Contents available at ScienceDirect

Diabetes Research and Clinical Practice

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

International Diabetes Federation

A systematic review and meta-analysis of exercise interventions in adults with type 1 diabetes

Jane E. Yardley [a,b], Jacqueline Hay [a], Ahmed M. Abou-Setta [c,d], Seth D. Marks [e], Jonathan McGavock [a,*]

[a] Manitoba Institute of Child Health, University of Manitoba, Winnipeg, MB, Canada
[b] University of Alberta, Augustana Campus, Camrose, AB, Canada
[c] George & Fay Yee Centre for Healthcare Innovation, University of Manitoba, Winnipeg, MB, Canada
[d] Winnipeg Regional Health Authority, Winnipeg, MB, Canada
[e] Department of Pediatrics, University of Manitoba, Winnipeg, MB, Canada

ARTICLE INFO

Article history:
Received 18 June 2014
Received in revised form
27 August 2014
Accepted 15 September 2014
Available online 7 October 2014

Keywords:
Physical activity
Glycemic control
Type 1 diabetes

ABSTRACT

Aims: Conflicting evidence exists regarding the benefits of physical activity for long-term blood glucose control in adults with type 1 diabetes (T1D). The object of this systematic review was to determine the effects of physical activity on long-term blood glucose control in T1D adults.

Methods: PubMed/Medline, Embase, CENTRAL, SPORTdiscus, Global Health and ICTRP were searched up to October 2013 for randomized trials of aerobic or resistance exercise training in T1D adults. Exercises had to be performed at least twice weekly for a minimum of two months. The primary outcome was glycated hemoglobin (HbA_{1c}). Secondary outcomes included cardiorespiratory fitness and insulin dose.

Results: Six randomized trials were identified (323 adults); sample sizes ranged from $n = 6$ to $n = 148$ participants receiving the intervention. Five trials had an unknown risk of bias; one trial was deemed to be at high risk of bias. Exercise frequency varied from twice weekly to daily, with intensities (50–90% VO_{2peak}), and session durations (20–120 min) varying widely. Four trials reported HbA_{1c}, which decreased with exercise training (mean difference [MD] −0.78% (−9 mmol/mol), 95% CI −1.14 (−13 mmol/mol) to −0.41 (−5 mmol/mol); $p < 0.0001$; I^2 0%) compared with controls. Exercise training improved cardiorespiratory fitness by 3.45 ml/kg/min (95% CI 0.59 to 6.31, $p = 0.02$, I^2 0%) compared with controls. One trial reported an effect on insulin dose (MD −0.4 U/kg, 95% CI −0.53 to −0.27, $p < 0.00001$) compared to controls.

Conclusion: There are currently insufficient well-designed studies to ascertain the true effect of exercise training on HbA_{1c} in individuals with T1D, but current results are promising.

1. Background

Regular physical activity is associated with multiple health benefits for individuals with type 1 diabetes (T1D) [1]. Increased physical activity is associated with a lower risk of complications and an increased life expectancy [2], however, more than 60% of adults with T1D do not achieve recommended levels of physical activity [3]. Children with T1D also face barriers to achieving recommended physical activity

* Corresponding author. Tel.: +1 204 480 1359.
E-mail address: jmcgavock@mich.ca (J. McGavock).
http://dx.doi.org/10.1016/j.diabres.2014.09.038
0168-8227/

targets [4]. In addition to conventional barriers to exercise (i.e. lack of time, work pressure, environmental conditions, low energy etc.), fear of hypoglycaemia [5] and a lack of evidence for any beneficial effect of exercise on long-term glycemic control likely contribute to low physical activity rates in individuals with T1D.

Clinical practice guidelines recommend 150 min of moderate (50–70% of person's maximum heart rate) to vigorous (>70% of person's maximum heart rate) physical activity weekly for adults with T1D [6,7]. Due to the dearth of evidence available on this topic, the appropriate dose (type, duration, frequency, intensity) of physical activity needed for improved glycemic control in this population remains unclear. In contrast to the well-documented benefits of physical activity for glycemic control among individuals with type 2 diabetes (T2D) [8,9], experimental studies of exercise training in T1D individuals have yielded conflicting results. Recent systematic reviews of trials of physical activity for glycemic control in persons with T1D failed to address these inconsistencies as they have either (1) included quasi experimental trials [1,10]; (2) pooled data from short term training studies (2–8 weeks) and acute studies [11] and/or (3) included studies of interventions that combined diet and exercise training [1,10,12]. One recent meta-analysis of physical activity and/or sedentary behavior intervention studies in children with T1D, included only randomized controlled trials [13] and found a significant improvement in glycemic control (HbA_{1c}) with exercise training [mean difference −0.85% (95% CI, −1.45 to −0.24%)]. A comparable systematic review and meta-analysis in adults is currently unavailable in the literature. Therefore, a focused systematic review of the literature was conducted to examine the state of the scientific literature regarding randomized trials of exercise training interventions lasting more than eight weeks with exercise performed at least twice weekly in individuals with type 1 diabetes.

2. Methods

Using a previously published protocol [14], a systematic review applying methodological approaches outlined in the Methodological Expectations of Cochrane Intervention Reviews [15] was conducted and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses criteria [16]. An expert panel from multiple fields (pediatrics, endocrinology, clinical epidemiology, exercise physiology) formulated the review question, reviewed the search strategies and review methods, and provided input throughout the review process.

2.1. Populations, interventions, comparators, outcome measures, settings and study designs (PICOS)

The primary research question for this analysis was: ''In adolescents and adults (aged 15–50 years) living with T1D, does a structured physical activity intervention lead to clinically meaningful reductions in glycated hemoglobin (HbA_{1c}) compared to a non-exercising control condition?'' To address this question, only randomized, controlled trials of adults diagnosed with T1D were included.

Inclusion criteria for trials included in the review were: (1) the majority of participants (≥80%) had to be between 15 and 50 years old and diagnosed with type 1 diabetes mellitus; (2) trials had to be prospective, randomized and controlled with a non-exercising T1D control group; and (3) the exercise intervention consisted of supervised or unsupervised aerobic, resistance or combined physical activity offered at least twice weekly for longer than eight weeks. Trials were excluded if they (1) involved animals; (2) included participants with cystic fibrosis, type 2 diabetes mellitus, monogenic forms of diabetes, secondary diabetes, or with $HbA_{1c} < 7.0\%$ (53 mmol/mol); (3) included co-dietary intervention, behavioral modification not directly related to physical activity, or acute exercise only (i.e. single exercise session); (4) used a quasi-experimental design (e.g., alternate randomization, randomization according to hospital number, non-randomized trials (e.g. cohort and case-control studies, cross-over or cluster randomized trials

The primary outcome measure was HbA_{1c} assessed at the end of the active intervention. Secondary outcomes included maximal oxygen uptake, weight (kg), daily insulin dose, cardiovascular risk factors, body mass index and occurrence of adverse events in both groups.

2.2. Search strategy for identification of studies

Trials without language restriction published up to October 2013 that met inclusion criteria were identified using individualized search strategies prepared for the following databases: PubMed (National Library of Medicine), EMBASE (Ovid), CENTRAL (the Cochrane Library—Wiley), CINAHL (EbscoHost), Global Health (Ovid), and SPORTDiscus (EbscoHost). The PubMed strategy is presented in Appendix 1. Further, a forward search was performed in Scopus and Web of Science to identify additional citations. To identify ongoing or planned trials, we searched the World Health Organization's International Clinical Trials Registry Platform for relevant registrations. Finally, abstracts, conference proceedings and the references lists of relevant narrative and systematic reviews were searched and included trials were hand-searched for possible relevant citations.

Two reviewers independently screened the titles and abstracts (when available) of search results to determine if studies met the inclusion criteria. Reports were classified as: include, exclude, unclear, or duplicate of another citation. The full text of citations classified as ''include'' or ''unclear'' by either reviewer were retrieved for formal review. Two reviewers independently assessed the full text of each potentially included trial by using a standardized form outlining the predetermined inclusion/exclusion criteria. Disagreements were resolved by discussion between the two reviewers or by another reviewer's adjudication, as needed.

2.3. Data extraction and management

Two independent reviewers (JY, JH) extracted information using standardized, piloted forms. Disagreements were resolved through consensus and with the assistance of another reviewer (JM), if consensus was not achieved. From each trial the following information was extracted: author, year and language of publication, source of funding, study