Journal of Holistic Performance
ISSN: 2463-7238 DOI: 10.26712/072019
Published: 5/7/2019
CLINICAL TRIAL | PEER-REVIEWED

Can a 'Carbohydrate Tolerance Questionnaire' Predict Outcomes from Diets Differing in Carbohydrate Content? A Pilot Study

Cliff J. d C. Harvey, Grant M. Schofield, Caryn Zinn, Simon J. Thornley

cliff@hpn.ac.nz

Abstract

Background

Clinical trials and experience suggest that there is a wide variation in how people respond to different dietary protocols. Clinical experience suggests that there are common signs of relative carbohydrate 'tolerance' that might predict cardiometabolic and anthropometric outcomes resulting from differing diets and the optimal allocation of carbohydrate restriction that might be most suited to the individual.

Objective

We believed that people with a higher carbohydrate intolerance score (CIS) determined from completing a carbohydrate tolerance questionnaire (CTQ) would achieve larger changes in cardiometabolic and anthropometric measures of health from greater magnitudes of carbohydrate restriction.

Methods

Seventy-seven healthy participants were randomised to a very low carbohydrate ketogenic diet (VLCKD), low-carbohydrate diet (LCD), or moderate-low carbohydrate diet (MCD), containing 5%, 15% and 25% total energy from carbohydrate respectively, for 12-weeks.

Anthropometric and metabolic health measures were taken at baseline and 12 weeks, and symptoms of carbohydrate withdrawal and mood evaluated by questionnaires. The association between CIS and changes in anthropometric and cardiometabolic markers and mood and symptoms of carbohydrate withdrawal were made by undertaking multiple linear regression. Differences between beta coefficients describing the outcome - CIS relationship by group were determined by an interaction term, testing for significance at a p-value < 0.05.

Results

Baseline carbohydrate tolerance was associated with improvement in serum triglycerides (TG) overall, (Beta = -0.025, p = 0.073) and in the VLCKD group (Beta = -0.034, p = 0.055). The only CIS-outcome relationship to vary significantly between groups was for change in body mass index (BMI); p = 0.007, with higher carbohydrate intolerance inversely associated with the change in BMI in the MCD group (Beta = -0.309, p = 0.032). Higher CIS was also associated with more severe symptoms of carbohydrate withdrawal (Beta = 0.214, p = 0.084) and increased mood disturbance (Beta = 0.044, p = 0.060). There was also a weak association between CIS and mood disturbance in the VLCKD group (Beta = 0.083, p = 0.014).

Conclusions

Our findings demonstrate that those with higher CIS are more likely to benefit from low-carbohydrate diets for the improvement of triglyceride concentrations. Subjects with higher scores are also more likely to experience mood disturbance and symptoms of carbohydrate withdrawal. The questionnaire might be useful for clinicians to allocate those with the highest CIS to a more moderately restricted plan to mitigate symptoms of carbohydrate withdrawal and effects on mood and to offer greater improvements in BMI. However, at this time and contrary to our hypothesis, due to the lack of clear between-group significance, it is unclear whether it can accurately predict the efficacy of dietary allocations for the individual.

Introduction

Low-carbohydrate diets (LCDs) and very low-carbohydrate ketogenic diets (VLCKDs) are routinely used for the management of a range of health conditions, including neurological disorders, obesity, diabetes, other conditions on the spectrum of metabolic syndrome, and various cancers.[1-11] They are also used widely in the general population to achieve weight-loss and maintenance,[12] improve satiety, and reduce hunger.[13-15] Despite the potential offered by LCDs, and the common use of these diets by the general public, there is little evidence for the superiority of greater carbohydrate restriction compared to more moderate restriction both overall,

and for whom greater restriction might be more effective.

Furthermore, there is little research available to support the use of tools to guide the degree of carbohydrate restriction for individual patients. For example, while it has been suggested that a 'metabolic type' with a physiological preference to oxidation of protein, carbohydrate or a 'mixed type' can be indicated by a simple dietary and lifestyle questionnaire,[16] a pilot trial of rugby players in New Zealand found that test results did not match up with laboratory analysis of fat and carbohydrate oxidation rates.[17] To our knowledge, there is also no accepted or validated questionnaire that might indicate the usefulness of diets differing in carbohydrate restriction for the improvement of anthropometric or cardiometabolic measures of health.

The present pilot study aimed to evaluate changes in cardiometabolic and anthropometric measures, and mood and symptoms of carbohydrate withdrawal, resulting from a twelve-week dietary intervention differing in the magnitude of carbohydrate restriction, relative to baseline scoring on a carbohydrate tolerance questionnaire (CTQ). We hypothesised that those with a higher 'carbohydrate intolerance score' (CIS) at baseline would benefit more from greater carbohydrate restriction.

Materials and Methods

Population

Seventy-seven participants, 25 males, 52 females (mean age: 39 years, range: 25 to 49; mean BMI 27 kg/m^2, range: 20-39) were recruited between the 7th and 19th of August 2017 and gave written, informed consent to participate in this 12-week, randomised, clinical intervention study. The study took place between 11th September and 10th December 2017. Collection of data and analysis was performed at AUT's Human Potential Centre, Auckland, New Zealand.

Inclusion and exclusion criteria

Participants were required to be healthy and between the ages of 25 and 49 years. Exclusion criteria were; underweight (< 18.5 BMI kg/m^2), diagnosed with diabetes, diagnosed with any serious medical condition, having previously following a ketogenic diet, or being a current or former client of any of the researchers in clinical practice.

Ethical approval

The trial was registered by the Australia New Zealand Clinical Trial Registry. (ACTRN12617000421336p). Ethics approval for this study was granted by the Southern Committee of the Health and Disability Ethics Committee of New Zealand. 17/STH/60

Dietary interventions and allocation

Participants completed baseline testing of blood and basic anthropometric measures and a lead-in dietary recording week to identify habitual calorie intake. The study statistician prepared a randomised sequence to one of three low-carbohydrate diet plans which advised intakes of either 5%, 15%, or 25% of total energy (TE) from carbohydrate. The randomisation was stratified by gender, with investigators blinded to treatment allocation at both baseline and follow-up. Participants were assigned to the next treatment group according to their order of recruitment. The primary researcher responsible for initial statistical analysis was blinded to the treatment group allocation until this analysis had been completed.

Diet plans, which included macronutrient and calorie allocation and a sample menu plan, were individualised to the participant, with energy intake determined by the mean reported energy consumed per day in the lead-in dietary recording week. Advice was given to limit protein intake to 1.4 g/kg/day (weight at baseline testing), consistent with the International Society of Sports Nutrition guidelines for optimal protein intake for performance.[18] Participants were advised to adhere as strictly as possible to the energy and macronutrient prescription for the first three weeks of the intervention. For the final nine weeks of the intervention, they were advised to eat *ad libitum* but to adhere as closely as possible to the carbohydrate energy limit for their treatment group as a percentage of their TE. Usual exercise patterns were continued. Dietary intake was recorded by participants in a mobile application (Fat Secret) with the researchers able to obtain real-time entry on a partner mobile application (Fat Secret Pro). Results were monitored for safety and compliance by the primary researcher and research assistants tasked with data-monitoring. Figure 1 profiles the instructions for the dietary allocations over the 13-week study course. Participants were instructed to contact either the clinical nutritionist or the registered dietitian in the research team for any assistance during the study duration.

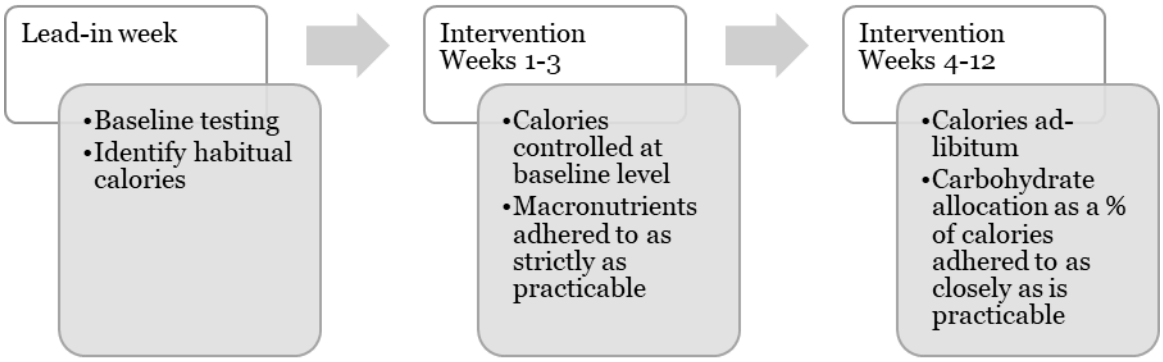

Figure 1. Flow-chart showing instructions for the dietary allocations

Carbohydrate Tolerance Questionnaire

The CTQ was compiled from qualitative indicators of expected carbohydrate 'tolerance' from the experience of the authors, with additional input from industry colleagues. The questionnaire was put through a 4-stage process of content analysis and peer review with a cohort of academics and experienced nutrition practitioners. This involved the creation of the questionnaire by the primary and tertiary authors, followed by feedback and additions from the rest of the research team, additional peer-review by two additional practitioner-researchers, and final adjustment by the research team. The CTQ included the following statements: *When I gain weight, I tend to put it on my tummy/around my middle, If I don't eat regularly/every few hours I suffer energy 'crashes', or mood/mental disturbance [i.e. 'hangry'], I crave sweet and/or starchy foods often, I snack on sugary or starchy food to relieve headaches/irritability/craving/excessive hunger*; ranked on a 5-point Likert scale (Not at all, Seldom, Occasionally, Often, Almost always). These results were ranked from 1 to 5 and added to create a combined CIS out of a total possible score of 20. The greater the CIS score, the greater the expected carbohydrate 'intolerance'. The CTQ was administered to participants at baseline.

Anthropometry

The following measures were taken, height (m), weight (kg), waist circumference (cm) at the narrowest point between the lowest rib and the iliac crest, and hip circumference (cm) at the widest point of the hips and buttocks. These measures were then used to derive BMI, waist-hip ratio, and the waist-height ratio. Records

were taken at both baseline and at the end of follow-up.

Blood measures

Following an overnight fast, blood samples were obtained from participants, before the first meal, via venipuncture by a certified phlebotomist from an antecubital vein and collected into PST Vacutainer tubes using lithium-heparin as the anticoagulant (Becton Dickinson). Within 15 minutes of collection, tubes were centrifuged at 1500 revolutions per minute for 10 min at +4°C, and plasma samples were transferred into clean polypropylene tubes and frozen at −80°C until analyses were conducted using specific diagnostics assays on a Roche Modular analyser (P800 and E170). Blood samples were analysed for total cholesterol (Total-c), low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, triglycerides (TG), C-reactive protein (CRP), gamma-glutamyl transferase (GGT), alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), glucose and uric acid on the P800 module. Insulin and C-peptide concentrations were measured on the E170 module. All analytical biomarkers were measured at baseline and immediately following the 12-week intervention. The total duration of the assay for each analyte was less than 20 min based on the electrochemiluminescence principle (ruthenium-conjugated monoclonal antibodies) for the E170 module and specific enzyme assay methods for the P800 module. Quantitative results were determined via instrument-specific full point calibration curves and validated with specific controls.

Mood and symptoms questionnaires

Participants were instructed to complete a questionnaire including one relating to keto-induction symptoms (Symptom-Q) and a simplified 5-point scale indicator of mood state (Figure 2) developed by the lead author. The Symptom-Q was developed based on published reports of symptoms observed in the early phase of subjects starting a ketogenic diet. One question was asked ("In the past 24 hours to what extent have you experienced the following symptoms?") for any of: headache, constipation, diarrhoea, stomach or intestinal pain, intestinal bloating, change in breath odour, muscle cramps, muscle weakness, skin rash, difficulty concentrating, light-headedness, and craving for sugary or starchy foods. These responses were reported on a 5-point Likert scale, and scored as 0) Not at all, 1) Mild, 2) Moderate, 3) Severe, and 4) Intolerable. Individual symptoms scores were added to form an overall sum of symptoms scores (SOSS) between 0 and 48 for analysis.

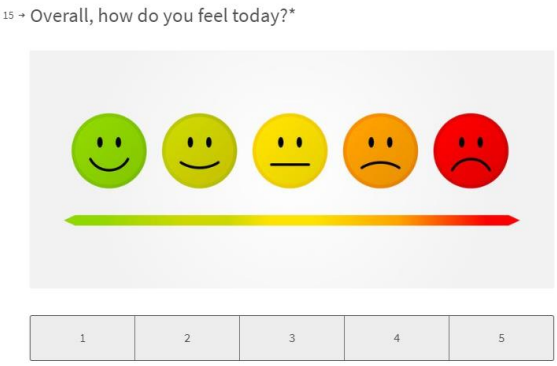

Figure 2. 5-point mood disturbance scale

Statistical analyses

The association between CIS and the change from baseline in anthropometric and cardiometabolic markers, and mood and symptoms of carbohydrate withdrawal, were made by undertaking multiple linear regression for the CIS and treatment group as independent variables with change in outcome measures as dependent variables. The hypothesis that the linear relationship between CIS and outcome change varied by group was tested for by including an interaction term in the model and evaluating the *p*-value from a likelihood ratio test. Whether or not this was statistically significant, the results of the model including the interaction term are presented, to explore the hypothesis of whether the CIS-outcome association varied by degree of carbohydrate restriction (treatment group), since the numbers of participants in each group are small, and the likelihood ratio may be under-powered. A *p*-value of less than 0.05 was used as the threshold for significance. Beta coefficients from regression models, therefore, represent the mean change in outcome associated with a one unit increase in CIS.

Results

A total of 283 people was assessed for eligibility with 206 excluded and 77 included for randomisation to the trial groups (Figure 3). Ten participants withdrew after they were randomised. Two failed to comply with guidelines to submit baseline data and withdrew from the study (one male, one female), and three females withdrew due to changes in personal circumstances, including two who became pregnant. A further five withdrew due to challenges arising from following the diets: two female participants found the dietary allocation of carbohydrate too difficult to sustain (one each in the 5% and 15% allocation groups). One did not want to use the food app; one felt that she could not maintain her sports performance on 15% total energy from carbohydrate; and one female in the 5% allocation group reported amenorrhea and reduced strength and power, despite improved mental clarity. A further 28 failed to present for post-intervention measurements. This left 39 participants with follow-up results available for analysis.

There were no significant differences in baseline characteristics between completers and non-completers and no meaningful difference in the number of

non-completers by group, with 50%, 50%, and 48% of participants not completing post-intervention measures in the MCD, LCD, and VLCKD groups, respectively. The CIS did not differ significantly between groups (p = 0.129) but did differ between individuals at baseline, as did all subscales, suggesting that the measures used could show validity (all results $p < 0.001$).

Mean baseline levels of TG were, however, 36% higher at baseline in those lost to follow-up compared to those who were not, even though the difference between the two distributions was not significant ($p = 0.08$). There was also no significant variation for age, gender, or ethnicity between the groups, in the participants analysed. At baseline, blood measures were all within reference ranges except for Total cholesterol (Total-c) which had an overall mean of 5.31 mmol/L (SD = 1.29) for completers, and a significant between-group difference ($p = 0.005$).

Baseline characteristics of those included for analysis are presented in Table 1, by randomised treatment group.

Table 1. Baseline characteristics of study participants

	Treatment group					
	MCD (n=12)	**LCD (n=13)**	**VLCKD (n=14)**	**Total (n=39)**	**Test**	***p*-value**
Age mean (SD)	39.1 (6.6)	38.9 (8.3)	38.7 (7.1)	38.9 (7.1)	ANOVA	0.992
Gender (%)					Fisher's	0.198
Female	10 (83.3)	6 (46.2)	9 (64.3)	25 (64.1)		
Male	2 (16.67)	7 (53.85)	5 (35.71)	14 (35.9)		
Ethnicity (%)					Fisher's	0.733
Asian	1 (8.3)	0 (0.0)	1 (7.1)	2 (5.1)		
European	8 (66.7)	11 (84.6)	10 (71.4)	29 (74.4)		
Maori	2 (16.7)	1 (7.7)	3 (21.4)	6 (15.4)		
Pacific	0 (0.0)	1 (7.7)	0 (0.0)	1 (2.6)		
Other ethnicity	1 (8.3)	0 (0.0)	0 (0.0)	1 (2.6)		
Carbohydrate Intolerance Score mean (SD)	9.2 (2.3)	9.6 (2.8)	11.5 (3.8)	10.2 (3.2)	ANOVA	0.129
Total energy (Kcal) mean (SD)	1435 (293)	1567 (666)	1805 (857)	1603 (649)	ANOVA	0.378
Weight (kg) mean (SD)	76.3 (14.9)	90.4 (20.0)	76.8 (11.2)	81.2 (16.6)	ANOVA	0.046
Height (m) mean (SD)	1.70 (0.10)	1.76 (0.08)	1.74 (0.09)	1.73 (0.09)	ANOVA	0.245
BMI (kg/m^2) mean (SD)	26.4 (3.23)	29.1 (4.92)	25.5 (2.77)	27.0 (3.96)	ANOVA	0.050
Glucose (mmol/L) mean (SD)	5.54 (0.43)	5.38 (0.47)	5.44 (0.44)	5.45 (0.44)	ANOVA	0.673
Total cholesterol (mmol/L) mean (SD)	5.20 (1.3)	4.57 (0.61)	6.10 (1.37)	5.31 (1.29)	ANOVA	0.005
Triglyceride (mmol/L) mean (SD)	0.79 (0.2)	0.99 (0.36)	0.92 (0.22)	0.90 (0.27)	ANOVA	0.184
Insulin (pmol/L) mean (SD)	63.1 (37.3)	81.1 (39.4)	41.6 (17.6)	61.4 (35.8)	ANOVA	0.012

SD: standard deviation; BMI: body mass index

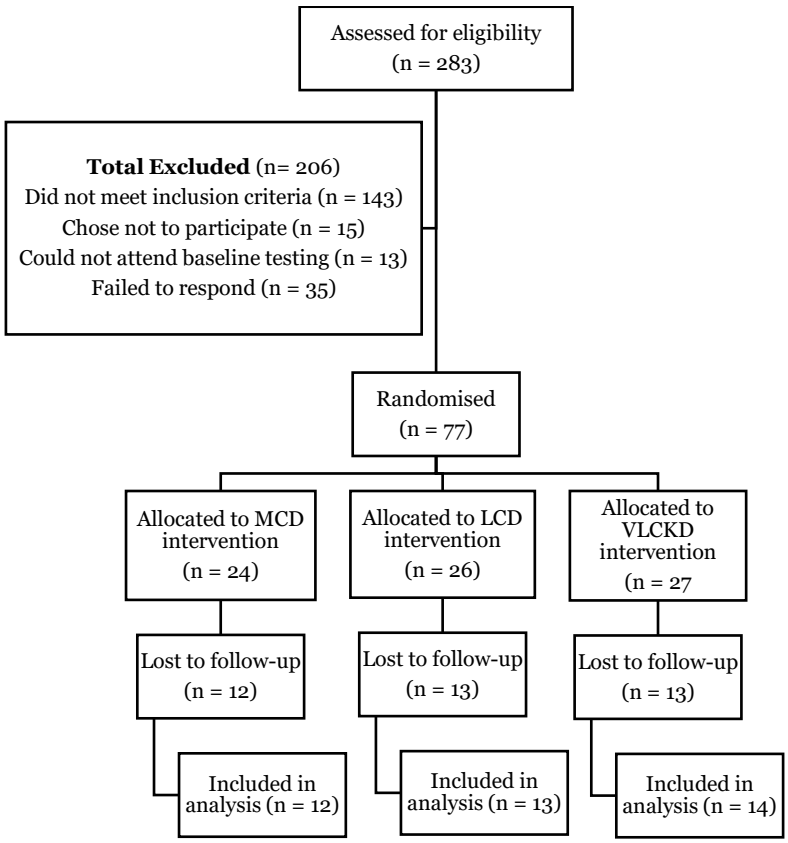

Figure 3. Flow-chart showing participant recruitment, randomisation, allocation, and loss-to-follow-up

Predictive value of CIS to change in outcome measures

The outcome measures which were most convincingly associated with CIS were for change in TG (Beta = -0.025, p = 0.073) and change in HDL cholesterol (Beta = 0.029, p = 0.106). This means that higher CIS scores at baseline were associated with more beneficial changes in TG and HDL cholesterol. On average, people with higher CIS had less marked improvements in BMI at the end of follow-up (Figure 4a) and the association between CIS and change in BMI differed significantly between interventions (p = 0.007) with relative carbohydrate intolerance associated with improvements in BMI in the MCD group only (a result that was also significant within that group) as shown in Figure 4b. The other interventions did not reach within-group thresholds for significance. Reduction in TG relative to CIS approached the threshold for significance in the VLCKD group only. Results are presented in Table 2. In subscale analysis the only measure to show meaningful and significant results was the interaction for *I snack on sugary or starchy food to relieve headaches/irritability/ craving/excessive hunger* and TG, with an increase in this

subscale score related to a greater improvement in TG (Beta = -0.0834, p = 0.050). This subscale approached the threshold for significance for HDL with higher scores related to an improvement in HDL (Beta = 0.088, p = 0.100). However, this interaction did not differ significantly within or between the intervention groups.

Table 2. Association between CIS and change in key outcome measures over twelve weeks by group

	Treatment group Beta-coefficient and p-value		
Outcome measures*	Moderate-Low Carbohydrate	Low Carbohydrate	Very Low Carbohydrate
Total cholesterol	Overall β = -0.017 ; p = 0.82†		
	0.034	-0.012	-0.068
	p = 0.81	p = 0.94	p = 0.62
	p for interaction = 0.891‡		
LDL cholesterol (mmol/L)	Overall β = -0.045 ; p = 0.51†		
	0.016	-0.045	-0.086
	p= 0.89	p = 0.77	p = 0.49
	p for interaction = 0.882‡		
HDL cholesterol (mmol/L)	Overall β = -0.029 ; p = 0.11†		
	0.047	0.007	0.018
	p = 0.44	p = 0.79	p = 0.45
	p for interaction = 0.773‡		
Triglycerides (mmol/L)	Overall β = -0.025 ; p = 0.073†		
	-0.060	0.027	-0.034
	p = 0.12	p = 0.40	p = 0.055
	p for interaction = 0.103‡		
BMI (kg/m²)	Overall β = -0.026 ; p = 0.627†		
	-0.309	0.213	0.073
	p = 0.032	p = 0.061	p = 0.275
	p for interaction = 0.007‡		

* All measures are change-from-baseline. BMI: body mass index. LDL: low-density lipoprotein. HDL: high-density lipoprotein

† β refers to the beta coefficient of the overall linear regression between carbohydrate intolerance score (CIS) and change in outcome measures.

‡ This p-value relates to a regression model of CIS and treatment group as independent variables and change in outcome as dependent variables. The p-value relates to the interaction term, testing for a significant difference in the CIS-change in outcome by treatment group.

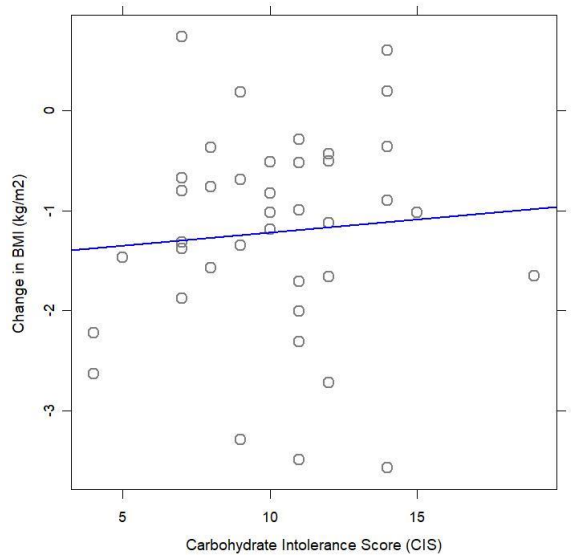

Figure 4a. Scatter plot illustrating the relationship between body mass index (BMI) and carbohydrate intolerance score (CIS) at baseline. The blue line is the linear regression.

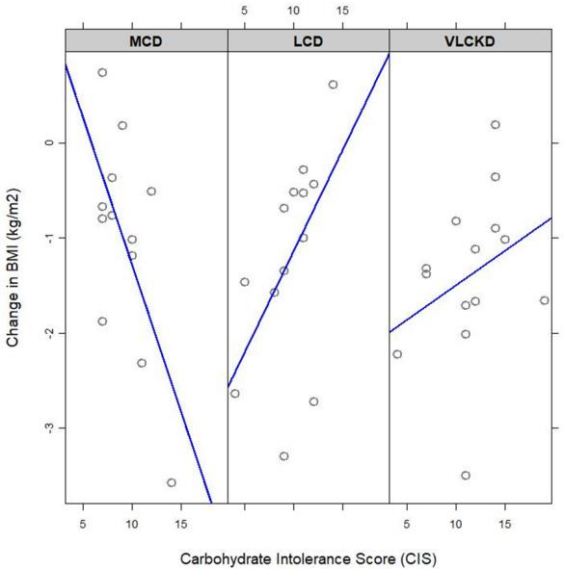

Figure 4b. Scatter plot of change in body mass index (BMI) and carbohydrate intolerance score (CIS) at baseline, by intervention group. MCD: Moderate-low carbohydrate diet; LCD: Low-carbohydrate diet; VLCKD: Very-low-carbohydrate ketogenic diet. Blue lines are the linear regressions.

Associations for symptoms and mood

A higher baseline CIS was associated with greater symptoms of carbohydrate withdrawal (Beta = 0.214) and mood (Beta = 0.044), although neither was statistically significant (p = 0.084 and 0.060 respectively). Between-group differences were not statistically significant, and the only significant within-group association was for an increase in mood disturbance associated with greater CIS in the VLCKD intervention. An increase in symptoms of carbohydrate withdrawal related to the severity of carbohydrate intolerance at baseline also approached the threshold for significance in the VLCKD group. (Table 3).

Table 3. Association between CIS and change in symptoms and mood

	Treatment group		
	Beta-coefficient and *p*-value		
Outcome measures*	Moderate-Low Carbohydrate	Low Carbohydrate	Very Low Carbohydrate
Symptoms of carbohydrate withdrawal	Overall β = 0.214 ; *p* = 0.084†		
	0.070	0.162	0.242
	p = 0.85	*p* = 0.49	*p* = 0.096
	p for interaction = 0.880‡		
Mood disturbance	Overall β = 0.044 ; *p* = 0.060†		
	-0.015	0.008	0.083
	p = 0.81	*p* = 0.82	*p* = 0.014
	p for interaction = 0.185‡		

* All measures are change-from-baseline.

† β refers to the beta coefficient of the overall linear regression between carbohydrate intolerance score (CIS) and change in outcome measures.

‡ This p-value relates to a regression model of CIS and treatment group as independent variables and change in outcome as dependent variables. The p-value relates to the interaction term, testing for a significant difference in the CIS-change in outcome by treatment group.

Discussion

Principal findings

We believed that the higher the CIS, the greater the benefit to health outcomes from greater magnitudes of carbohydrate restriction. Overall, these findings suggest that a CIS might be beneficial to indicate the magnitude of carbohydrate restriction most beneficial for improvements in key outcome measures of health. The CTQ created for this study is useful for identifying people that are likely to benefit from lower-carbohydrate interventions for improvements in their important cardiometabolic markers of HDL cholesterol and TG. People with high scores on this questionnaire are also more likely to suffer most from symptoms resulting from carbohydrate withdrawal and mood disturbance when beginning a carbohydrate-restricted diet. However, the CTQ was not useful for distinguishing between different levels of carbohydrate-restriction diets for outcome measures, except for BMI. In this case, a higher CIS was associated with greater improvements from a moderately low-carbohydrate intervention when compared to one that is more restrictive. Therefore, based on these preliminary results, those with a higher CIS might be best allocated to a moderately restricted low carbohydrate diet, initially, rather than one that is more heavily restrictive. This is also indicated by per group analysis in which symptoms of carbohydrate withdrawal were increased relative to baseline CIS, approaching the threshold for significance (i.e. $p < 0.1$) and significant worsening of mood disturbance in the VLCKD group relative to 'worseness' of baseline CIS. This Beta-value of 0.083 ($p = 0.014$) could provide for an approximate increase in mood disturbance of 42% for those maximally 'carbohydrate-intolerant' and, as such could be an appreciable factor in the interplay between diet, baseline intolerance, and mood.

Interestingly, in a secondary analysis, we found that this might have resulted from greater relative changes in carbohydrate intake as a proportion of TE by group. While there was a higher intake of carbohydrate overall in the MCD group, those with a higher CIS were more likely to have had a greater relative reduction in carbohydrate as a percentage of daily energy intake (Beta = -1.052, $p = 0.20$) when compared to positive associations between change in carbohydrate intake and CIS in the LCD and VLCKD groups. Similarly, greater improvements in TG and HDL cholesterol relative to CIS were seen in the MCD group and might be attributable to the association between CIS and change in carbohydrate intake independent of the absolute magnitude of carbohydrate intake.

Strengths and weaknesses of the study

To our knowledge, this pilot study is the first to compare commonly purported signs of *carbohydrate intolerance* and the effect this might have on outcomes from differing low-carbohydrate diets.

It was a randomised trial, including regular food tracking, along with real-time researcher monitoring and feedback and advice and information provided to participants from a competent team with extensive experience in the prescription of LCDs and VLCKDs. As such, we believe it provides a valuable addition to the literature to help inform clinical practice.

Our study was limited by small sample size and by 49% of participants not completing the intervention or presenting for follow-up testing. This was expected, as high dropout rates are common in dietary studies. A systematic review of low-carbohydrate diets vs low-fat, calorie-restricted diet interventions showed an overall attrition rate of 36%, with a higher rate of attrition in low-fat, high-carbohydrate interventions.[19] Despite high drop-out rates being common in dietary studies, few participants in this study reported dropping out due to challenges with the diets allocated, and most dropouts were instead due to failure to present for testing rather than a failure to adhere to the diet. These numbers were almost identical between the intervention groups. Participants who failed to present were asked to provide reasons for (not) doing so. Two participants responded, stating a clash with work and inability to attend due to parental responsibilities. It is therefore unclear whether there were other factors, outside of scheduling or other logistical challenges, that affected participants completing the study. The final numbers included in our analysis due to attrition, therefore, resulted in a lack of statistical power.

The study did not include a group with a higher carbohydrate allocation consistent with existing dietary guidelines of 45-65% of energy derived from carbohydrate.[20] Because of the possible predictive value of baseline CIS on mood, symptoms, TG, HDL, and BMI changes resulting from these low-carbohydrate diet allocations overall, a comparison with a higher-carbohydrate, lower-fat diet, might provide a better evaluation of the predictive value of carbohydrate 'tolerance' questionnaires.

Meanings and practical implications of the study

The key research question of this pilot study was whether relative carbohydrate intolerance, as indicated by a CTQ born of clinical experience, could predict anthropometric, cardiometabolic, and subjective mood and symptoms outcomes from differing magnitudes of carbohydrate restriction. There is a likely predictive value of greater *carbohydrate intolerance* on

mood disturbance, symptoms of carbohydrate withdrawal, and TG, HDL cholesterol, and BMI. This could provide the clinician with valuable information to tailor dietary prescriptions more effectively for the client. Additionally, it could allow the practitioner to provide more information about changes in mood and symptoms of carbohydrate withdrawal that might occur, in anticipation of starting a lower-carbohydrate diet.

Unanswered questions and directions for future research

Clinical experience and several of this study's findings suggest that a higher CIS might indicate the use of a low-carbohydrate diet overall and a moderately carbohydrate-restricted diet to improve BMI, TG and HDL cholesterol. However, this might be a result of the magnitude of relative carbohydrate restriction, irrespective of the absolute carbohydrate intake; research with larger numbers of participants and a higher-carbohydrate comparison group is necessary to further explore this hypothesis. While the questionnaire was subjected to some content analysis and peer-review by experienced nutrition practitioners and researchers, it has not yet been validated and should it be utilised in future research, it will need to undergo more thorough validity and reliability testing.

Conclusions

Our findings demonstrate that those with higher CIS are more likely to benefit from low-carbohydrate diets for the improvement of triglyceride concentrations. Subjects with higher scores are also more likely to experience mood disturbance and symptoms of carbohydrate withdrawal. The questionnaire might also be useful to allocate those with the highest CIS to a more moderately restricted plan to mitigate symptoms of carbohydrate withdrawal and effects on mood and to potentially offer greater improvements in BMI. However, at this time and contrary to our hypothesis, due to the lack of clear between-group significance, it is unclear whether it can accurately predict the efficacy of dietary allocations for the individual. To investigate this hypothesis further, additional research, with larger sample sizes, and a higher-carbohydrate control-group is required.

Acknowledgements

We are grateful to the participants in this study. We acknowledge the support of our colleagues at the Human Potential Centre, AUT University, especially Catherine Crofts and Dee Holdsworth-Perks, and Fabrice Merien; and the Holistic Performance Institute. Specifically, we would like to acknowledge the assistance of Amberleigh Jack, Bella Marinkovich, Emily White, and Lulu Caitcheon who assisted with data collection; phlebotomists, Brenda Costa-Scorse and Claudia Barclay; Kirsten Beynon for lab assistance during data collection and analysis, Dave Shaw for his co-operation during data-collection, and Eric Helms and Nigel Harris for advice about the study design and methods.

Abbreviations

Carbohydrate intolerance score (CIS), carbohydrate tolerance questionnaire (CTQ), very-low-carbohydrate ketogenic diet (VLCKD), moderate-low carbohydrate diet (MCD), low-carbohydrate diet (LCD), total cholesterol (Total-c), low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, triglycerides (TG), C-reactive protein (CRP), gamma-glutamyl transferase (GGT), alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP).

Author affiliations

All authors: Human Potential Centre, Auckland University of Technology, Auckland, NZ

Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

Authors' contribution

CJdCH, GMS, CZ, and SJT designed research; CJdCH conducted research; CJdCH, and SJT analysed data; CJdCH wrote the paper, with editing assistance from GMS, CZ and SJT. CJdCH had primary responsibility for final content. All authors read and approved the final manuscript.

Data availability

The raw, deidentified r-data files used to support the findings of this study are available from the corresponding author upon request.

Funding statement

All funding was provided by the Human Potential Centre, AUT.

Received: Accepted: Published:

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