A time for exercise: the exercise window

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Abstract

How blood glucose responds to exercise depends on the timing of the physical activity with respect to the proximate meal. Although study after study has confirmed this, many researchers still report results without specifying exercise timing. This laxity could be the source of some of the uncertainties and inconsistencies found in the field. In place of the current practice of using the binary categorization of the feeding cycle into pre-meal and post-meal periods, we look at it as consisting of four time intervals: the pre-meal period plus the early, mid- and late postprandial periods. Two of these intervals stand out. Pre-meal exercise uses endogenous glucose and muscle glycogen as the main fuels offering varying effects on glycemia. Exercise during the mid-postprandial period uses exogenous glucose as the main fuel. Exogenous glucose is abundant in the blood during the 30 to 90 min post-meal period, rendering this interval a unique opportunity to use up the excess glucose as fuel for moderate aerobic exercise, thereby blunting the glucose surge. Hypoglycemia risk is minimal during this exercise window. The continuing arrival of glucose from the gut in copious amounts minimizes the risk for hypoglycemia. The role of different modes of exercise and combinations during the mid-postprandial period on metabolic markers remains to be explored.
What is new?

The pre-meal/post-meal binary categorization of the feeding cycle can be profitably modified using the quartet: pre-meal, early, mid- and late postprandial periods. The pre-meal (counterregulation, steady glucose) and mid-postprandial (insulin action, surging glucose) intervals stand out. The mid-postprandial period offers a window of opportunity to diabetes patients to exercise and blunt the glucose surge without fear of hypoglycemia. The early and late postprandial periods are “grey” segments, constantly vulnerable to intrusion by hepatic glucose.
A time for exercise: the exercise window

Introduction

In 1982, a team of Canadian scientists reported in the American Journal of Physiology how exercise affected blood glucose levels (20). The exercise was a moderately paced treadmill walk that started 30 min post-meal and lasted for 45 min. Although the focus of the study lay elsewhere, the graphical results presented in the paper pointed to an intriguing possibility: could physical activity be used to drain off – in real time -- the exogenous glucose entering the bloodstream from the food being digested along the alimentary canal? The authors noted that “with exercise, glycemia returned rapidly to fasting levels . . .” in healthy people and in those with type 1 diabetes. Since then, a large number of studies have come out featuring exercise timings that vary widely: pre-meal, 15 min post-meal, 30 min post-meal, 45 min post-meal and one hour to several hours post-meal (2, 7). Many others, however, have been inexplicably silent on the timing of the exercise in relation to meal. These studies have also used various exercise intensities, durations, frequencies and combinations thereof. Now, 34 years later, it is still not clear what exercise conditions would best improve the key metabolic parameters, HbA1c and lipids. Translational efforts are exceedingly slow in this critical area. This report suggests a somewhat more refined framework than the binary pre-meal – post-meal categorization of the feeding cycle to help account for how meals and exercise influence blood glucose levels and other metabolic measures. The remainder of this paper reviews existing studies that point to the utility and rationale of this approach.
Research over several decades now has shown that blood glucose levels are sensitive to various exercise conditions: timing, intensity, duration, frequency and sequencing of exercise (2, 7). Light to moderate exercise pre-meal raised postprandial glucose, but a similar walk post-meal lowered glucose levels (4, 5). Remarkably, an hour-long, energy-intensive interval exercise gave the opposite results: it was the pre-meal exercise that improved glycemia (25).

Exercising in the late postprandial period could lead to hypoglycemia (7). In people with type 1 diabetes, delayed nocturnal hypoglycemia, which usually follows high-intensity or resistance exercise, is a problem as well (17, 30). For many with type 1 diabetes, fear of hypoglycemia has been a potent deterrent against partaking in exercise activities. This and extra carbohydrate intake, meant to prop up falling blood glucose levels, lead to weight gain. Insulin pumps and continuous glucose monitoring have made the task of regulating the insulin dose much simpler (although these gadgets and associated procedures remain beyond the reach of the vast majority of diabetes patients worldwide.)

Published accounts where no information on exercise timing is forthcoming show inconsistent results for the effects of exercise on HbA1c (9, 10, 15). The reviews and meta-analyses reporting on HbA1c have generally yielded only small improvements except in a few cases where the improvements have been quite impressive (9, 10, 15). What is common to virtually all of these studies is the absence of information on the timing of the exercise bout with respect to meals.

The physiology
The complex exercise – glycemia connection can be best understood by considering exercise timing, the sources of glucose and the hormones involved. The post-meal period is far from monolithic and, in fact, consists of three segments defined by the rise and fall of the glucose flux: early (0-30 min), mid- (30-90 min) and late (> 90 min) postprandial periods. Categorization of the feeding cycle in this manner is reasonable and warranted because, unlike the relatively tranquil pre-meal period, the post-meal period is quite eventful, especially in people with diabetes, what with the ebb and flow of the blood-glucose concentration (3). The dome of the glucose peak, where exogenous glucose is abundant in the blood, is pegged as the 30-90 min post-meal interval.

In this formulation two intervals stand out: pre-breakfast (where counterregulation is active) and mid-postprandial (where insulin action prevails). The other two intervals are in grey areas where the potential for intrusion by hepatic glucose is constantly present. It is, however, in the late postprandial period that hypoglycemia mostly lurks. Fortuitously, the new framework comes with a built-in antidote for the fear of hypoglycemia harbored by many diabetes patients. Start and finish the daily exercise session within the bounds of the mid-postprandial period, and patients are assured of plentiful supplies of blood glucose.

The dominant source of endogenous glucose, the liver plays a crucial role in glucose dynamics. The hormones controlling blood glucose levels during exercise are insulin, glucagon and catecholamines. The pre-breakfast period is characterized by low insulin-to-glucagon ratios. Levels of catecholamines go up with high-intensity exercise (18). Moderate exercise during insulin action lowers glucose levels while moderate exercise during counterregulation stabilizes
it (2, 22). As for high intensity pre-meal exercise, markedly elevated hepatic glucose production leads to substantial post-exercise hyperglycemia (2, 7, 12, 13) before any glucose lowering effect sets in (2, 6, 12, 21). In this scenario, the extent of hepatic glucose production holds the key to glycemia. In the mid-postprandial period, hepatic glucose production is suppressed, free fatty acids remain low and meal-derived glucose is pouring in, making the 30-90 min interval the right time to drain off any excess glucose using moderate physical activity (1, 20, 24). What is apparent here is the improvement of insulin sensitivity through insulin-mediated and contraction-mediated glucose transport, nipping the post-meal surge in the bud – in real time at that. The goal of timely exercise is to deny meal-derived glucose the chance to build up in the blood. This denial not only avoids the serious long term consequences of repeated microvascular damage but may reduce abnormal fat distribution.

**Exercise timing**

A 2013 review on exercise timing concluded that post-meal exercise of moderate intensity is superior to pre-meal exercise for dealing with hyperglycemia (7). Moderate exercise during the mid-postprandial period improved glucose consistently (1, 2, 4, 5, 11, 14 20, 22, 24, 26, 29). Glucose lowering has been less efficient during the early (23) and late (5) postprandial periods presumably because of the involvement of hepatic glucose. In the mid-postprandial period, exercise starting at 30 min after the first bite into the meal showed the most effective blunting of the glucose surge (1, 20, 24) (Table 1). As Nelson and colleagues demonstrated decades ago, by intervening at the right time with an exercise bout of the right intensity, it is possible to keep the post-meal glucose peak from forming altogether (1, 20, 24). This tactic also minimizes the
hypoglycemia risk because the continued arrival of glucose from the gut serves as a protective measure.

Table 1 summarizes representative studies (4, 14, 20, 21, 23, 27, 28) done during the four segments of the feeding cycle. A few cautionary observations are in order here. The glucose responses shown use different measures: the quoted area-under-the-curve (AUC) values may refer to the “total,” “incremental” or unspecified variety. Also, hyperglycemia reduction can be just for the meal or for the whole day. But the overall trend is apparent: intervention starting closer to the 30 min mark in the mid-postprandial period with exercise of moderate intensity yields better glycemic control. Tellingly, these studies were not done for the purpose for which they are being cited here and as such whatever support they offer to the considerations laid out in this paper may be deemed independently proffered.

Same timing, different intensities

In two studies healthy people exercised at 30 min post-meal for 60 min at different intensities, 50% VO$_{2\text{max}}$ and 71% VO$_{2\text{max}}$ (24, 19). The lower intensity exercise normalized the glucose level in 15 min and kept it at that level throughout the exercise, thereby blunting the peak well (24). At the higher intensity, after the initial drop, glucose started going up 20-min into the exercise bout and hyperglycemia persisted until the exercise ended (19). When Manders and colleagues compared two intensities, 35% VO$_{2\text{max}}$ and 70% VO$_{2\text{max}}$, at 60 min post-meal in people with type 2 diabetes, the lower intensity exercise offered the better glycemic outcome (16). At the high end of the moderate intensity range, shorter duration of exercise may be needed to keep hepatic glucose at bay.
Coordinating meals and exercise

A practical approach to moderating the 24-h glucose profile is to have one big meal, preferably breakfast, as the designated “exercise meal” and two smaller meals plus two or three snacks. This meal plan, along with mid-postprandial exercise would lower hyperglycemia after breakfast, lunch and dinner (29). This lifestyle also minimizes the risk for hypoglycemia. The alternative, of course, is to exercise three times a day. Light exercise for 15 min after every meal showed some blunting of the peaks, but the energy expenditure was not enough to produce a significant effect (5, 29). Taken together, the studies shown in Table 1 hold the promise of an even better glycemic response to moderate activity starting 30 min post-meal (1, 2, 20, 24). Moderate post-meal exercise can be done every day, the effects on glycemia are additive (28).

There's work to do

Although there is good evidence that the right time to start the moderate exercise session for maximum benefit is some 30 min after the start of the meal (20, 24), data on HbA1c and lipids are scarce. Immediate (real time), short term (48-72 hours) and long term (3 months) effects of moderate aerobic exercise on metabolic measures (HbA1c, levels of lipids, liver fat, and markers of oxidative stress) in the mid-postprandial period remain to be explored.

Focusing research efforts on the mid-post-meal period is critical for accelerated translation: physical activity is the one means available to vast populations living with diabetes in the impoverished corners of the world. Moreover, if diabetes patients follow the current guidelines and exercise moderately before breakfast or work out intensely any time other than in the mid-
postprandial period, chances are that glucose levels go up right after the physical activity (4, 5, 12, 13).

Conclusion

Although many studies extant inexplicably do not specify the timing of the exercise in relation to the meal, enough data exist to suggest the rationale and utility of looking at the feeding cycle as consisting of four segments: the pre-meal, early postprandial, mid-postprandial and late postprandial periods. The mid-postprandial period (30 – 90 min post-meal) offers a unique opportunity to diabetes patients to manage hyperglycemia, with minimal risk of hypoglycemia, using a moderate aerobic activity. When exercise timing and intensity are taken into account blood glucose levels respond to the physical activity in a predictable and consistent manner.

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Table 1. Glucose response to moderate aerobic exercise at different timing

<table>
<thead>
<tr>
<th>Exercise Mode</th>
<th>Population</th>
<th>Timing</th>
<th>Intensity &amp; duration</th>
<th>Favorable Glycemic Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-meal (21)</td>
<td>T2D</td>
<td>“before breakfast”</td>
<td>60-75% HR(_{\text{max}}) for 60 min</td>
<td>Hyperglycemia/day reduced by 12-15% (delayed effect)</td>
</tr>
<tr>
<td>Early postprandial (23)</td>
<td>T1D</td>
<td>15 min post-meal</td>
<td>65% VO(_{2\text{max}}) for 30 min</td>
<td>Hyperglycemia for the meal reduced by one third</td>
</tr>
<tr>
<td>Mid-postprandial (20)</td>
<td>T1D and Healthy</td>
<td>30 min post-meal</td>
<td>55% VO(_{2\text{max}}) for 45 min</td>
<td>“...glycemia returned rapidly to fasting levels.”</td>
</tr>
<tr>
<td>Mid-postprandial (14)</td>
<td>T2D</td>
<td>45 min post-meal</td>
<td>53% VO(_{2\text{max}}) for 45 min</td>
<td>4 h glucose-AUC for the meal reduced by 50%</td>
</tr>
<tr>
<td>Mid-postprandial (4)</td>
<td>People with metabolic syndrome</td>
<td>60 min post-meal</td>
<td>60% VO(_{2\text{max}}) for 45 min</td>
<td>3 h glucose-AUC for breakfast reduced by 22%</td>
</tr>
<tr>
<td>Mid-postprandial (27)</td>
<td>T2D</td>
<td>90 min post-meal</td>
<td>50% (W_{\text{max}}) for 30 min</td>
<td>Hyperglycemia/day reduced by 24%</td>
</tr>
<tr>
<td>Late postprandial (28)</td>
<td>T2D with and w/o insulin</td>
<td>150 min post-meal</td>
<td>50% (W_{\text{max}}) for 45 min</td>
<td>Hyperglycemia/day reduced by 33%</td>
</tr>
</tbody>
</table>

T2D- type 2 diabetes; T1D- type 1 diabetes; AUC-area under the curve
References


