Contents available at ScienceDirect

Diabetes Research and Clinical Practice

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

Brain-derived neurotrophic factor, insulin like growth factor-1 and inflammatory cytokine responses to continuous and intermittent exercise in patients with type 1 diabetes

Aleksandra Żebrowska [a,*], *Barbara Hall* [b], *Adam Maszczyk* [c], *Rafał Banaś* [d], *Joanna Urban* [e]

[a] *Department of Physiological and Medical Sciences, The Jerzy Kukuczka Academy of Physical Education, Mikołowska 72A, 40-063 Katowice, Poland*

[b] *School of Health Science, University of Salford, Allerton Building, Frederick Road Campus, Salford M6 6PU, England, United Kingdom*

[c] *Department of Sports Theory, The Jerzy Kukuczka Academy of Physical Education, Mikołowska 72A, 40-063 Katowice, Poland*

[d] *Hospital and Health Center, Hospital Road Box 507, Chetwynd, BC V0C 1J0, Canada*

[e] *Department of Biological Science, Thompson Rivers University, 805 TRU Way, Kamloops, BC V2C 0C8, Canada*

ARTICLE INFO

Article history:
Received 28 February 2018
Received in revised form
14 August 2018
Accepted 29 August 2018
Available online 1 September 2018

Keywords:
Diabetes
Exercise training
BDNF
IGF-1/IGFBP-3 ratio
Neuroregeneration

ABSTRACT

Aims: Type 1 diabetes mellitus (T1DM) is an important risk factor for cognitive decline and motor dysfunction due to progressive muscular atrophy. Chronic hyperglycemia may be responsible for impaired vascular function, loss of muscle mass, and morphological abnormalities in the myocytes. For the proper functioning of the neuromuscular system, two crucial growth factors are necessary: brain-derived neurotrophic factor (BDNF) and insulin-like growth factor-1 (IGF-1), whose reduced expressions have been implicated in progressive neuropathy and muscle atrophy in patients with T1DM.

The aim of the study was to compare the effects of two different exercise regimes (continuous and intermittent) on BDNF, IGF-1, blood glucose and inflammatory cytokine responses in young adults with and without Type 1 diabetes.

Methods: Fourteen patients (aged: 26.9 years) with T1DM and age-matched adults without diabetes participated in a 40 min continuous exercise (ExC, 50% of lactate threshold) and a high intensity intermittent exercise (ExInt, 120% of lactate threshold). During the study the patients performed self-monitoring of blood glucose levels (SMBG) under glycemic control. The effects of ExC and ExInt on BDNF, IGF-1, insulin like growth factor binding protein (IGFBP-3), insulin (INS), vascular endothelial growth factor (VEGF), transforming growth factor beta (TGF-β) and tumor necrosis factor alpha (TNF-α) were analyzed.

Results: BDNF and IGF-1 baseline serum levels were significantly lower in the T1DM

Abbreviations: T1DM, type 1 diabetes mellitus; BDNF, brain-derived neurotrophic factor; IGF-1, insulin-like growth factor-1; ExC, continuous exercise; ExInt, intermittent exercise; CG, control group; HbA1, glycated haemoglobin; VO_2max, maximal oxygen uptake; LAT, lactate threshold; HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; VE, pulmonary ventilation; CO_2, carbon dioxide output; MET, metabolic Equivalent; INS, insulin; IGFBP-3, insulin like growth factor binding protein-3; VEGF, vascular endothelial growth factor; TGF-β, transforming growth factor beta; TNF-α, tumor necrosis factor alpha; BG, blood glucose; $SatO_2$, pulse oxygen saturation; SMBG, self-monitoring of blood glucose

* Corresponding author.
E-mail addresses: a.zebrowska@awf.katowice.pl (A. Żebrowska), a.maszczyk@awf.katowice.pl (A. Maszczyk), jurban@tru.ca (J. Urban).

https://doi.org/10.1016/j.diabres.2018.08.018

patients compared to the healthy controls, but we found that ExInt and ExC significantly increase the secretion of BDNF and IGF-1 levels. Significant increases in BDNF and TGF-β levels, higher blood glucose decline, and a lower incidence of hypoglycaemia in ExInt compared to ExC were observed. Lower IGFBP-3 concentrations were revealed in T1DM patients in response to ExInt compared to ExC, suggesting a positive effect on IGF-1/IGFBP-3 ratio and the bioavailability of IGF-1.

Conclusions: According to our results physical exercise has beneficial effects on serum BDNF and IGF-1 levels. A high-intensity intermittent exercise may be more effective at reducing the risk of exercise-induced glycaemic disorders in the T1DM patients as compared to continuous exercise.

1. Introduction

Type 1 diabetes mellitus (T1DM) is commonly associated with pathological complications, such as nephropathy and neuropathy. Previous studies report that diabetes is also an important risk factor for cognitive decline and motor dysfunction due to progressive muscular atrophy [1–3]. The severity of neuromuscular complications in poorly controlled diabetic patients is associated with an accumulation of advanced glycation end-products, impaired vascular function, oxidative stress and altered neurotrophic support [4,5]. Chronic hyperglycemia may be responsible for the loss of muscle mass, muscle fiber atrophy, and morphological abnormalities in their mitochondria [3]. These pathological changes are thought to be responsible for the reduced muscle strength and impaired postural stability. A decreased strength in the distal muscles is related to an increased risk of developing foot ulcers, subsequently impairing walking performance [1,2,6,7]. Previous human and animal studies have highlighted BDNF, IGF-1 and VEGF as the key factors that may have beneficial effects on cognition, skeletal muscle strength, and endothelial function in the micro- and macrocirculation in patients with diabetes [8,9,10], although the underlying mechanisms in response to physical effort still need to be clarified.

Brain-derived neurotrophic factor (BDNF) and insulin-like growth factor-1 (IGF-1) are the two crucial growth factors for the proper functioning of the neuromuscular system. Their reduced expressions and serum concentrations in patients with T1DM have been implicated in progressive neuropathy and muscle atrophy [3,10,11].

Regular physical exercise is recommended for patients with diabetes [12–14], but current literature data does not support any one argument for or against the benefits of physical exercise on glucose control in patients with T1DM. Regular physical activity has a positive effect on overall health in individuals with type 1 diabetes who are in good metabolic control and without long-term complications. However, patients who have proliferative nephropathy or neuropathy should avoid exercise conditions that can result in high arterial blood pressures [15]. Exercise training ameliorates some of the negative impacts of diabetes on the body composition, blood lipid profile, blood pressure, skeletal muscle capillarization, and aerobic performance [16,17]. Exercise increases glucose transport via insulin-independent pathway, enhances synthesis of glucose transporters (i.e. GLUT-4), and increases insulin sensitivity, all of which result in lowering the insulin requirements in management of diabetic patients [18]. Recent studies of T1DM patients have shown that combining a moderate-intensity continuous exercise (ExC) with a high-intensity intermittent exercise (ExInt) may be more effective at reducing hyperglycaemia and minimizing the risk of hypoglycaemia [19,20]. The glucose metabolism and the response of glucoregulatory hormones to the continuous and intermittent exercise in patients with T1DM have been explored widely in the previous studies [20–22]. Little is known however, about the impact of different exercise protocols on the levels of brain-derived neurotrophic factor, insulin-like growth factor-1, and their binding protein in patients with type 1 diabetes.

The aim of this study was to assess the effects of continuous and intermittent exercise on brain-derived neurotrophic factor, insulin-like growth factor-1 and their binding protein-3, glycaemic control and concentrations of inflammatory cytokines in subjects with and without type 1 diabetes.

2. Methods

2.1. *Subjects*

Fourteen patients (7 females and 7 males; aged: 26.9 ± 5.9 years) with T1DM (average duration of disease 12.1 ± 7.7 years) and age matched healthy adults participated in the study. All patients were treated with recombinant human insulin (NovoRapid Novo Nordisk, Denmark; Lantus SoloStar, Sanofi-Aventis, Germany or Humalog Eli Lilly, Nederland) and were receiving multiple insulin injections daily. No individual with established diabetic complications, personal history of other metabolic or cardiovascular diseases and acute infection one week prior to the study was included in the study.

The control group consisted of healthy subjects (7 females and 7 males) with a mean age of 24.1 (5.9), without impaired fasting glucose (fasting blood glucose concentration: 70–99 mg/dL). A linear Douglas Altman's nomogram was used to calculate the total sample size.

Participants' body mass and body composition were determined from bioelectrical impedance analysis (BIA; InBody Data Management System, Biospace, Korea). The groups were