Preventive Medicine Reports 12 (2018) 94–100

Contents lists available at ScienceDirect

Preventive Medicine Reports

journal homepage: www.elsevier.com/locate/pmedr

The associations of sedentary time and breaks in sedentary time with 24-hour glycaemic control in type 2 diabetes

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ARTICLE INFO

Keywords:
Sedentary lifestyle
Physical activity
Glucose
Type 2 diabetes

ABSTRACT

The aim of this study was to investigate the associations of accelerometer-assessed sedentary time and breaks in sedentary time with 24-h events and duration of hypoglycaemia (< 3.9 mmol/l), euglycaemia (3.9–7.8 mmol/l), hyperglycaemia (> 7.8 mmol/l) and above target glucose (> 9 mmol/l). Thirty-seven participants with type 2 diabetes (age, 62.8 ± 10.5 years; body mass index, 29.6 ± 6.8 kg/m^2) in Glasgow, United Kingdom were enrolled between February 2016 and February 2017. Participants wore an activity monitor (activPAL3) recording the time and pattern of sedentary behaviour and a continuous glucose monitoring (CGM, Abbott FreeStyle Libre) for up to 14 days. Linear regression analyses were used to investigate the associations. Participants spent 3.7%, 64.7%, 32.1% and 19.2% of recording h/day in hypoglycaemia, euglycaemia, hyperglycaemia and above target, respectively. There was a negative association between sedentary time and time in euglycaemia (β = −0.44, 95% CI −0.86; −0.03, p = 0.04). There was a trend towards a positive association between sedentary time and time in hyperglycaemia (β = 0.36, 95% CI −0.05; 0.78, p = 0.08). Breaks in sedentary time was associated with higher time in euglycaemia (β = 0.38, 95% CI 0.00; 0.75, p = 0.04). To conclude, in individuals with type 2 diabetes, more time spent in unbroken and continuous sedentary behaviour was associated with poorer glucose control. Conversely, interrupting sedentary time with frequent breaks appears to improve glycaemic control. Therefore, this should be considered as a simple adjunct therapy to improve clinical outcomes in type 2 diabetes.

1. Introduction

Type 2 diabetes is a chronic non-communicable disease affecting > 90% of the global diabetes population (415 million) (International Diabetes Federation, 2015). The principal therapeutic goal of diabetes management is to achieve good glucose control in order to prevent diabetes-related complications (Bonora et al., 2001; Reid, 2010; Tancredi et al., 2015). However, daily glucose fluctuates widely outside the recommended range in people with type 2 diabetes even with diet management and oral anti-diabetes agents (Bonakdaran and Rajabian, 2009; Hay et al., 2003; Paing et al., 2017). This could be due to the heterogeneous and progressive nature of type 2 diabetes. Factors such as age, sex, body mass index (BMI), duration of diabetes and lifestyle all impact on glucose control (Franks et al., 2013; Hartz et al., 2006). It is therefore important to identify and target the modifiable lifestyle factors, in addition to oral anti-diabetes agents, to improve glucose control in type 2 diabetes.

Among lifestyle factors, sedentary time (time spent sitting or reclining) shows a consistent association with the risk of type 2 diabetes (Wilmot et al., 2012). Additionally, prolonged sedentary time is reported as a risk factor for high 2-h postprandial glucose and insulin resistance (Healy et al., 2007; Helmerhorst et al., 2009; Sardinha et al., 2017). In contrast, there is an emerging experimental evidence that breaks in sedentary time improve glucose metabolism through muscle contraction and insulin dependent and independent glucose uptakes (Bergouignan et al., 2016). A break in sedentary time is generally defined as a period of non-sedentary activity (e.g. standing or walking) in between two sedentary conditions (e.g. sitting or reclining posture) (Tremblay et al., 2017). In well-controlled laboratory settings and quasi-free-living settings, experimental studies showed that

Abbreviations: CGM, Continuous glucose monitoring; GLUT4, Glucose transporter 4; MET, Metabolic equivalent task; IL, Interleukin; TNF, Tumour necrosis factor

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https://doi.org/10.1016/j.pmedr.2018.09.002
Received 3 April 2018; Received in revised form 29 August 2018; Accepted 4 September 2018
Available online 05 September 2018

interrupting sedentary time with short frequent breaks reduces post-prandial glucose, daily glucose and insulin resistance (Chastin et al., 2015; Dempsey et al., 2016; Duvivier et al., 2017). However, limited evidence is available that this is the case in actual free-living settings and that more frequent interruption of sedentary time in normal daily living is associated with better glucose control. Therefore, the present study aimed to explore the associations of sedentary time and breaks in sedentary time with glycaemic control measured as events and time in hypoglycaemia, euglycaemia, hyperglycaemia and above target glucose, using concurrent and continuous glucose and activity data in free-living settings.

2. Methods

The present study was a cross-sectional study and was approved by the University Ethics Committee (UEC) of University of Strathclyde. This study was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants.

2.1. Participants

Eligible participants were individuals with type 2 diabetes aged 18 years and over. Exclusion criteria were age < 18 years, pregnancy, insulin therapy, alcohol and substance abuse, liver and renal diseases and cancer. Recruitment was achieved through advertising within the staff of two universities, the Diabetes UK website, Diabetes Balance magazine and diabetes support groups in the Glasgow area.

2.2. Study protocol

This cross-sectional study was carried out between February 2016 and February 2017 and consisted of two short visits to the University laboratory or convenient location (e.g. participant's home). At the first visit, a continuous glucose monitoring (CGM, Abbott FreeStyle Libre) sensor was inserted into the subcutaneous tissue on the back of upper arm, and an activPAL3 activity monitor (PAL Technologies, Glasgow, UK) was attached to the anterior aspect of the right thigh, after the device was waterproofed. Demographic data were collected by the researcher. Participants were then requested to wear the CGM and activPAL3 for up to 14 days of normal daily living and to follow habitual diet. The activPAL3 and real-time glucose measurements provided by the CGM might influence participants' diet and physical activity patterns. To minimise this, they were reminded to maintain habitual diet and lifestyle throughout the study. To record diet, medication, bedtime and waking time; participants were provided with 24-h Dietary Recall Forms and sleep diary. Participants attended a second visit to remove the CGM and activPAL3.

2.3. Covariates

Demographic data included age, gender, body mass index (BMI), anti-diabetes medication, alcohol consumption and smoking status. Smoking status was classified as non-smoker and smoker, and alcohol consumption was classified as non-consumer, low consumer (≤14 units per week) and high consumer (> 14 units per week). For each participant, carbohydrate intake in each day was calculated using 24-h Dietary Recall Form and Carbs & Cals Counter, and carbohydrate intake in each day was then averaged to estimate carbohydrate intake per day (Cheyette et al., 2013).

2.4. Glucose monitoring and glucose control measurements

The CGM (Freestyle Libre) used in this study measures interstitial glucose every 15 min for up to 2 weeks, and glucose data are retrieved wirelessly by the reader every 8 h. This is a well-tolerated consumer grade device, and the interstitial glucose measurements by this device are as accurate as capillary blood glucose (Bailey et al., 2015). The glucose data from the CGM were downloaded to a personal computer using FreeStyle Libre software (version 1.0). Global guideline for type 2 diabetes by the International Diabetes Federation was used to define thresholds for glucose control measures: events and time in hypoglycaemia (glucose < 3.9 mmol/l), euglycaemia (glucose 3.9–7.8 mmol/l), hyperglycaemia (glucose > 7.8 mmol/l) and above target (glucose > 9 mmol/l) (International Diabetes Federation Guideline Development Group, 2014). This is an evidence-based guideline targeting HbA_{1c} < 53 mmol/mol (7%) to reduce diabetes-related complications, and 36% of national guidelines were also based on this guideline (Home et al., 2013). Daily events and time in hypoglycaemia, euglycaemia, hyperglycaemia and above target were computed using the glucose data from 00:00 to 00:00 h of two consecutive days. The first and final days, which do not have full 24-h recording, were excluded. Average daily events and time in hypoglycaemia, euglycaemia, hyperglycaemia and above target were then calculated. However, daily missing glucose data points can influence time in hypoglycaemia, euglycaemia, hyperglycaemia and above target because each missing glucose data point represents 15 min missing data time. Therefore, normalisation method was applied to deal with missing glucose data points and to calculate time spent in glucose control measures (e.g. Time in hypoglycaemia [% of recording h/day] = [Average daily time in hypoglycaemia / (24 h − Average daily missing data time)] × 100). Inclusion or exclusion criteria were not considered regarding missing glucose data points. HbA_{1c} was self-reported by participants and it was based on their personal records from their last visits to diabetes clinic, diabetes specialist nurse (DSN) and general practitioner (GP).

2.5. Sedentary time, breaks in sedentary time and physical activity measurements

The activPAL3 was used to monitor sedentary time, breaks in sedentary time and physical activity of each participant. This is a small (53 × 35 × 7 mm) validated accelerometer and has been routinely used in clinical trials and epidemiological studies (Grant et al., 2006; Grant et al., 2008; Kozey-Keadle et al., 2011). This device records the start and duration of sitting, lying, standing and stepping for up to two weeks. The data were downloaded using the activPAL3™ software (version 7.2.32).

To determine daily sedentary time, time spent in sitting or lying posture between 00:00 to 00:00 h of two consecutive days was calculated, after sleeping time was removed using the sleep diary and activPAL events file (Chastin et al., 2014; Edwardson et al., 2016). The sleep diary, which still needs to be validated, was developed by our research group, and the sleep diary was used in conjunction with activPAL events file (Edwardson et al., 2016). A break in sedentary time was considered as a transition from sitting or lying condition to standing or stepping condition during waking hours. For each participant, daily sedentary time and number of breaks in sedentary time were first calculated, and average sedentary time and number of breaks per day were then computed. Average standing time, walking time and moderate to vigorous physical activity (MVPA) time per day were also calculated. A cadence greater or equal to 100 steps/min was considered as MVPA (Marshall et al., 2009).

2.6. Statistical analysis

Sample size calculations were based on a previous study, which reported the association between breaks in sedentary time and high 2-h plasma glucose (R^2 = 0.21) (Healy et al., 2008). Assuming a statistical power of 85%, an alpha of 0.05 and six predictors, we estimated that 37 participants would be required to detect significant association between breaks in sedentary time and glucose control measures.

Participants with minimum 3 days of concurrent and continuous glucose and activity data were included in final analysis. Linear