Concurrent low-carbohydrate, high-fat diet with/without physical activity does not improve glycaemic control in type 2 diabetics

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Aim: This study aimed to determine if a low-carbohydrate, high-fat diet (LCHFD) provides any benefits of glycaemic control in patients with type 2 diabetes mellitus, either alone or in conjunction with physical activity.
Methods: Type 2 diabetics ($n = 39$) were assigned into either a concurrent physical activity and LCHFD group (DiExG), LCHFD only group (DietG) or control group (ConG).
Results: No significant ($p > 0.05$) changes were observed in glycated haemoglobin (HbA1c), glucose and insulin in either the DiExG (HbA1c: $p = 0.592$; 8.3% decrease, glucose: $p = 0.477$; 11.1% decrease and insulin: $p = 0.367$; 44.1% increase) or DietG (HbA1c: $p = 0.822$; 0% change, glucose: $p = 0.108$; 11.0% decrease and insulin: $p = 0.976$; 4.2% decrease) group.
Conclusions: In this study, neither an LCHFD alone nor in combination with a physical activity programme succeeded in eliciting improvements in insulin sensitivity in the type 2 diabetics. As such, adoption of a LCHFD, either alone or in combination with physical activity, should not unequivocally be part of the treatment approach for type 2 diabetics. Furthermore, it should carefully be weighed against the benefits of more balanced dietary and/or physical activity interventions.

Keywords: glucose, glycated haemoglobin, HbA1c, insulin, physical activity

Introduction

Type 2 diabetes mellitus is a global health problem of pandemic proportions and currently affects more than 171 million people.[1] Those with the condition are characterised as being insulin resistant with an inadequate insulin response to maintain a normal concentration of glucose in the blood.[2] It is estimated that type 2 diabetes mellitus accounts for 90–95% of all diabetic conditions.[3] Insulin is a hormone that regulates blood glucose levels in the body and controls glucose entry into the body's tissue cells.[4] Following a meal, blood glucose levels rise while insulin activates an intracellular signal, leading to the translocation of glucose from intracellular compartments to the cell surface. This then, in turn, results in glucose uptake and normalisation of the blood glucose levels[5] due to a glucose transporter type 4 (GLUT4), a protein that is found primarily in adipose tissue and striated muscle.[6] In type 2 diabetics, when an individual's blood glucose levels are high, GLUT4 is released in a non-stimulated state, which prevents the protein from reaching the surface of the cells and affects the transport of glucose into muscle and fat cells. This causes glucose to remain in a state that cannot be used by the body for energy and other processes.[5]

Type 2 diabetes mellitus is considered a chronic and progressive metabolic disorder caused by a poor lifestyle[3] and the condition has a direct relationship with a sedentary lifestyle and an unhealthy diet. Treatment typically focuses on the patient's self-management, which involves daily blood glucose monitoring, oral medication and/or insulin injections, in combination with a specific diet and regular physical activity.[7] In addition to blood glucose monitoring, glycated haemoglobin (HbA1c), as a determination of the average state of glycemia over several months, is an important measurement for the monitoring and management of diabetes mellitus as it relates to the development of long-term diabetic complications.[8]

Low-carbohydrate, high-fat diets (LCHFD) have become a popular diet strategy, with supposed benefits of glycaemic control in patients with type 2 diabetes mellitus.[9] This type of diet typically involves a carbohydrate intake of 50 grams (g) or less per day or diets as having less than 20% carbohydrate and 40–60% dietary fat content.[10] Proposed benefits of such a diet, compared with a high-carbohydrate, low-fat diet (HCLFD), are that it has been demonstrated to decrease basal serum insulin levels, assist in the removal of water from the body, and increase satiety and the dissolution of glucose stores. This may be due to LCHFD also being proposed to increase the thermal effects of food digestion, effectively increasing energy expenditure.[11] However, limited research has been conducted on the effects of a LCHFD on glycaemic control in type 2 diabetics.[12] While LCHFDs may prove to have health-promotion benefits, Foster et al. (2003)[9] reported that the most recommended diets for weight loss in type 2 diabetics are the adverse HCLFDs.

Aerobic physical activity is considered to be part of the gold standard for the treatment regime of type of 2 diabetes mellitus. According to Boulé et al. (2003),[13] aerobic physical activity needs only reflect an improvement from a sedentary state. This is because an increase in physical activity provides more benefits than only lowering blood glucose; it also improves body composition, feelings of well-being and an individual's ability to perform activities of daily living (ADLs) and reduces overall morbidity.[14]

Problematically, the incidence of type 2 diabetes mellitus has greatly increased in the past 20 years.[1] Internationally, according to the International Diabetes Federation (IDF), 366 million individuals had diabetes in 2012 rising to 425 million in 2017.[15] This alarming trend has necessitated the need to determine the efficacy of novel possible treatment methods, such as LCHFD, either alone or as an adjunct to physical activity in an attempt to improve insulin sensitivity (and associated co-morbidities) in the type 2 diabetic.

Methods

Study population and sample
This research was approved by the Institutional Review Boards of the University of Zululand, South Africa (Ethical Clearance number: UZREC 171110–030 PGD 2017/164) and employed a pre-test–post-test design with two experimental groups and one control group. Participants were recruited from patients registered at the Richards Bay Diabetic Clinic and surrounding area in Zululand, KwaZulu-Natal, South Africa. Following written informed consent, participants were screened and received approval from a medical doctor at the clinic for participation in the study. The screening process included past and current medical history, a physical examination and questions/diagnostic procedures, and required testing to determine each participant's eligibility based on inclusion criteria and relative/absolute contraindications to exercise.[4] Thirty-nine type 2 diabetics were assigned into either a concurrent physical activity and LCHFD group (DiExG), LCHFD only group (DietG) or control group (ConG), whose members continued with their normal daily activities.

Assessment
Blood samples were obtained following an overnight 9- to 12-hour fast, and 48 hours before and after the study period. Venous blood was drawn, and centrifuged serum and plasma were frozen at −80°C. Serum levels of HbA1c, glucose and insulin were assayed using a Bio-Rad Variant 11 (Bio-Rad Laboratories Ltd, Johannesburg, South Africa) and Centaur XP Siemens apparatus (Siemens Healthcare GmbH, Erlangen, Germany).

Intervention
Low-carbohydrate, high-fat diet component
Using a popular diet book published by a lay press,[16] trained research staff instructed DietG and DiExG participants to restrict intake of carbohydrates to less than 50 g of carbohydrates per day[10] for the 16-week intervention period. Adherence to the diet was measured by self-report food records. During the first meeting, participants were instructed on how to document food intake and were given handouts with examples of how to complete the records. Staff provided a single set of instructions that were not altered over the course of the study.

Physical activity component
The DiExG group followed a 16-week programme consisting of a physical activity programme entailing walking a minimum of 10 000 steps daily for most days of the week measured using a pedometer (HJ 112, Omron Healthcare Inc., Kyoto, Japan)[17] in combination with the LCHFD requiring participants not to consume more than 50 g of carbohydrates per day.[10] The promotion of participation in exercise is increasingly important and one such promotional strategy is to encourage walking; many organisations such as the British Heart Foundation (2005: http://www.bhf.org.uk) utilise the cumulative strategy recommending a minimum of 10 000 steps per day for most

days of the week.[18] In addition to the LCHFD records, DiExG participants received a personal physical activity logbook to record their number of steps daily. Staff provided a single set of instructions that were not altered over the course of the study.

Control component
The ConG group were required to continue their normal activities throughout the 16-week period as 10 000 steps is not normally achievable through routine daily activities.[18]

Statistical analysis
Variables were reported as mean ± standard deviation (SD). Results are expressed as means. The averages and correlation levels between the scores in relation to the different parameters were calculated using the paired-samples t-test. Data were also processed using one-way analysis of variance (ANOVA), with a subsequent independent t-test. A p-value of ≤ 0.05 was considered statistically significant. Statistical analyses were performed with the Statistical Package for the Social Science (SPSS) for Windows, Version 25.0 software (IBM Corp, Armonk, NY, USA).

Results
Of the initial 39 patients with type 2 diabetes mellitus who were eligible to participate in the study, 35 patients (DiExG: $n = 12$, DietG: $n = 10$, ConG: $n = 13$) completed the study and were included in the final analysis. Four patients were excluded from analysis in the study as they were unable to be tested throughout the 16 weeks. There were no significant ($p > 0.05$) differences found in all three groups for HbA1c, glucose and insulin (Table 1). Following the 16-week experimental period, no significant changes were found in HbA1c, glucose and insulin for either the DiExG, DietG or ConG.

Discussion
This study aimed to determine if an LCHFD provides any benefits of glycaemic control in patients with type 2 diabetes mellitus, either alone or in conjunction with physical activity, as a practical means for addressing this global health problem. The present study found no noteworthy benefit when type 2 diabetics followed a 16-week LCHFD or concurrent LCHFD and physical activity programme. This finding is in contrast to Haimoto et al. (2008),[19] Miller et al. (2011)[20] and Nanri et al. (2015)[1] who found that an LCHFD led to a decrease in HbA1c and improved glycaemic control. These studies may have elicited these results as they restricted carbohydrate consumption by 45–60%, which is hardly sustainable. The addition of a physical activity programme was proposed to be an appropriate adjunct to an LCHFD as exercise has the potential to provide many benefits for an individual with diabetes mellitus.[22] Some of the specific benefits that exercise has for DM include possible improvements in blood glucose control (specifically for DM type II), improved insulin sensitivity, lowered medication requirement, reduction in body fat (thus increasing insulin sensitivity), cardiovascular benefits, stress reduction (thus maintaining balance with counter-regulatory hormones) and even the prevention of developing DM type II.[22] In this regard, exercise may assist in the uptake of glucose into muscles even in the absence of insulin.[23] This statement may be somewhat supported by the present study in that while the DiExG group was found to have a non-significant decrease in HbA1c and glucose levels, this group was also found to have a non-significant increase in insulin levels by 44.1% at post-test, possibly indicating increased insulin resistance. The present study and several studies for even longer periods (of up to four months)

Table 1: HbA1c, glucose and insulin in type 2 diabetics following a 16-week low-carbohydrate, high-fat diet (LCHFD) with/without physical activity

	Group	Pre-test	Post-test	*p*-value	% difference
HbA1c (%)	DiExG	7.3 ± 1.8	6.7 ± 1.4	0.592	↓8.3
	DietG	5.8 ± 0.7	5.8 ± 0.4	0.822	0.0
	ConG	7.8 ± 1.9	8.1 ± 1.8	0.937	↑ 3.8
Glucose (mmol/l^{-1})	DiExG	8.1 ± 2.6	7.2 ± 1.2	0.477	↓ 11.1
	DietG	6.4 ± 0.8	5.7 ± 0.7	0.108	↓ 11.0
	ConG	7.6 ± 1.8	8.0 ± 1.9	0.824	↑ 5.0
Insulin (µIU/ml^{-1})	DiExG	20.9 ± 16.1	37.4 ± 47.4	0.367	↑ 44.1
	DietG	28.5 ± 23.5	27.3 ± 23.5	0.976	↓ 4.2
	ConG	30.1 ± 26.4	34.4 ± 23.7	0.879	↑ 12.5

Values are means ± SD.
DiExG: concurrent physical activity and LCHFD group; DietG: LCHFD only group; ConG: control group; HbA1c: glycated haemoglobin; mmol/l^{-1}: millimoles per litre; µIU/ml^{-1}: microliter.

failed to demonstrate that walking can be the appropriate exercise modality to result in health and glycaemic control improvements, even in type 2 diabetics, especially when intensity is self-determined in the case of cumulative strategy recommendations.[24] In this regard, Fritz and Rosenqvist (2001),[25] Mitranun et al. (2014)[26] and Gainey et al. (2016)[27] demonstrated that walking can improve glycaemic control in type 2 diabetics, although exercise that includes at least intervals of higher intensity has a more significant impact on health promotion, and especially on HbA1c levels. It is important to note that these studies utilised target intensities (i.e. 50–70% maximum heart rate) and did not utilise self-determined intensities as in the present study and that of Fritz et al.[24]

While the efficacy of a healthy lifestyle can be supported in type 2 diabetics by undertaking regular physical activity and diet and avoiding harmful habits, such as smoking and alcohol consumption, many important questions remain regarding the effectiveness of LCHFDs in improving health outcomes, especially in type 2 diabetics. In addition, although physical activity is considered a 'gold standard' in the management of type 2 diabetes mellitus, it appears that the prescription of 10 000 steps daily without any regard for intensity may not be quite as effective in improving health outcomes, and especially glycaemic control, in type 2 diabetics.

There are several limitations to this study. This study was conducted for a relatively short timeframe of 16 weeks and it is unclear whether any of the changes outlined would have been sustained following the completion of this study. Additionally, because of the relatively small sample, results should not be generalised to the entire diabetic population. Although there are many problems with using self-report measures, they will continue to be a popular methodology. The drawbacks associated with physical activity measurement via pedometry too are acknowledged; more specifically, the use of a pedometer as both a measurement tool and an intervention device should be highlighted as a potential confounding factor. Therefore, in the future, pedometer-driven intervention trials should consider the use of alternative, yet sensitive objective means of assessing changes in physical activity in conjunction with wearable devices that monitor and record target intensities. These devices should be sealed and returned weekly to the researchers for download of raw data.

Conclusions
In this study, neither an LCHFD alone nor in combination with a physical activity programme failed to elicit improvements in

insulin sensitivity in the type 2 diabetics. As such, adoption of an LCHFD, either alone or in combination with physical activity, should not unequivocally be part of the treatment approach for type 2 diabetics and should carefully be weighed against the benefits of more traditional, balanced dietary and/or physical activity interventions. In addition, this study provides evidence that the use of cumulative strategies such as the 10 000 steps method should be reduced as this disregards other important factors of exercise design, such as target exercise intensities. This is especially critical given that exercise intensity and duration have been recognised as the primary determinants of muscle glucose uptake during exercise.[18]

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