Safe exercise options for people with diabetes

Elsamma Chacko*

ABSTRACT

People with diabetes can tame post-meal glucose surges in real time by doing a 30 min moderate aerobic exercise starting 30 min after the start of the major meal(s) of the day. Although glycogen-depleting high-intensity activities offer many health benefits, including insulin sensitivity improvement through muscle glycogen replenishment, these can also result in wide glucose fluctuations signified by post-exertion hyperglycaemia and delayed hypoglycaemia. Data obtained in previous studies, viewed holistically, strongly indicate that a short bout (10 min) of high intensity exercise before the daily aerobic activity during the mid-postprandial period three times a week can lead to better health without jeopardizing glycaemia. Long duration pre-meal exercises have resulted in glycaemia improvement: light walks for 120 min improve fasting glucose and high intensity interval (the fast/slow design) exercises of long duration (>60 min) looks promising for overall glycaemia.

Introduction

When healthy people exercise, it does not matter much whether they do so pre-meal or post-meal, or at what intensity or for how long. Blood glucose remains steady except for a small bump after meals. Pre-breakfast exercise where insulin-to-glucagon ratio is low uses free fatty acids, endogenous glucose and muscle glycogen as fuels. Training during fasting increases glycogen content and GLUT-4 protein levels and improves body composition and physical health through molecular adaptations. Exercising post-meal, when insulin-to-glucagon ratio remains high blood glucose is the main fuel until the exogenous supply becomes low. At that point human body reverts to using endogenous glucose along with free fatty acids and muscle glycogen. The two hormone systems, counterregulatory hormones and insulin, working in tandem keep the glucose in the normal range.

People with diabetes, on the other hand, have little room to maneuver. They have to pay close attention to a number of factors to stay out of trouble. Their blood sugar levels can undergo wild swings if they exercise without regard to timing, intensity, duration, frequency and sequence of exercise. Managing hyperglycaemia and avoiding hypoglycaemia pose challenges in the daily lives of patients with type-2 and type-I diabetes. This commentary concerns the safe exercise options for people with diabetes.

Exercise timing

Although most studies extant do not specify exercise timing, those who do show that the timing of the physical activity in relation to the proximate meal matters significantly when it comes to blood glucose levels [1-10].

Moderate exercise

A moderate pre-meal exercise can raise postprandial glucose in people with insulin resistance [1-4]. Although moderate post-meal exercise improves glucose levels [5,6], decades of evidence support the finding that the mid-postprandial period (30-90 min post-meal) offers diabetes patients a unique opportunity to do a moderate aerobic exercise to blunt the post-meal glucose surge in real time [7,8]. Exercise

Connecticut Valley Hospital, 1000 Silver Street, Middletown, CT 06457, USA
**Author for correspondence: elsammac@msn.com*

KEYWORDS
- diabetes
- glucose
- exogenous

during the early and late postprandial intervals may trigger endogenous glucose resulting in suboptimal glycaemic advantage [9]. Physical activity in the late postprandial interval may precipitate exercise-induced hypoglycaemia in some people [5,10].

Intense exercise

High-intensity exercise comes with significant health benefits [11-15] and as such elicits much more complex responses than moderate exercise.

Table 1 shows the acute and short term glucose responses to high-intensity or resistance exercise obtained in various laboratory settings by previous investigators. The studies picked for inclusion in the table necessarily specify exercise timing (Only a few representative studies could be accommodated here). The glucose response is expressed in different units, glucose-AUC reduction or decrease in hyperglycaemia prevalence–either for the day or for the meal.

An intense pre-meal exercise of short duration can offer post-exertion hyperglycaemia [16] and delayed hypoglycaemia [17]. Post-exertion hyperglycaemia goes with high intensity continuous exercise (HICE) (Table 1) [16] and high intensity interval exercise (HIIE) where the fast component is alternated with rest (Table 1) [18]. High intensity exercise triggers catecholamine up to 15 times the normal level [19]. These anaerobic activities cause significant glycogen depletion in liver and muscle and lactate accumulation during high glucose turn-over [19]. The extra glucose arriving from the liver is the main contributor to the post-exertion hyperglycaemia. Muscle glycogen depletion is a good thing for glycaemia because it increases insulin sensitivity during glycogen replenishment [16,20]. The insulin sensitivity improvement usually is a delayed effect [16] but it can last for 24 hrs or even beyond [16,20]. This can, however, also raise the risk for exercise-induced [5,10] or delayed hypoglycaemia [17]. The feat of achieving improved insulin sensitivity without post-exertion glucose elevation is quite doable by paying attention to the timing, design and duration of the high-intensity exercise activity.

Post-exertion hyperglycaemia remains modest with resistance exercise (Table 1) [21] and interval exercise when the intense activity alternates with the moderate activity (fast/slow

Table 1. Glucose response to different exercises at different timing, intensity, design and duration.

Type of exercise and Feeding interval	Population	Intensity (high-intensity part) and duration	Acute effect for the meal	Short term effect for the day	Conclusion: effect of exercise on glucose
HICE fasting [16]	T2D & healthy men	100-110% VO2 max, 13 min	Post exercise Hyperglycaemia worse for T2D	Increased insulin sensitivity	Short duration HICE, fasting, offers post-exertion Hyperglycaemia
HIIE fasting [18]	T1D & healthy	30 s fast/4 min rest; 4-10 cycles	Post exercise Hyperglycaemia worse for T1D	-	Short duration HIIE fast/rest design, fasting, offers post-exertion Hyperglycaemia
HIIE fasting *vs.* 80 min post-meal [30]	T2D	100% VO2 peak × 1 min/40% × 3 min, 15 cycles; total >60 min	ppg-AUC -24.8% *vs.* -11.5%	ppg-AUC -37% *vs.* -5%	Long- duration HIIE, fast/slow design, is better fasting; long duration HIIE post-meal make glycaemia worse
Resistance Pre-dinner *vs.* 45 min post-dinner [21]	T2D	Moderate Resistance for 45 min	ppg-AUC -18% vs -30%	-	Resistance exercise is better post-dinner than pre-dinner
High-Intensity interval 90 min post-meal [28]	T2D	90% HRmax for 10 min		ppg-AUC -35% hyperglycaemia -65%	Short-duration HIIE mid-postprandial is good

T2D: Type 2 diabetes; T1D: Type 1 diabetes; AUC: Area under the curve; ppg: Postprandial glucose; HICE: High-intensity cont; ex.: HIIE-HI interval ex.

rather than fast/rest) [4] under fasting conditions. It makes sense to speculate that hepatic glucose output leads to post-exertion hyperglycaemia whereas muscle glycogen replenishment and intermittent moderate physical activity modulate glucose levels by increasing glucose transport to the muscles. On the other hand, all these high-intensity exercises, when done during the mid-postprandial interval, lead to modest hyperglycaemia compared with the high levels seen following pre-meal exercises [21-23]: when exogenous glucose is plentiful in the blood, hepatic glucose production is suppressed.

Duration

Marmy-Conus and colleagues observed that glucose levels go down initially when healthy men did aerobic exercise at 71% VO2 max starting 30 min post-meal. Twenty min into the activity, however, these levels started to go up and remained high until the end of the exercise [24]. Under identical timing, many subjects (healthy and type 1 diabetes) could walk for up to 60 min at lower intensities without compromising glucose levels [7,25,26]. Additionally, Manders and colleagues showed that glycaemia was worse with 30 min of exercise at 70% Wmax at 60 min post-meal compared with 60 min of exercise at 35% Wmax, in people with type 2 diabetes [27]. In these mid-postprandial exercises, hepatic glucose output appeared to be spared initially, when exogenous glucose was abundant in the blood but then, as digestion waned, the liver was pressed into action to make up for the energy requirements of high intensity exercise. That is, done post-meal, high intensity exercise must be of short duration not to trigger hepatic glucose output (Table 1) [28]. Starting the exercise at 30 min post-meal–the starting point of the mid-postprandial interval–might also help by providing more fuel [7,25].

Two pre-meal studies with prolonged exercise durations demonstrated beneficial glycaemic effects. Borer et al. compared two two-hour bouts of moderate exercise (43% Wmax) during both pre-meal and post-meal periods in healthy post-menopausal women [29]. It was the pre-meal study that improved fasting glucose, an effect attributable to liver glycogen depletion. A recent study, where both duration and intensity were high, used an hour-long interval exercise (15 min, 100% HRmax) under fasting conditions to show overall glycaemia improvement (Table 1) [30]. Here the mechanism could be the significant depletion of both liver glycogen and muscle glycogen. In pre-meal studies when intensity or duration are shorter, the insulin sensitivity improvement for the day is only 12-15% [4,20].

High intensity exercise of short duration is preferable during mid-postprandial period–if glycaemic improvement is the goal. Long duration high intensity interval exercise (where the fast component alternates with the slow component), pre-meal, improves glycaemia because of marked glycogen depletion [30].

Frequency

Moderate exercise post-meal [31] can be done every day. The insulin sensitivity improvements are additive. High intensity exercises are best done no more than three times a week [32]; the body, especially the muscles, need the intervening restful days to recover from the intense physical work and the muscles also must have their depleted glycogen stock replenished. Another reason to limit the high intensity forms of exercise to 3 days a week is this: if insulin sensitivity improvements continue beyond 24 hrs [16,33], why disrupt that salutary effect with the unwelcome possibility of glucose levels going up? In a recent meta-analysis on the effect of intensity on HbA1c, out of seven studies, HbA1c reduction was better when the training was done three times a week compared with five times a week [34].

Sequence

A post-meal study directly compared the sequence {resistance exercise before aerobic exercise} with {aerobic before resistance} in patients with type-I diabetes and found that the former was decidedly better glycaemically [35]. Glucose levels came down during both the resistance exercise and the aerobic activity. The glycaemia improvement during the recovery period is likely the result of additional glucose uptake via the glycogen replenishment process.

Options for high-intensity exercise

The evidence available from the studies where timings are specified (Tables 1) points to pre-breakfast and mid postprandial as the intervals to focus on when considering glycaemic effects. When exercising post-meal, it is critical not to trigger hepatic glucose output [21-23,28] and during pre-meal, the more the glycogen depletion there is the better [29,30].

■ The mid-postprandial option

The goal of mid-postprandial exercise is to tame the post-meal glucose surge of the biggest meal (preferably breakfast) of the day [7,8]. A moderate activity for 30 min or a light activity for up to 60 min starting 30-45 min before the anticipated peak will do [7,8,25,26]. A short bout (10 min) of high intensity (interval, continuous or resistance) exercise [21-23,28] before the daily aerobic exercise three times a week may offer additional insulin sensitivity improvement (Table 1) [21,28].

■ The pre-meal option

A light walk for long duration, ~120 min, before breakfast can deplete liver glycogen and improve fasting glucose in one day [29]. A good glycogen depleting exercise, high-intensity interval exercise of fast/slow design (Table 1) [30] of long duration, >60 min, would offer overall glycaemia benefit.

It is important to personalize the lifestyle. Ideally one big meal, the exercise meal, two small meals and 2-3 snacks would offer moderate glucose profile, improved satiety and minimal hypoglycaemia risk. The young and otherwise healthy diabetes patients have both options. Most diabetes patients might pick the post-meal option with or without the high-intensity or resistance exercise.

Summary

The evidence supports the following exercise conditions for glucose control:

1. Light to moderate aerobic exercise for 30-60 min, during the mid-postprandial period can tame post-meal glucose surges in real time.

2. Under fasting conditions, HIIE of fast/slow design and resistance exercise are better than HICE and HIIE fast/rest design to prevent post-exertion hyperglycaemia.

3. High-intensity exercise earlier in the day (breakfast) is preferred for preventing hypoglycemia.

4. Exercise of long duration during the fasting hours offers significant glycogen depletion.

5. High-intensity exercise of short duration during mid-postprandial interval may not result in post-exertion hyperglycaemia or trigger hepatic glucose output.

6. High-intensity exercise three times a week is favored for better glycaemia benefits.

7. High-intensity exercise before aerobic is better than aerobic before high-intensity.

Conclusion

A moderate mid-postprandial exercise can tame post-meal glucose surges in real time. High-intensity exercise can improve glycaemia if insulin sensitivity improvement can be achieved without the post-exertion hyperglycaemia or hypoglycaemia. Post exertion glucose elevation is modest when any of the high intensity exercises is done during the mid-postprandial interval or a high intensity interval exercise where fast component is alternated with slow component or resistance exercise is done under fasting conditions. High-intensity exercise of short duration post-meal and high-intensity exercise of long duration pre-meal offer glycaemia benefits. Hypoglycaemia risk seems minimal with these two exercise options, especially if exercise is done before or after breakfast. Short and long term studies are needed to explore the effects of these two options further on hypoglycaemia and cardio-metabolic markers. Such targeted efforts may help with accelerated translational drives.

Funding

This work received no specific funding.

Duality of interest

The author declares that there is no duality of interest associated with this manuscript.

References

1. Derave W, Mertens A, Muls E *et al*. Effects of post–absorptive and postprandial exercise on glucoregulation in metabolic syndrome. *Obesity*. 15, 704–711 (2007).
2. Colberg SR, Zarrabi L, Bennington L *et al*. Post–prandial walking is better for lowering the 6–8,14,15]glycemic effect of dinner than pre–dinner exercise in type 2 diabetic individuals. *J. Am. Med. Dir. Assoc.* 10, 394–397 (2009).
3. DiPietro L, Gribok A, Stevens MS *et al*. Three 15–min bouts of moderate post–meal walking significantly improves 24–h glycemic control in older people at risk for impaired glucose tolerance. *Diabetes. Care.* 36, 3262–3268 (2013).
4. Francois ME, Baldi JC, Manning PJ *et al*. 'Exercise snacks' before meals: a novel strategy to improve glycaemic control in individuals with insulin resistance. *Diabetologia.* 57, 1437–1445 (2014).
5. Haxhi J, di Palumbo A, Sacchetti M. Exercising for metabolic control: is timing important? *Ann. Nutr. Metab.* 62, 14–25 (2013).
6. Chacko E. Exercising tactically for taming postmeal glucose surges. *Scientifica.* (2016).
7. **a.)** Chacko E. A time for exercise: the exercise window. *J. Appl. Physiol.* (2016). **b.)** Commentaries on Viewpoint: A time for exercise: the exercise window. [9 teams of authors]. *J Appl Physiol* 122, 210-213 (2017). **c.)** Elsamma Chacko. Last Word on ViewPoint: A time for exercise: the exercise window. *J Appl Physiol* 122, 214 (2017).
8. van Dijk JW, Venema M, van Mechelen W *et al*. Effect of moderate–intensity exercise versus activities of daily living on 24–hourblood glucose homeostasis in Male patients with type 2 diabetes. *Diabetes. Care.* 36, 3448–3453 (2013).
9. Rasmussen OW, Lauszus FF, Hermansen K. Effects of postprandial exercise on glycemic response in IDDM subjects. *Diabetes. Care.* 17, 1203–1205 (1994).
10. Praet SF, Manders RJ, Lieverse AG *et al*. Influence of acute exercise on hyperglycaemia in insulin–treated type 2 diabetes. *Med. Sci. Sports. Exerc.* 8, 2037–2044 (2006).
11. Gibala M. Molecular responses to high–intensity interval exercise. *Appl. Physiol. Nutr. Metab.* 34, 428–32 (2009).
12. Strasser B, Pesta D. Resistance Training for Diabetes Prevention and Therapy: Experimental Findings and Molecular Mechanisms. Biomed. Res. Int. 2013, 805217 (2013).
13. Cassidy S, Thoma C, Houghton D *et al*. High–intensity interval training: a review of its impact on glucose control and cardiometabolic health. *Diabetologia.* 60, 7–23 (2017).
14. Kessler HS, Sisson SB, Short KR. The potential for high–intensity interval training to reduce cardiometabolic disease risk. *Sports. Med.* 242, 489–509 (2012).
15. Jelleyman C, Yates T, O'Donovan G *et al*. The effects of high–intensity interval training on glucose regulation and insulin resistance: a meta–analysis. *Obesity. Rev.* 16, 942–961 (2015).
16. Kjaer M, Hollenbeck CB, Frey–Hewitt B *et al*. Glucoregulation and hormonal responses to maximal exercise in non–insulin–dependent diabetes. *J. Appl. Physiol.* 68, 2067–2074 (1990).
17. Maran A, Pavan P, Bonsembiante B. Continuous glucose monitoring reveals delayed nocturnal hypoglycaemia after intermittent high–intensity exercise in non–trained patients with type 1 diabetes. *Diabetes. Technol. Ther.* 12, 763–768 (2010).
18. Harmer AR, Chisholm DJ, McKenna MJ *et al*. High–intensity training improves plasma glucose and acid–base regulation during intermittent maximal exercise in type 1 diabetes. *Diabetes. Care.* 30, 1269–127 (2007).
19. Marliss EB, Vranic M. Intense exercise has unique effects on both insulin release and its roles in glucoregulation. *Diabetes*. 51, S271–S283 (2002).
20. Oberlin DJ, Mikus CR, Kearney ML *et al*. One bout of exercise alters free–living postprandial glycemia in type 2 diabetes. *Med. Sci. Sports. Exerc.* 46, 232–238 (2014).
21. Heden TD, Winn NC, Mari A *et al*. Post–dinner resistance exercise improves postprandial risk factors more effectively than pre–dinner resistance exercise in patients with diabetes. *J. Appl. Physiol.* 118, 624–634 (2015).
22. Szewieczek J, Dulawa J, Strzalkowska D *et al*. Impact of the short–term, intense exercise on postprandial glycaemia in type 2 diabetic patients treated with gliclazide. *J. Diabetes. Complicat.* 21, 101–107 (2007).
23. Larsen JJS, Dela F, Madsbad S *et al*. The effect of intense exercise on postprandial glucose homeostasis in Type II diabetic patients. *Diabetologia*. 42, 1282–1292 (1999).
24. Marmy–Conus N, Fabris S, Proietto J *et al*. Preexercise glucose ingestion and glucose kinetics during exercise. *J. Appl. Physiol.* 81, 853–857 (1996).
25. Nelson JD, Poussier P, Marliss EB *et al*. Metabolic response of normal man and insulin–infuseddiabetics to postprandial exercise. *Am. J. Physiol.* 242, E309–E316 (1982).
26. Shin YH, Jung HL, Ryu JW *et al*. Effects of pre–exercise meal on plasma growth hormone response and fat oxidation during walking. *Prev. Nutr. Food. Sci.* 18, 175–180 (2013).
27. Manders RJ, Van Dijk JW, van Loon LJ. Low–intensity exercise reduces the prevalence of hyperglycaemia in type 2 diabetes. *Med. Sci. Sports. Exerc.* 42, 219–225 (2010).
28. Gillen JB, Little JP, Punthakee Z *et al*. Acute high–intensity interval exercise reduces postprandial glucose response and prevalence of hyperglycaemia in patients with type 2 diabetes. *Diabetes. Obes. Metab.* 14, 575–577 (2012).
29. Borer KT, Wuorinen EC, Lukos JR *et al*. Two bouts of exercise before meals, but not after meals, lower fasting blood glucose. *Med. Sci. Sports. Exerc.* 41, 1606–16149 (2009).
30. Terada T, Wilson BJ, Myette–Cote *et al*. Targeting specific interstitial parameters with high–intensity interval exercise and fasted–state exercise in type 2 diabetes. *Metabolism*. 2016, 599–608 (2016).
31. van Dijk JW, Tummers K, Stehouwer CDA *et al*. Exercise therapy in type 2 diabetes. Is daily exercise required to optimize glycaemic control. *Diabetes. Care.* 35, 945–954 (2012).
32. Snowling NJ, Hopkins WJ. Effects of different modes of exercise training on glucose control and risk factors for complications in type 2 diabetic patients. *Diabetes. Care.* 11, 2518–2527 (2006).
33. Little JP, Jung ME, Wright AE *et al*. Effects of high–intensity interval exercise versus continuous moderate–intensity exercise on postprandial glycemic control assessed by continuous glucose monitoring in obese adults. *Appl. Physiol. Nutr. Metab.* 39, 835–841 (2014).
34. Liubaoerjijin Y, Terada T, Fletcher K *et al*. Effect of aerobic exercise intensity on glycaemic control in type 2 diabetes: a meta–analysis of head–to–head randomized trials. *Acta. Diabetol.* 53, 769–781 (2016).
35. Yardley JE, Kenny GP, Perkins BA *et al*. Effects of performing resistance exercise before versus after aerobic exercise on glycaemia in type 1 diabetes. *Diabetes. Care.* 35, 669–675 (2012).