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Effects of postmeal exercise on postprandial glucose excursions in people with type 2 diabetes treated with add-on hypoglycemic agents

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ABSTRACT

Aims: Type 2 diabetes treatment primarily focuses on reducing hyperglycemia, including postprandial glucose excursions. Hypoglycemic agents are used clinically to lower fasting and postprandial glucose. Metformin is the first-line therapy; however, if metformin is inadequate then 'add-on' hypoglycemic agents are implemented. Postmeal exercise has been shown to lower postprandial glucose. The aim of this study was to assess if postmeal exercise provides additional glucose-lowering benefit, beyond medication alone, in those on add-on hypoglycemic agents.

Methods: Postprandial glucose excursions in eight participants with type 2 diabetes (Age: 60 ± 10.7, HbA_{1C}: 7.9 ± 2.3) being treated with add-on hypoglycemic agents were assessed during both drug-treated sedentary and drug-treated postmeal exercise conditions. Continuous glucose monitoring was used to assess peak and area under the glucose curve (AUC) during exercise, as well as peak within a 2-h time window, 2-h total and 2-h incremental AUC after a standardized breakfast meal. Postmeal exercise consisted of 3 × 10-min intervals of treadmill walking at 50% maximal oxygen uptake.

Results: Glucose peak (drug only: 13.8 ± 3.7, drug/exercise: 9.9 ± 2.7 mmol/L; $p = 0.02$) and AUC (drug only: 500 ± 136, drug/exercise: 357 ± 89 mmol/L × 40 min; $p = 0.03$) were reduced during postmeal exercise. Breakfast 2-h incremental AUC was also reduced (drug only: 585 ± 291, drug/exercise: 330 ± 294; $p = 0.047$).

Discussion: Post-breakfast exercise lowered glucose during the exercise bout, although this effect was not sustained on later meals.

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1. Introduction

Type 2 diabetes is a metabolic disease characterized by defects in insulin action and/or insulin secretion, which ultimately contribute to hyperglycemia [1]. Hyperglycemia has been associated with the development of macrovascular and microvascular disease [2]. Thus, treatment of type 2 diabetes centers on regaining glycemic control [3]. Clinical glucose targets include both fasting and postprandial components of hyperglycemia [3].

Pharmacologic therapies that reduce hyperglycemia are currently the foundation of type 2 diabetes treatment [3]. Metformin is an oral biguanide used to reduce fasting glucose and is the first-line therapy [4]. However, metformin is typically inadequate for long-term glycemic control likely due to the progressive nature of the disease [5]. When this occurs, additional hypoglycemic agents, termed "add-on" therapies, are implemented into treatment regimens. There are a variety of drug classes that are used as add-on therapies, such as sulphonylureas, dipeptidyl peptidase-4 inhibitors (DPP-4 Is), and glucagon-like peptide-1 (GLP-1) receptor agonists [6]. Currently, the American Diabetes Association does not prioritize these drug classes for treatment. Instead, selection of the appropriate add-on therapies depends on several factors including cost, tolerability, side-effects, and co-morbidities [3].

Exercise is also a cornerstone of type 2 diabetes treatment due to improvements in skeletal muscle insulin sensitivity that occur after an exercise bout [7]. Exercise may have added benefits if it is appropriately timed to the postmeal period [8]. Exercising during the postprandial period has been shown to cause acute reductions in postprandial glucose [9–13]. As a result, postmeal exercise is gaining interest as a potential glucose-lowering method for people with type 2 diabetes [8]. Postmeal exercise exploits the non-insulin dependent process of glucose uptake that occurs during skeletal muscle contraction. Thus, postmeal exercise may be an effective approach for lowering glucose during all stages of disease progression, including those with severe type 2 diabetes who have dysfunctional insulin secretion.

Since hypoglycemic agents and exercise are prescribed together for patients with type 2 diabetes, recent attention has been given to the interactive effects of these two treatment modalities [14–16]. Some data suggest that the combination of metformin monotherapy and exercise may not always lead to additive glucose-lowering effects [17,18]. On the other hand, some studies show that exercise and sulphonylurea treatment have additive effects [19–22], although these studies did not time exercise to the postprandial phase. To our knowledge, the effects of postmeal exercise during treatment with add-on hypoglycemic agents has not been tested.

It is currently unknown how the combination of postmeal exercise and treatment with add-on hypoglycemic agents will affect postprandial glucose in people with type 2 diabetes. The main objective of this study was to determine if postmeal exercise lowers peak postprandial glucose within a 2-h time window of the postprandial breakfast phase in people with type 2 diabetes being treated with add-on hypoglycemic agents. It was hypothesized that the combination of postmeal exercise and add-on hypoglycemic agents would result in a lower peak postprandial glucose response compared to treatment with add-on hypoglycemic agents alone. We also tested the lasting effects of post-breakfast exercise on the subsequent glycemic responses to standardized lunch and dinner meals later in the day.

2. Materials and methods

2.1. Participants

Eight participants were recruited for this study from the local community using website postings and newspaper advertisements. Participants had to be between the ages of 18–75 years of age, and were recruited based on their diabetes medication regimen defined as being treated with more than just metformin monotherapy, but not on insulin. Participants were excluded from this study if they had severe diabetes-related complications including nephropathy, renal, or liver disease. This study was approved by the Western Institutional Review Board. All participants provided written informed consent prior to study participation.

2.2. Study design

This study used a repeated measures design to assess the effects of postmeal exercise on peak postprandial glucose excursions in people with type 2 diabetes being treated with add-on hypoglycemic agents, but not on insulin. The mode of exercise was treadmill walking. Participants completed a single continuous glucose monitoring protocol consisting of back to back testing days with the following 2 conditions: one sedentary day and one postmeal exercise day. To avoid potential residual effects of the exercise, the sedentary day was always conducted prior to the postmeal exercise day. During study protocols, participants did not deviate from their physician prescribed treatment regimens. Timing of medication was standardized within each participant, meaning hypoglycemic agents were taken at the same time during both sedentary and exercise conditions.

2.3. Study procedures

2.3.1. Baseline testing

Height, weight, HbA_{1C}, age, current clinical diagnoses, medication usage, and body composition via dual X-ray absorptiometry scan (GE Lunar, Fairfield CT, USA) were collected at the initial visit. In addition, submaximal exercise testing on a treadmill was conducted to estimate maximal oxygen consumption. The purpose of this test was to determine the appropriate parameters of treadmill walking (speed/grade) needed to achieve an exercise bout of 50% maximal oxygen uptake. For this submaximal exercise testing protocol, walking speed was held constant and percent grade was increased by 1% every 2 min until 85% of age-predicted maximum heart rate was reached. During each exercise stage, heart rate (Polar