Nutrition, Metabolism & Cardiovascular Diseases (2014) **24**, 956–962

Available online at www.sciencedirect.com

Nutrition, Metabolism & Cardiovascular Diseases

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

Sedentary time and markers of inflammation in people with newly diagnosed type 2 diabetes

C.L. Falconer [a,b,*], A.R. Cooper [a,b], J.P. Walhin [c], D. Thompson [c], A.S. Page [a], T.J. Peters [d], A.A. Montgomery [e,f], D.J. Sharp [f], C.M. Dayan [g], R.C. Andrews [d]

[a] *Centre for Exercise, Nutrition and Health Sciences, School for Policy Studies, University of Bristol, UK*
[b] *National Institute for Health Research Bristol Biomedical Research Unit in Nutrition, Diet and Lifestyle, University of Bristol, UK*
[c] *Department for Health, University of Bath, Bath, UK*
[d] *School of Clinical Sciences, University of Bristol, Bristol, UK*
[e] *Nottingham Clinical Trials Unit, University of Nottingham, Nottingham, UK*
[f] *School of Social and Community Medicine, University of Bristol, Bristol, UK*
[g] *Institute of Clinical Diabetes and Metabolism, Cardiff University School of Medicine, Cardiff, UK*

Received 26 November 2013; received in revised form 18 March 2014; accepted 20 March 2014
Available online 26 April 2014

KEYWORDS
Sedentary time;
Type 2 diabetes;
Breaks in sedentary time;
Inflammation

Abstract *Background and aims:* We investigated whether objectively measured sedentary time was associated with markers of inflammation in adults with newly diagnosed type 2 diabetes.
Methods and results: We studied 285 adults (184 men, 101 women, mean age 59.0 ± 9.7) who had been recruited to the Early ACTivity in Diabetes (Early ACTID) randomised controlled trial. C-reactive protein (CRP), adiponectin, soluble intracellular adhesion molecule-1 (sICAM-1), interleukin-6 (IL-6), and accelerometer-determined sedentary time and moderate-vigorous physical activity (MVPA) were measured at baseline and after six-months. Linear regression analysis was used to investigate the independent cross-sectional and longitudinal associations of sedentary time with markers of inflammation.

At baseline, associations between sedentary time and IL-6 were observed in men and women, an association that was attenuated following adjustment for waist circumference. After 6 months of follow-up, sedentary time was reduced by 0.4 ± 1.2 h per day in women, with the change in sedentary time predicting CRP at follow-up. Every hour decrease in sedentary time between baseline and six-months was associated with 24% (1, 48) lower CRP. No changes in sedentary time between baseline and 6 months were seen in men.
Conclusions: Higher sedentary time is associated with IL-6 in men and women with type 2 diabetes, and reducing sedentary time is associated with improved levels of CRP in women. Interventions to reduce sedentary time may help to reduce inflammation in women with type 2 diabetes.

Introduction

Type 2 diabetes is one of the most prevalent chronic diseases worldwide, contributing significantly to the global burden of disease [1]. Diabetes is an independent risk factor for cardiovascular disease (CVD) and in people with CVD, the presence of diabetes worsens prognosis [2]. Chronic inflammation is implicated in the pathogenesis of type 2 diabetes and in the development of CVD and other

* Corresponding author. NIHR Biomedical Research Unit in Nutrition, Diet and Lifestyle, Level 3, University Hospitals Bristol Education Centre, Upper Maudlin Street, Bristol BS2 8AE, UK. Tel.: +44 1173421759.
E-mail address: Catherine.falconer@bristol.ac.uk (C.L. Falconer).

0939-4753
http://dx.doi.org/10.1016/j.numecd.2014.03.009

diabetic complications including diabetic retinopathy [3]. Inflammatory cytokines secreted by adipose tissue are involved in the regulation of glucose metabolism and insulin resistance, and also in other inflammatory processes linked to an increased CVD risk [4]. For example, high levels of C-reactive protein (CRP) are related to risk of future CVD in people with type 2 diabetes [5]. The inflammatory nature of type 2 diabetes is partly mediated through increased adiposity [6], with hepatic CRP secretion suggested to increase in response to an adiposity-related increase in another inflammatory cytokine, interleukin-6 (IL-6). Adiposity is also associated with reduced levels of adiponectin [7], an anti-inflammatory cytokine with anti-atherogenic properties. Other, non-adipose, markers of inflammation such as soluble intracellular adhesion molecule-1 (sICAM-1), are independently associated with risk of CVD and provide information on the inflammatory state of the vasculature [8].

Regular physical activity is a cornerstone in the prevention and treatment of type 2 diabetes due to its actions on glucose control, and blood pressure [9] and is also known to reduce inflammation in people with type 2 diabetes [10], therefore providing a potential avenue for intervention to reduce CVD risk. However, people with type 2 diabetes have low levels of physical activity with few meeting physical activity recommendations of 30 min moderate to vigorous physical activity (MVPA) on five days of the week [11]. There is increasing interest in the role that sedentary behaviours may play in adult health. Higher levels of time spent sedentary are associated with an increased risk of type 2 diabetes, cardiovascular disease, and cardiovascular and all-cause mortality [12,13], independently of levels of physical activity. In addition, detrimental cross-sectional associations between sedentary time objectively measured with accelerometers and waist circumference, HDL-cholesterol and insulin resistance have been shown in both healthy individuals [14] and those with type 2 diabetes [15]. In adults with newly diagnosed type 2 diabetes, MVPA accounts for 3.2% of the day in contrast to 61.5% of the day spent sedentary [15], and reducing sedentary time may thus provide an alternative approach to managing health status in such individuals.

There is evidence that prolonged sedentary time may impact upon inflammation [16,17]. However, the mechanism by which this occurs and how much of the effect is mediated through differences in MVPA and adiposity is not well understood. Studies in healthy individuals or those at risk of type 2 diabetes have demonstrated higher levels of objectively measured sedentary time to be associated with CRP, independently of MVPA [14,18,19], and one study reported evidence of a sex difference, with self-reported sitting time associated with inflammation in women, but not men [20]. However, all associations were attenuated when adjusted for BMI [20]. To date, no studies have investigated the independent associations of objectively measured sedentary time with inflammatory biomarkers in individuals with type 2 diabetes.

Therefore, the aim of the present study was to investigate the sex-specific associations of objectively measured sedentary time with selected inflammatory biomarkers in individuals with newly diagnosed type 2 diabetes. If such associations are present, they may indicate an alternative route to improve health in people with type 2 diabetes.

Methods

Participants

This paper presents a secondary data analysis from the Early ACTivity in Diabetes (Early ACTID) study, a randomised controlled trial of physical activity and diet in the management of type 2 diabetes. This study has been described in detail previously [21]. Briefly, participants with newly diagnosed type 2 diabetes were recruited through primary care in the South West of England. Eligible participants had a clinical diagnosis of type 2 diabetes in the previous 6 months and were aged 30–80 years at diagnosis. Participants were excluded on the basis of uncontrolled diabetes (HbA1c $>$ 10% [85.8 mmol/mol]), blood pressure $>$ 180/100 mmHg, LDL-cholesterol $>$4 mmol/l, and body mass index (BMI) $<$ 25 kg/m^2 or body weight $>$180 kg. Telephone screening was performed on 1634 participants, of whom 712 were eligible for face-to-face screening and 593 were enrolled in the study. All participants provided written informed consent prior to participation and ethical approval was obtained from the Bath Hospital Research Ethics Committee (05/Q2001/5). This study is registered (number ISRCTN92162869).

Metabolic and anthropometric outcomes

Venous blood samples were obtained following an overnight fast and analysis was conducted by individuals blinded to the patient's identity. Serum was analysed for IL-6, sICAM-1 and adiponectin using commercially available solid phase ELISAs (Quantikine, R and D Systems Inc., Abingdon; US). High sensitivity serum CRP was determined using an automated high sensitivity immunoturbidimetric assay and RX Daytona clinical chemistry analyser (Randox Laboratories Ltd., UK). Average intra- and inter-assay coefficient of variation (CV) was established from the repeated analysis of 20–60 samples at different concentrations. The intra-assay CV was 3%, 5%, 6% and 9% for CRP, adiponectin, sICAM-1 and IL-6, respectively. The inter-assay coefficient of variation was 6–7% for all assays except IL-6 which was 16%. Body weight and height were measured to the nearest 0.1 kg and 0.5 cm, respectively with participants wearing light, indoor clothing and without shoes. Waist circumference was measured at the midpoint between the lowest rib and anterior iliac. Social deprivation was measured using the Index of Multiple Deprivation (IMD) score, a measure of local area deprivation that takes into account income, employment, health and disability, education and training, housing and services, living environment and crime, based on re-