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Targeting specific interstitial glycemic parameters with high-intensity interval exercise and fasted-state exercise in type 2 diabetes

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ABSTRACT

Aims. To compare the acute glycemic responses to a bout of high-intensity interval exercise (HIIE) and energy-matched moderate-intensity continuous exercise (MICE) performed under fasted and postprandial conditions.

Methods. A randomized, controlled, crossover design was used. Ten individuals with type 2 diabetes were each tested in five experimental conditions after an overnight fast: 1) fasted-state HIIE ($HIIE_{fast}$); 2) post-breakfast HIIE ($HIIE_{fed}$); 3) fasted-state MICE ($MICE_{fast}$); 4) post-breakfast MICE ($MICE_{fed}$); and 5) no exercise (control). MICE was performed at workload corresponding to 55% of $\dot{V}O_{2peak}$, whereas HIIE was composed of repetitions of three minutes at workload corresponding to 40% followed by one minute at workload corresponding to 100% $\dot{V}O_{2peak}$. Interstitial glucose was monitored by continuous glucose monitoring over 24 h under standardized diet and medication.

Results. Fasted-state exercise attenuated postprandial glycemic increments ($p < 0.05$) to a greater extent than post-breakfast exercise did. HIIE reduced nocturnal and fasting glycemia on the day following exercise more than MICE did (main effect: both $p < 0.05$). Compared to the control condition, $HIIE_{fast}$ lowered most interstitial glycemic parameters, i.e., 24-h mean glucose (−1.5 mmol·l^{-1}; $p < 0.05$), fasting glucose (−1.0 mmol·l^{-1}; $p < 0.05$), overall postprandial glycemic increment (−257 mmol·360 min·l^{-1}; $p < 0.05$), glycemic variability (−1.79 mmol·l^{-1}; $p < 0.05$), and time spent in hyperglycemia (−283 min; $p < 0.05$).

Abbreviations: CGM, continuous glucose monitoring; HR, heart rate; HIIE, high intensity interval exercise; $HIIE_{fast}$, fasted-state high intensity interval exercise; $HIIE_{fed}$, post-breakfast high intensity interval exercise; iAUC, incremental area under curve; MAGE, mean amplitude of glycemic excursion; MICE, moderate intensity continuous exercise; $MICE_{fast}$, fasted-state moderate intensity continuous exercise; $MICE_{fed}$, post-breakfast moderate intensity continuous exercise; PAL, physical activity level; PAR-Q+, physical activity readiness questionnaire; RER, respiratory exchange ratio; T2D, type 2 diabetes; $t^{-1}_{>10.0\ mmol\cdot l}$, time spent in glucose concentration > 10.0 mmol·l^{-1}; $t^{-1}_{<4.0\ mmol\cdot l}$, time spent in glucose concentration < 4.0 mmol·l^{-1}; $\dot{V}CO_2$, carbon dioxide production; $\dot{V}O_2$, oxygen consumption; $\dot{V}O_{2peak}$, peak oxygen consumption.

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Conclusion. This study showed that HIIE is more effective than MICE in lowering nocturnal/fasting glycemia. Exercise performed in the fasted state reduces postprandial glycemic increments to a greater extent than post-breakfast exercise does. Performing HIIE under fasted condition may be most advantageous as it lowered most aspects of glycemia.

1. Introduction

Elevated blood glucose, including postprandial and fasting hyperglycemia [1], as well as labile glycemic concentrations [2], has been identified as an independent risk factor for the development of diabetic complications. There have been several meta-analyses demonstrating that, on average, exercise has a clinically meaningful impact on glycemic control as measured by glycated hemoglobin (HbA_{1c}) in individuals with type 2 diabetes (T2D) [3,4]. However, it is less clear whether exercise can be tailored to favor preferential reductions in specific glycemic parameters.

A recent systematic review investigating the effects of exercise on interstitial glycemic parameters measured by continuous glucose monitoring (CGM) showed that aerobic exercise typically lowers postprandial but not fasting glucose [5]. Postprandial hyperglycemia is considered to be more strongly associated with insulin resistance at the level of skeletal muscles, whereas fasting glycemia reflects hepatic insulin resistance [6]. Thus, it is possible that some types of exercise improve muscular insulin sensitivity but have little effects on the hepatic insulin sensitivity. Additionally, it is also possible that the negligible effect of exercise on circulating fasting glucose concentrations is due to a short-lasting effect of traditionally used exercise interventions because circulating fasting glucose concentration is often measured on the day subsequent to exercise.

Modification to exercise interventions in order to favor different effects on muscle versus liver glycogen could have different effects on various glucose parameters. Two such strategies may be high-intensity and fasted-state exercise. An increasingly appreciated approach to increase exercise intensity in T2D is high-intensity interval exercise (HIIE) [7–11], which involves alternating between repetitions of high-intensity exercise bouts (≥70% of maximum or peak oxygen consumption [12], or 80%–100% of maximal heart rate [13,14]) and lower-intensity recovery periods. Brief bouts of high intensity exercise facilitate muscular glycogenolysis and may stimulate translocation of glucose transporters to a greater degree than lower intensity continuous exercise does [14,15]. Consequently, glucose uptake during exercise, as well as post-exercise insulin sensitivity, is expected to differ between HIIE and moderate-intensity continuous exercise (MICE; typically defined as 40%–60% of maximum or peak oxygen consumption) [16]. In addition, a previous study has shown that HIIE suppresses hepatic glucose production and thereby fasting blood glucose of individuals with T2D [17].

Glycemic responses to exercise may also be manipulated by altering carbohydrate availability. Although performed predominantly on non-diabetic individuals, pre-prandial exercise resulted in more sustained reduction of blood glucose concentration compared to postprandial exercise, presumably because of greater depletion of hepatic glycogen stores [18]. Therefore, the effects of fasted-state exercise on glycemic parameters may differ from those of post-meal exercise.

To date, no study has simultaneously investigated the effects of HIIE and energy-matched MICE, and the effects of fasted-state and postprandial exercise on glycemic parameters. The primary purpose of the study was to compare the effects of HIIE and MICE, as well as fasted-state and post-breakfast exercise, on daily mean, postprandial and fasting interstitial glycemia. A secondary purpose was to contrast the aforementioned glycemic responses following each of the four exercise conditions (fasted-state HIIE and MICE, and post-breakfast HIIE and MICE) with a sedentary, control condition. We hypothesized that HIIE and fasted-state exercise would improve interstitial fasting and postprandial glycemia to greater degrees than MICE and post-breakfast exercise, respectively. We also hypothesized that the combination of HIIE and fasted-state would improve both fasting and postprandial glycemia.

2. Materials and Methods

2.1. Research Design

A randomized controlled crossover research design was used. Each participant was studied under five separate experimental conditions: fasted-state HIIE ($HIIE_{fast}$), post-breakfast HIIE ($HIIE_{fed}$), fasted-state MICE ($MICE_{fast}$), post-breakfast MICE ($MICE_{fed}$), and no exercise (control), in random order separated by 48 h. The randomization of the condition order was performed separately for each participant with no additional methods, such as counterbalancing, to control the order. Forty-eight hours was chosen as previous research demonstrated that the glucose-lowering effect of morning exercise is negligible on the second day [19]. Each experimental period consisted of 24 h during which interstitial glycemic parameters were assessed using CGM.

2.2. Participants

Ten individuals were recruited through advertisement and by contacting volunteers listed in the Alberta Diabetes Institute databank. Inclusion criteria for the study were: 1) diagnosed with T2D; 2) non-smoker; 3) 45–75 years of age; 4) post-menopausal for at least one year; 5) not on exogenous insulin; 6) blood pressure < 140/90; 7) HbA_{1c} < 10% (<86 $mmol \cdot mol^{-1}$), 8) no history of T2D-related complications. All participants provided written informed consent. Ethical approval was obtained from the University of Alberta Health Research Ethics Board.

2.3. Preliminary-Testing

Volunteers reported to a laboratory at the University of Alberta to complete the physical activity readiness questionnaire (PAR-Q+) [20], screening and medical information