition to reducing the meal bolus insulin by 75% 60 minutes before performing aerobic exercise, improves time in target compared with no adjustments. For patients receiving MDIs who perform resistance exercise lasting ~ 45 minutes, a reduction in basal insulin of 10% to 20% is generally helpful in maintaining BG concentrations in the target range. In a study by Yardley et al (44), patients receiving MDIs reduced basal insulin by 10% on exercise days and found that BG levels dropped more drastically with aerobic exercise versus resistance exercise. However, the 10% basal insulin reduction with resistance exercise may not be enough to protect these patients from late-onset nocturnal hypoglycemia (44). Therefore, in addition to reducing basal insulin by 10% to 20%, mealtime bolus insulin reductions may also be required to combat postexercise hypoglycemia (Table 4).

Table 3
Basal insulin adjustment strategies for patients receiving continuous subcutaneous insulin infusion

	Exercise (~30 min)	Exercise (~60 min)	After exercise
Aerobic: moderate-to-vigorous intensity continuous exercise	50% basal reduction, performed 60–90 min before exercise) or 100% basal reduction at exercise onset*	50%–80% basal reduction performed 60–90 min before exercise) or 100% basal reduction at exercise onset*	20% basal reduction overnight from bedtime lasting 6 h
Resistance: weight lifting	No reduction typically performed	50% basal reduction, performed 60–90 min before exercise)	20% basal reduction overnight from bedtime for 6 h
Brief intense anaerobic (sprinting, powerlifting)	Not applicable: Exercise typically lasts seconds to minutes		No reduction typically performed†
Mixed: intermittent aerobic and anaerobic	100% basal reduction at exercise onset*	50% basal reduction, performed 60–90 min before exercise) or 100% basal reduction at exercise onset*	20% basal reduction overnight from bedtime for 6 h

Suggested starting points for basal insulin reductions for various types and durations of exercise (not all recommendations have been formally tested). Basal rate adjustments are typically made when the exercise is performed in the fasted state or several (3+hours) after a meal. For activities that occur soon after meals (within 3 hours), bolus insulin should be adjusted (see Table 2). Knowing the type of activity that is being performed will guide the basal rate adjustments, as described previously. This summary table is based on studies conducted in patients with type 1 diabetes (35, 37, 44, 45).

* Carbohydrate may be required, since insulin levels may not drop fast enough during the activity.

† Postexercise hyperglycemia should be treated with a bolus insulin correction rather than a basal rate change.

Table 4
Basal insulin adjustment strategies for patients receiving multiple daily injection therapy

	Single exercise bout (up to 60 minutes)	Unusually active day (≥90 minutes accumulated)
Aerobic: moderate-to-vigorous intensity continuous exercise	No reduction typically performed	20%–30% long-acting insulin reduction*
Resistance: weight lifting	No reduction typically performed	10%–20% long-acting insulin reduction*
Brief intense anaerobic (sprinting, powerlifting)	Not applicable: Exercise typically lasts only a few minutes	
Mixed: intermittent aerobic and anaerobic	No reduction typically performed	20%–30% long-acting insulin reduction*

Suggested starting points for basal rate reductions for various types and durations of exercise (not all recommendations have been formally tested). Basal rate adjustments for patients receiving multiple daily injections are appropriate if the planned activity is prolonged and the activity is performed either in the fasted state or several hours after a meal such that bolus insulin cannot be reduced (i.e. 3 or more hours). In all situations with multiple daily injection therapy, additional carbohydrates may be required, particularly if no basal rate adjustments are made. This summary table is based on studies conducted in patients with type 1 diabetes (21, 23, 44), but these suggestions may also be applied to patients with type 2 diabetes.

* This applies to long-acting (insulin glargine, detemir) and intermediate-acting (neutral protamine Hagedorn) insulins only. Patients on a split-dose basal insulin regimen can reduce the morning basal dose to protect against exercise-induced hypoglycemia and may lower the evening dose to further protect against nocturnal hypoglycemia. Doses of ultra-long-acting insulin (e.g. degludec) should not be adjusted for exercise.

For those individuals using ultra-long-acting insulin (i.e. degludec), basal adjustments for exercise are generally not recommended, since the glycemic impact will be prolonged. More research is needed to accommodate exercise in the era of ultra-long-acting basal insulins.

Carbohydrate Intake for Exercise

Although this review focuses primarily on insulin dose adjustments for exercise, patients should be aware that carbohydrate ingestion is perhaps a simpler approach to reduce exercise-associated hypoglycemia. Some earlier examples of carbohydrate supplementation strategies include ingestion of 30 to 60 g of carbohydrate per hour for prolonged exercise (>1 hour) at ~60% of maximal heart rate (49,50). It should be noted that this amount of carbohydrate intake equates to about 120 to 240 kcal, equivalent to about half of the energy expended during mild aerobic exercise. This caloric intake may not be desirable from an energy balance perspective if weight loss is a goal of exercise.

Carbohydrates can generally be avoided or significantly reduced in situations of short duration, high-intensity anaerobic sprints because hypoglycemia risk is low *during* this type of exercise. In addition, exercising at times of the day when either glucose excursions are common (i.e. after a large carbohydrate meal) or when insulin levels are lowest (i.e. fasting) may be ideal for those wishing to exercise for weight loss.

A Zone-Based Approach to Exercise Adjustments

Figure 3 provides a general schematic of strategies for aerobic and mixed forms of exercise based on initial BG levels and the amount of circulating insulin at the start of exercise. Zone 1 (BG in target range, low insulin levels) typically requires only a small amount of carbohydrate intake during exercise (<0.5 g per kilogram per hour of exercise) to maintain BG levels in a normal range. Zone 1 can be achieved if insulin levels are reduced in anticipation of exercise and a limited amount of carbohydrate is consumed before the activity. If higher amounts of carbohydrate intake are desired for performance reasons (up to 75 g/ hr), some insulin based on CGM readings is typically required (51), thereby placing the individuals in zone 2. Zone 2 (BG in target range, relatively high insulin levels) is a common scenario for patients at the start of aerobic exercise who have not lowered insulin levels in advance of the activity. Because of the relatively high circulating insulin levels, BG concentrations can be expected to drop shortly after exercise is initiated, and hypoglycemia risk will be high unless carbohydrates are consumed. Patients can still maintain reasonable BG levels (5.0–15.0 mmol/L, 90–270 mg/dL) by increasing carbohydrate intake (up to ~60 g/hr) to offset the increase in insulin sensitivity while they lower basal insulin levels, if possible (patients receiving CSII only). Zone 3 (high pre-exercise BG levels, low circulating insulin levels) may require a small dose of insulin to correct for hyperglycemia and limit ketone production before the start of exercise (i.e. 30%–50% of correction dose). Zone 4 (high BG levels, moderate to high insulin levels) may be a result of high carbohydrate intake before exercise relative to the insulin dosage (i.e. a slight bolus insulin reduction) or from competition stress. In this setting, patients can begin mild to moderate aerobic exercise (~40%–60% maximal aerobic capacity), since BG levels will likely drop during the activity. Patients receiving a CSII have an advantage over those receiving MDIs with this zone-based approach, since the former group can observe the level of "on board" or "active" bolus insulin on the pump device before starting exercise and can lower or suspend insulin delivery if BG levels trend toward hypoglycemia during the activity. Zone 5 (i.e. hypoglycemia) can be observed before exercise if excessive insulin was administered for the carbohydrates consumed at the meal or snack before exercise (Figure 3, right side of the panel) or if prolonged fasting or recent exercise has occurred (Figure 3, left side of the panel). In this situation, exercise should be delayed until carbohydrate ingestion occurs (~20–30 g) and/or basal insulin levels are reduced (patients receiving a CSII only).

Special Consideration for Patients with Type 2 Diabetes Receiving Insulin

Most of the published literature to date concentrates on insulin adjustment strategies for exercise in patients with type 1 diabetes. As in patients with type 1 diabetes, in patients with type 2 diabetes, an aerobic exercise session has an immediate lowering effect on BG levels (52–56). In general, higher pre-exercise BG concentration, longer exercise duration and a higher heart rate are all associated with a greater reduction in BG concentration (57). Patients with type 2 diabetes receiving insulin or sulfonylureas are at risk for developing hypoglycemia during exercise (58), and for those receiving insulin, the risk is increased if they start exercise with a lower BG concentration (59). The drop in BG levels during exercise is likely related to the recruitment of additional glucose transport proteins in skeletal muscle that are contraction mediated (60).

Although insulin-stimulated glucose uptake is generally impaired in people with type 2 diabetes, muscular glucose uptake is near normal (61). Therefore low- to moderate-intensity exercise generally

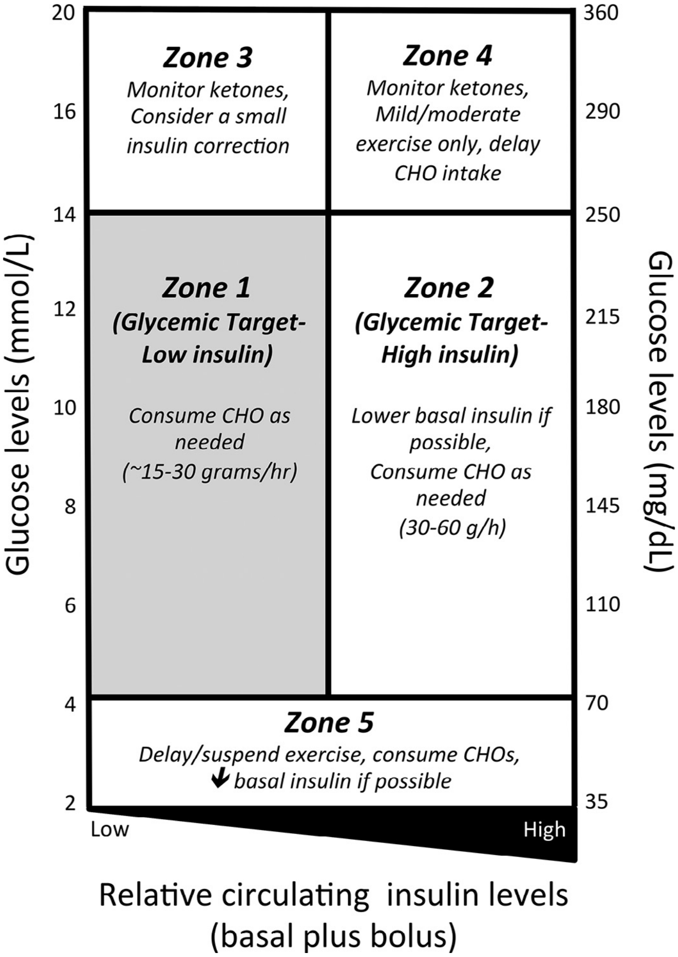

Figure 3. Carbohydrate and insulin strategies for aerobic exercise based on starting blood glucose (BG) concentration and relative "on board" insulin levels: A zone-based approach. Zones 1 to 5 represent BG ranges and relative insulin levels at the start of exercise and suggested strategies for safe performance of exercise (e.g. monitor ketone levels, delay exercise, consume carbohydrates, lower basal insulin if possible). Zone 1 (i.e. BG in targeted range, low insulin) is suitable for prolonged aerobic exercise and for anaerobic and mixed exercise. Zone 2 (i.e. BG in targeted range, high insulin) is suitable for prolonged aerobic exercise but typically requires some carbohydrate feeding and/or basal insulin reductions if possible (patients receiving continuous subcutaneous insulin infusion only). Anaerobic and mixed exercise can be initiated. Zone 3 (i.e. high BG levels, low insulin) requires ketone monitoring before exercise and insulin administration if ketones are elevated above trace level. Exercise should be avoided until control is re-established. Zone 4 (i.e. high BG levels, high insulin) also requires ketone monitoring to confirm that ketones are low before start of moderate-intensity aerobic exercise. (Note: Circulating insulin concentrations may be lower than estimated levels because of infusion-set blockage in patients receiving continuous subcutaneous insulin infusion). Zone 5 (i.e. hypoglycemia with or without elevated insulin levels) requires carbohydrate feeding before the start of exercise (~15–30 g, depending on the amount of insulin in the circulation). In all of these zones, close BG monitoring is advised. CHO, carbohydrate.

causes a mild reduction in BG levels as glucose uptake by the working muscles increases. If exercise is performed after a meal, postprandial hyperglycemia is blunted in patients with type 2 diabetes, even though exercise limits the rise in insulin after the meal (62). The immediate improvements in glucose tolerance and insulin sensitivity after exercise can last from 24 to 72 hours (63).

Although mild hypoglycemia can occur during exercise in patients with type 2 diabetes, it appears to be much less common than in those with type 1 diabetes. Plöckinger et al (64) found only 3 cases of exercise-induced hypoglycemia (all mild) in 122 patients who performed 30 minutes of aerobic exercise with unadjusted basal insulin (glargine or NPH). In patients with type 2 diabetes, exercising for just 30 minutes at a time when BG levels are elevated after a meal (i.e. > 7.0 mmol/L, 126 mg/dL) provides significant improvements in overall BG concentration and is not typically associated with increased risk of hypoglycemia (65).

Current Issues and Future Directions

In spite of its numerous health benefits, regular exercise remains a challenge for most patients with diabetes who are receiving insulin therapy. An important recommendation for all patients is to be more vigilant with BG monitoring before, during and after exercise and to use real-time CGM when possible. Ideally, future studies geared toward improving automated insulin delivery systems should integrate exercise settings and/or other strategies to increase exercise safety. One possibility is the prophylactic use of small dosages of glucagon, given subcutaneously, in patients who are at risk for exercise-induced hypoglycemia.

Conclusion

Insulin dose adjustments are often required for patients with diabetes in preparation for exercise. These insulin adjustments differ depending on the intensive insulin therapy used to manage diabetes (i.e. MDIs vs. CSII). Also, because of the high interindividual variability in BG responses to exercise, the insulin adjustment strategies outlined here should be taken simply as starting points. A number of factors can affect the insulin strategies used for exercise including the intensity, duration and type of activity being performed. In general, the bolus insulin dose should be reduced by 25% to 75%, depending on the duration and intensity of exercise, for activities that occur in the postprandial state. To reduce the risk of hypoglycemia for prolonged aerobic exercise well after meal absorption (i.e. 3 or more hours after a meal), basal insulin dose reductions are recommended well before (60–90 minutes) the start of exercise, when possible. For anaerobic exercise, adjustments in insulin are often not required during the activity, but small bolus insulin corrections may be required after exercise if hyperglycemia ensues.

Patients with type 1 diabetes often experience postexercise nocturnal hypoglycemia. They should be encouraged to monitor BG levels more closely after unusual and prolonged activity. For patients receiving CSII, strategies to adjust bolus and/or basal insulin can be used before, during and after exercise; whereas patients receiving MDIs are often more restricted and require advance planning to make basal insulin adjustments for exercise the evening before or morning of activity. Ideally, planned activity should follow a regular pattern (i.e. same time of day, same intensity, same duration) so that insulin dose strategies can be incorporated routinely with some degree of fine-tuning based on individual responses. These starting-point strategies should help health-care providers further promote regular exercise for patients with diabetes.

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Author Contributions

DZ prepared the first draft of this review. MCR edited the first and subsequent drafts. DZ and MCR finalized and approved the submission.

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