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Effects of carbohydrate-restricted diets in the management of diabetes mellitus: review of scientific literature

Efeitos da restrição de carboidratos no manejo do diabetes mellitus: revisão de literatura científica

Abstract

This study aimed to evaluate, through a literature review, evidence of the use of diets with carbohydrate restriction in the management of diabetes mellitus (DM). Electronic and manual searches were conducted until April 2019, including works published from 2008 onwards. Studies on in vitro and animal research, literature reviews, books, monographs, dissertations, theses, case studies and case reports were excluded. The remaining articles were submitted to analysis of their methodological quality by the five-point JADAD Scale. Nineteen randomized studies with an average quality of three points were selected and analyzed regarding the types of diet used, adherence, type of DM, time of intervention, reported consumption of carbohydrates and results observed for the control and intervention group. Among the parameters chosen to measure the possible effects of diets, weight and BMI changes, Hb1Ac, variability or glycemic control, lipid profile and changes in insulin doses or medication used stood out. In four studies, no significant advantages were observed from a carbohydrate-restricted diet, and 15 studies reported improvements in one or more parameters. Such results can represent a great advantage in adopting this dietary strategy in the management of DM and in preventing complications of the disease. However, there are limitations in the studies, which need to have their hypotheses verified in the long term, and additional research must be carried out to configure an official strategy in the control of DM.

Keywords: Diabetes mellitus. Carbohydrate-restricted diet. High-protein and low-carbohydrate diet. Fat-restriction diet. Diet therapy.

Resumo

O objetivo do presente estudo foi avaliar, por meio de uma revisão da literatura, evidências da utilização de dietas com restrição de carboidratos no manejo do diabetes mellitus (DM). As buscas eletrônicas e manuais foram até abril de 2019, e incluíram trabalhos publicados a partir de 2008. Foram excluídos estudos de pesquisas in vitro e em animais, revisões de literatura, livros, monografias, dissertações, teses, estudos de caso e relatos de caso. Os artigos remanescentes foram submetidos à análise de sua qualidade metodológica pela Escala JADAD cinco pontos. Um total de 19 estudos randomizados e com qualidade média de três pontos foram selecionados e analisados quanto aos tipos de dieta utilizadas, adesão, tipo de DM, tempo de intervenção, consumo reportado de carboidratos e resultados observados para os grupos controle e intervenção. Dentre os parâmetros escolhidos para mensurar os possíveis efeitos das dietas, destacaram-se alteração de peso e IMC, Hb1Ac, variabilidade ou controle glicêmico, perfil lipídico e alteração nas doses de

insulina ou medicação utilizadas. Em quatro estudos não foram observadas vantagens significativas de uma dieta restrita em carboidratos, e 15 trabalhos relataram melhoras em um ou mais parâmetros. Tais resultados podem representar uma grande vantagem na adoção desta estratégia alimentar no manejo do DM e na prevenção de complicações da doença. Contudo, existem limitações nos estudos, que precisam ter suas hipóteses verificadas no longo prazo, e pesquisas adicionais devem ser realizadas para configurar uma estratégia oficial no controle do DM.

Palavras-chave: Diabetes mellitus. Dieta com restrição de carboidratos. Dieta rica em proteínas e baixa em carboidratos. Dieta com restrição de gorduras. Dietoterapia.

INTRODUCTION

Diabetes mellitus (DM), due to its high prevalence and morbidity, appears as a major public health problem, as a result of the complications it can generate, in addition to premature mortality.¹ It is well known that the delay in development and progression of such complications can only be achieved with an appropriate treatment in which it is possible to keep good glycemic control, that is, glycemia within the target most of the time.² Therefore, the use of a healthy eating strategy and specific for such patients is essential; and the quantity and quality of carbohydrates in the diet have long been notably an important dietary factor involved in glycemic control.³

Despite all the advances in the field of Medicine and Pharmacology, the management of DM is still far from adequate. Currently, the global average of glycated hemoglobin (HbA1c) in diabetic patients is 8.2%, and the American Diabetes Association (ADA) establishes that values below 7% are ideal for reducing the risk of complications. The biggest challenge to reach the expected goals for this DM control parameter is the difficulty in controlling postmeal plasma glucose, due to the mismatch between carbohydrate absorption and insulin action, which typically occurs after meals in patients with type 1 diabetes (DM 1), as well as the quantity and quality of carbohydrates consumed at meals, in individuals with type 2 diabetes (DM 2).^{4,5} Still, the Brazilian Diabetes Society (BDS), in its 2017-2018 guidelines, recommends a diet based on 45 to 60% of carbohydrates, and no less than 130g of carbohydrates per day, with a maximum of 5% coming from sucrose.⁶

DM reflects a disturbance in the glucose-insulin metabolism axis, with the absence of hormone production in a type of disease (DM 1); in the other, insulin resistance is the defining characteristic (DM 2). In both cases, the problem lies in the passage of blood glucose into the cells.⁷ Therefore, it is expected that carbohydrate restriction is the main DM management strategy, and this was the first approach to be used even before the discovery of insulin.⁸ From a physiological viewpoint, it can be argued that carbohydrates consumed in the diet must be controlled to achieve good glycemic control in patients with DM.^{9,10}

According to ADA, in a consensus published in 2019, reducing the total amount of carbohydrates for individuals with DM is the strategy that showed the greatest amount of evidence for the improvement of blood glucose, and several dietary patterns can be applied, according to the need and preference of each individual.¹¹ This position is in contrast to the aforementioned BDS recommendations.⁶

Knowing that DM can bring serious health complications and compromise the quality of life, and that there is still no satisfactory control for most people with the disease,^{12,13} it is necessary to update health professionals, so that they can provide an effective strategy to control this disease. Therefore, this study aimed to evaluate, through a literature review, evidence of the use of diets with carbohydrate restriction in the management of DM.

METHOD

This literature review was prepared according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) recommendations.¹⁴ The research included randomized clinical trials published from 2008 in English, Portuguese and Spanish. The databases LILACS-BIREME (Database of Latin American Literature in Health Science), SciELO (Scientific Electronic Library Online) and PubMed (maintained by the National Library of Medicine) were used. The search period was between August 2018 and June 2019.

The search was carried out using the keywords based on the Health Sciences Descriptors (DeCS) in Portuguese: *diabetes mellitus*, *dieta com restrição de carboidratos*, *dieta rica em proteínas e baixa em carboidratos*, *dieta com restrição de gorduras*, *dietoterapia*; and its respective terms in English: *diabetes mellitus*; *diet*,

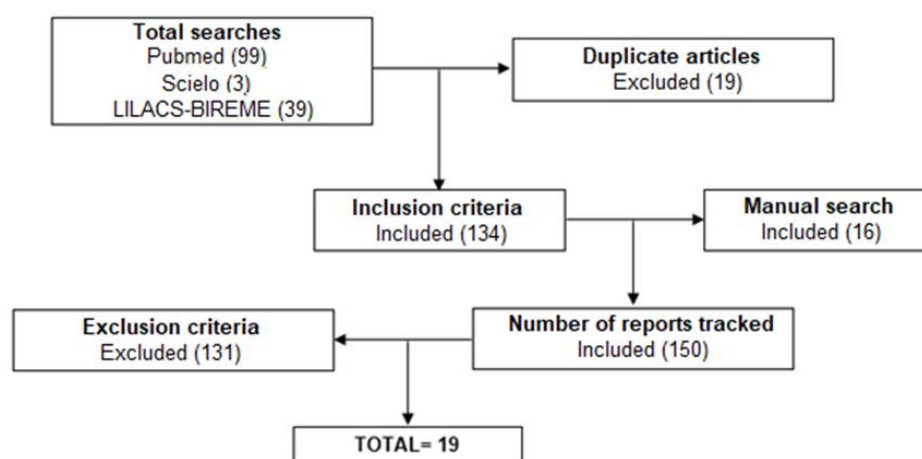
carbohydrate-restricted; diet, high protein low carbohydrate; diet, fat-restricted; diet therapy. For the selection of articles, the title and abstract of the articles were carefully read, and if considered relevant to the study, they were read in full. Other articles searched manually were added to the articles chosen after this stage, both in references of studies already selected, and in unsystematic searches of the theme. This strategy was used in order to recover original / main studies for each intervention.

Subsequently, in vitro and animal research studies were excluded, as well as literature reviews, observational studies, case studies and case reports. Articles that did not achieve an excellent quality score on the JADAD five-point scale (JADAD score on a 5-point scale) were also excluded.¹⁵ It is a mechanism for evaluating the methodological quality of scientific works, one of the main resources used to assess the quality of randomized controlled trials,¹⁶ divided into two parts. In the first, the maximum score of three points is accumulated through opposite answers (yes - 1 point; no - 0 point) for the criteria: (1) randomization, (2) double-blind and (3) losses (dropouts). In the second stage, the score is added, considering two criteria: (4) adequate randomization method and (5) adequate blinding. When a study scores two or less, it is considered of poor quality; and when it adds up to two points, it is evaluated with excellent quality.¹⁵

RESULTS

In the systematic search, 147 articles were found, 19 of which were excluded because they were duplicate results. Through manual search, 16 articles were found and included, resulting in 150 studies, of which 131 were disregarded due to the exclusion criteria. At the end of the process, 19 articles remained. For the representation of the results, the flowchart of the PRISMA method was used, as shown in figure 1.

Figure 1. Flowchart of the article selection process on the use of carbohydrate-restricted diets in the management of diabetes mellitus.



According to the JADAD Scale, the average quality of the studies selected in this systematic review was 3 (SD = 0.58), meaning that they can be considered quality and that they considered important factors to conduct a randomized clinical trial. Among the items identified as fundamental to the quality of the studies,¹⁵ all articles used the randomization method, and most of them (n = 15) described the procedure. Losses were reported in all studies, although none were double-blind.

The characteristics of the studies included here are described in chart 1. The selected studies were published between the years 2008 and 2018. The sample size ranged from 10 to 227 adult individuals, with type 1 or type 2 DM. The intervention time of the studies ranged between 18 days and 2 years in duration.

All individuals in the intervention groups received low-carbohydrate diets, and the total amount of this macronutrient varied between 14-49% of the total energy value (TEV) of the diet, or between 20-130 g of carbohydrates per day. In the diets applied to the control groups in each study, the amount of carbohydrate varied between 40 to 65% of the TEV in the diet in some studies; in others, they were classified as composed of an amount equal to or greater than 130g, 165g or 250g of carbohydrates per day. The diets used for the intervention and control groups were classified in terms of energy value as being isocaloric, non-isocaloric or of a similar caloric deficit for each participant, according to the individual total energy expenditure.

Chart 1. Main characteristics of selected studies on carbohydrate-restricted diets in the management of diabetes mellitus

| Source | Study type | Diet types | N and % of adherence | Diabetes type | Intervention time | TEV of diets | Diets composition | Observed results |
|---------------------------------------|--|-----------------------|--|---------------|-------------------|----------------------|---|--|
| Wang et al. (2018) ¹⁷ | Clinical trial, prospective, randomized, blind, controlled | IG: LCHF CG: LFD | I: IG=28 and CG=28 F: IG=24 (85.7%) and CG=25 (89.3%) | DM 2 | 3 months | Isocaloric diets | IG: 39% CHO and 42% LIP CG: 56% CHO and 26% LIP | LCHF was superior to LFD in glycemic control. It regulates cholesterol levels, reduced BMI, decreased insulin dose ($p<0.05$). |
| Watson et al. (2018) ¹⁸ | Clinical trial randomized | IG: LCHP CG: HC | I: IG=32 and CG=31 F: IG=23 (71.9%) and CG=21 (67.4%) | DM 2 | 24 weeks | Isocaloric diets | IG: 34% CHO, 29% PTN, 31% LIP CG: 48% CHO, 21% PTN, 24% LIP | Weight reduction, improvement in Hb1Ac, psychological well-being in both the LCHP and HC diet. LCHP diet shown to improve vitality ($p<0.05$). |
| Tay et al. (2017) ¹⁹ | Clinical trial randomized, blind, controlled | IG: LCD CG: LFD | I: IG=58 CG=57 F: IG=33 (56.9%) CG=28 (49.1%) | DM 2 | 2 years | Isocaloric diets | IG: 14% CHO, 28% PTN and 58% LIP (<10% sat.) CG: 53% CHO, 17% PTN, 30% LIP (<10% sat.) | Both diets achieved weight loss and reductions in HbA1c. LCD maintained greater reductions in the use of diabetes medication, and improvements in glycemia stability and blood lipid profile, without kidney damage, suggesting optimization of DM2 management ($p<0.05$). |
| Ranjan et al. (2017) ²⁰ | Clinical trial, cross-sectional, randomized and open | IG: LCD CG: HCD | I: IG=5 CG=5 F: IG=5 (100%) CG=5 (100%) | DM 1 | 18 days | Isocaloric diets | IG: \leq 50g CHO/day CG: \geq 250g CHO/day | LCD resulted in more euglycemia time, less hypoglycemia time and less glucose variability than HCD without changing glucose concentrations ($p<0.05$). |
| Saslow et al. (2017) ²¹ | Clinical trial, prospective, randomized | IG: VLCKD CG: MCCR | I: IG=16 CG=18 F: IG=14 (87.5%) CG=15 (83.3%) | DM 2 | 12 months | Non-isocaloric diets | IG: 20-50 g net CHO CG: 165 g CHO (40 – 50% VET), hypocaloric (-500 Kcal), LFD | In the VLCKD group there were greater reductions in HbA1c, greater weight loss and reduction in medications than those instructed to follow an MCCR diet. |
| Wycherley et al. (2016) ²² | Clinical trial, prospective, randomized | IG: VLCKD CG: HCD | I: IG=58 CG=57 F: IG=41 (70.7%) CG=37 (64.9%) | DM 2 | 12 months | Isocaloric diets | IG: 14% CHO, 28% PTN, 58% LIP (<10% sat) CG: 53% CHO, 17% PTN, 30% LIP (<10% sat) | Both diets, combined with general improvement in lifestyle, showed similar benefits in weight reduction, improvement in Hb1Ac and endothelial function ($p<0.05$). |

Chart 1. Main characteristics of selected studies on carbohydrate-restricted diets in the management of diabetes mellitus. (Continues)

| Source | Study type | Diet types | N and % of adherence | Diabetes type | Intervention time | TEV of diets | Diets composition | Observed results |
|--|---|---|---|---------------|-------------------|-------------------------|--|--|
| Raygan et al. (2016) ²³ | Clinical trial, prospective, randomized | IG: LCD CG: HCD | I: IG=28 CG=28 F: IG=28 (100%) CG=28 (100%) | DM 2 | 8 weeks | Similar calorie deficit | IG: 43-49% CHO, 36-40% LIP and 14-17% PTN CG: 60-65% CHO, 20-25% LIP and 14-17% PTN | LCD showed better results in reducing fasting blood glucose, and greater sensitivity to C-reactive protein ($p < 0.05$). HCD showed higher concentrations of glutathione and antioxidant capacity ($p < 0.05$). There was no significant difference between other metabolic markers. |
| Sato et al. (2016) ²⁴ | Clinical trial, prospective, randomized | IG: LCD CG: Dieta hipocalórica | I: IG=33 CG=33 F: IG=30 (90,9%) CG=32 (97%) | DM 2 | 6 months | Non-isocaloric diets | IG: <130 g CHO /day CG: Hypocaloric diet (28 kcal x ideal weight) | There was a greater reduction in the concentration of HbA1c in the LCD group ($p < 0.05$), as well as greater reduction in BMI ($p < 0.05$). |
| Krebs et al. (2016) ²⁵ | Clinical trial, prospective, randomized | IG: LCD CG: dieta livre com contagem de carboidratos | I: IG= 5 CG= 5 F: IG= 5 (100%) CG= 5 (100%) | DM 1 (adults) | 12 weeks | Non-isocaloric diets | IG: CHO <75 g/day | Decrease in Hb1Ac concentrations without adverse effects in the intervention group ($p < 0.05$). |
| Brinkworth et al. (2016) ²⁶ | Clinical trial, prospective, randomized | IG: LCD CG: HCD | I: IG= 58 and CG= 57 F: IG= 41 (70.7%) CG= 37 (64.9%) | DM 2 | 1 year | Isocaloric diets | IG: 14% CHO (<50 g/day), 28% PTN and 58% LIP (<10% sat) CG: 53% CHO, 17% PTN and <30% LIP (<10% sat) | There was no significant difference in weight loss, quality of life and psychological status results. Both diets, within a lifestyle modification program that includes physical training, improve these parameters. |
| Tay et al. (2014) ²⁷ | Clinical trial, prospective, randomized | IG: LCD CG: HCD | I: IG=58 CG=57 F: IG=46 (79.3%) CG=47 (82.4%) | DM 2 | 24 weeks | Isocaloric diets | IG: 14% CHO [<50 g/day], 28% PTN, and 58% LIP (<10% sat) CG: 53% CHO, 17% PTN, and 30% LIP | Both groups improved the concentrations of LDL, BP and fasting blood glucose ($p \geq 0.1$). In the LCD group there was an improvement in Hb1Ac concentrations and glycemic variability, as well as an increase in HDL concentrations ($p < 0.05$). |
| Rock et al. (2014) ²⁸ | Clinical trial prospective, controlled randomized | GI1: LCHF GI2: LFD CG: Dieta do programa UC | I: GI1=74, GI2=77, CG=76 F: GI1=73 (98.6%), GI2=76 (98.7%), CG=76 (100%) | DM 2 | 1 year | Similar calorie deficit | GI1: 45% CHO, 25% PTN and 30% LIP GI2: 60% CHO, 20% PTN and 20% LIP CG: 55% CHO, 15% PTN and 30% LIP | LCHF and LFD programs showed better results in glycemic control and weight loss than the UC Program proposed by the University. |
| Jonasson et al. (2014) ²⁹ | Clinical trial prospective, controlled randomized | IG: LCD CG: LFD | I: IG=30 CG=31 F: IG=30 (100%) CG=31 (100%) | DM 2 | 2 years | Isocaloric diets | IG: 25% CHO and 49% LIP CG: 49% CHO 29% LIP | Only LCD was found to significantly improve subclinical inflammatory status in type 2 diabetes ($p < 0,05$). |
| Guldbrand et al. (2014) ³⁰ | Clinical trial, prospective, randomized | IG=LCD CG=LFD | I: IG=30 CG=30 F: IG=25 (83.3%) CG=29 (96.7%) | DM 2 | 2 years | Isocaloric diets | IG: 20% CHO, 30% PTN and 50% LIP CG: 55-60% CHO, 10-15% PTN and 30% LIP | There were no significant differences between weight loss in the two groups, but after one year of intervention, the quality of life of the LCD group improved. |

Chart 1. Main characteristics of selected studies on carbohydrate-restricted diets in the management of diabetes mellitus. (Continues)

| Source | Study type | Diet types | N and % of adherence | Diabetes type | Intervention time | TEV of diets | Diets composition | Observed results |
|---------------------------------------|---|---|--|---------------|-------------------|-------------------------|--|---|
| Saslow et al. (2014) ³¹ | Clinical trial, prospective, randomized | IG: VLCKD CG: MCCR | I: IG=16 CG=18 F: IG=15 (93.8%) CG=18 (100%) | DM 2 | 3 months | Non-isocaloric diets | IG: 20-50 g netCHO CG: 165 g CHO (40 – 50% VET), hypocaloric (-500 Kcal), LFD | Decrease in HbA1c concentrations and medication doses ($p < 0.05$) and greater weight loss ($p = 0.09$) in the VLCKD group. |
| Goldstein et al. (2011) ³² | Clinical trial, randomized, controlled | IG: ATK (LCD) CG: ADA recommended diet | I: IG=26 CG=26 F: IG=14 (53.8%) CG=16 (61.5%) | DM 2 | 1 year | Non-isocaloric diets | IG: 25 g CHO/40 g CHO CG: 50-60% CHO, 10%-20% PTN and 30% LIP | There was no statistically significant advantage in terms of weight loss or glycemic control for the Atkins diet ($p < 0.05$). |
| Larsen et al. (2011) ³³ | Prospective, controlled, randomized | IG: LCHP CG: HCD | I: IG=53 CG=46 F: IG=48 (90.6%) CG=45 (97.8%) | DM 2 | 1 year | Isocaloric diets | IG: 40% CHO, 30% PTN and 30% LIP CG: 55% CHO, 15% PTN and 30% LIP | These results suggest that there is no superior metabolic benefit, in the long run, of a protein-rich diet over a high-carbohydrate diet in the treatment of type 2 diabetes ($p = 0.44$). |
| Davis et al. (2009) ³⁴ | Clinical trial randomized | IG: LCD CG: LFD | I: IG=55 CG=50 F: IG=47 (85.4%) CG=44 (88%) | DM 2 | 1 year | Non-isocaloric diets | IG: 20-25 g CHO/day incremented with 5g per week CG: 25% VET in LIP | Weight loss occurred more quickly in the LC group than in the LF group ($p < 0.05$), but within one year a similar weight reduction was observed in both diet groups. There was no significant change in A1C in any group in one year. There was no change in blood pressure, but a greater increase in HDL was observed in the LCD group ($p < 0.05$). |
| Wolever et al. (2008) ³⁵ | Clinical trial randomized | LCHF HCHGI HCLGI | I: 54 group LCHF, 56 group HCLGI, 52 group HCHGI F: 53 group LCHF (98.1%), 55 group HCLGI (98.2%), 48 group HCHGI (92.3%) | DM 2 | 1 year | Similar caloric deficit | 39% CHO and 40% LIP 47% CHO and 31% LIP 52% CHO and 27% LIP | Reduction of postmeal plasma glucose in the LCHF group. There was no difference in Hb1Ac compared to the other groups ($p < 0.05$). |

Subtitle: IG: intervention group; CG: control group; I: study start; F: end of study; Diets: LCHF: low carb high fat; LFD: low fat diet; LCHP: Low carb high protein; HC: High carb; LCD: low carb diet; HCD: high carb diet; VLCKD: Very low carb keto diet; MCCR: medium carbohydrate, low fat, calorie-restricted, carbohydrate counting diet; ATK: Atkins diet; HCHGI: high carb high glycemic index; HCLGI: High carb low glycemic index; TEV: Total energy value; CHO: carbohydrates; PTN: Proteins; LIP: fats; sat: saturated fats; net CHO: net carbohydrates.

Most studies selected for analysis in this review addressed intervention strategies with carbohydrate-restricted diets in patients with DM 2, and only two articles out of the 19 selected addressed patients with DM 1. There was still great variation in intervention time, the shortest time being 18 days and the longest, two years. Studies were highlighted in which the diets used for the intervention and control groups were isocaloric, but in some studies the diets had a different TEV or a similar caloric deficit was reported under the total energy expenditure of each individual. In addition, there was great variability between the proportions of macronutrients that made up each applied diet, as well as in the nomenclature adopted to classify each diet.

DISCUSSION

From the results of this study, there are few articles in which the impact of low-carbohydrate diets is investigated in DM 1 individuals compared to those conducted with DM 2 patients. Corroborating this finding, a literature review published in 2018 also reported only one randomized study carried out with DM 1 individuals, published after 2009.³⁶

A possible justification for this result is the fact that patients with DM 1 can monitor carbohydrate intake by counting carbohydrates in order to calculate pre-meal insulin doses, and thus control postprandial glucose concentrations. So patients can be taught to evaluate the carbohydrate content of the meal in grams, and how much the content to be ingested will represent in the insulin dose administered to maintain normoglycemia.³⁷ Thus it is inferred that knowing counting carbohydrates correctly and keeping continuous blood glucose monitoring enables DM 1 individuals to obtain optimal glycemic control, without the need to restrict the amount of carbohydrates in the diet.³⁸

However, some problems have been observed in practice, especially with regard to children with DM 1, who depend on parents or caregivers. There is a great tendency to underestimate the dose of insulin to be administered by counting carbohydrates, for fear of a situation of hypoglycemia, especially at larger meals, which has resulted in high concentrations of Hb1Ac and high postmeal plasma glucose.^{37,39,40} Furthermore, results of studies point to a general inability in the accuracy of carbohydrate counting among DM 1 individuals.^{37,41}

Regarding the intervention time of each diet, there was a great variation between the selected articles (between 18 days and 2 years). In order to gather a greater number of studies on the topic addressed, a minimum intervention time was not established as an inclusion criterion. However, in another systematic review study,⁴² the authors justify the exclusion of studies with an intervention time of less than 12 weeks because the main objective of the metabolic control of individuals with DM is to reduce the long-term implications of this pathology. This time does not apply for two of the 19 articles selected for this work.

It is important to note that 12 weeks is the average time for changes in the treatment of DM to have an effect on the result of Hb1Ac, the best parameter for predicting DM complications and fundamental in the assessment of the patient's glycemic control.⁴³ Thus, studies with an intervention time shorter than this may not have such significant effects to assert the quality of the intervention.

Among the articles selected by this study whose study time was less than 12 weeks, only parameters that undergo variation in the short term were evaluated, such as fasting glucose, euglycemia time, glycemic variability, and sensitivity to C-reactive protein.

In studies with a short intervention time, there is a limitation in assessing the individual's adherence to a type of diet, and whether it would be applicable in the long term, as well as the possible effects it would cause. Adherence among individuals allocated to the intervention groups in the selected studies ranged between 53.8% and 100%; and adherence among individuals randomized to the control group ranged from 49.1% to 100%.

An important issue to be raised regarding adherence to the diet is how challenging it can be to adopt a restrictive diet in the amount of carbohydrates for some individuals, especially when less drastic changes in diet and lifestyle are recommended by current Brazilian guidelines, easier to be followed in the long run.⁴⁴ Among the selected studies, three report 100% adherence of individuals in both the control and intervention groups, and they used the shortest intervention times (18 days, 8 weeks and 12 weeks).

Noaks and Windt report, in their literature review,⁴⁵ studies that demonstrate similar adherence between low carb high fat (LCHF) and low fat high carb (LFHC) diets,⁴⁶⁻⁴⁸ and one study that shows greater continuity of follow-up in individuals adopting the LCHF diet compared to those who adopted a low calorie and low fat diet.⁴⁹ The authors therefore conclude that the evidence points out that patients do not seem to find it more difficult to adhere to an LCHF diet than to any other dietary strategy. They add that due to their unique ability to reduce hunger, some patients may find that LCHF diets are more easily sustainable than LFHC diets that require conscious calorie restriction.

The diets applied to the intervention and control groups were isocaloric in ten among the 19 selected articles; six used non-isocaloric diets and in three studies the energy needs of each person were calculated individually, and a similar caloric deficit was applied to them. Authors who adopted isocaloric diets in order to compare them, or those who used the same calorie deficit based on individual energy needs, were able to more reliably observe the possible effects of changing the proportions of macronutrients in the diet, since the energy balance was similar between groups. In studies in which the diets were not isocaloric, one cannot isolate the possibility that a greater caloric deficit has occurred for the intervention or control group, and as a result, the results have favored one or other diet in terms of effectiveness.

Among the articles selected for this review, there was great variability regarding the definition and composition of each diet in terms of proportion. Diets with lower carbohydrate content, between 20-50g daily or representing up to 14% of the daily TEV, were classified by the authors as being very low carb keto diet (VLCKD), or ketogenic diet. There were also studies that, in their intervention diets, compensated for the reduction in the carbohydrate content by raising the content of only one macronutrient, being protein (low carb high fat, LCHP) or lipids (low carb high fat, LCHF), or just increased both in equal proportion (low carb diet, LCD). Most diets in the control group were named by the authors as being high in carbohydrates (high carb diet, HCD) or low in fat (low fat diet, LFD).

One can find in the literature several definitions for a carbohydrate-restricted diet, and the lack of consensus and standardization between these definitions makes it difficult to compare diets and their benefits. And although there is variation between studies and authorities, in the consensus published by ADA in 2019, in which several meta-analyses, cohort studies, observational studies and randomized controlled trials were analyzed, a definition for low carb was established as a diet containing between 26-50% of the energy value from carbohydrates, and very low carb those containing 20-50 g / day of carbohydrates or less than 26% of the energy value derived from carbohydrates.^{11,50-52} In this work, however, several authors have classified diets with higher levels of this macronutrient as LCD.^{17,18,23,28,33,35} Therefore, although there are benefits in adopting diets with reduced levels of carbohydrates by patients with DM, it is difficult to establish the most appropriate percentage of macronutrient restriction that is sufficient to observe the improvements caused by the food strategy and that also result in greater adherence of patients.

To measure the possible effects of diets applied to the intervention groups, the authors of the elected articles were based on parameters which stood out: weight change and BMI, Hb1Ac, variability or glycemic control, lipid profile and change in insulin doses or medication used. Among the 19 studies, in four there were no significant advantages of a carbohydrate-restricted diet when compared to other diets indicated for the management of DM. However, in 15 studies, improvements were observed in one or more parameters among those mentioned above.

The improvement in glycemic control and Hb1Ac concentrations is attributed, by the authors, to the fact that individuals on a carbohydrate-restricted diet are able to maintain less variability in blood glucose

concentrations.^{17,19,20,21,24,25,27,31} Consequently, this reduces the need to use adjuvant pharmacology in the treatment of DM.^{17,19}

Still in their discussions, the authors relate the observation of weight reduction and BMI to lower caloric intake, due to the sacietogenic effect that low carb diets cause; and the improvement of the lipid profile as a result of increased total consumption of unsaturated fats and reduced levels of triglycerides.^{17,19,27,34}

Such results may represent a great advantage in adopting this dietary strategy in the management of DM, mainly in the prevention of complications arising from poor disease control.⁵³ Among the complications, there are mainly microvascular and macrovascular disorders, which result in retinopathy, nephropathy, neuropathy, coronary disease, cerebrovascular disease, peripheral arterial disease; disorders in the musculoskeletal system, gastrointestinal system, cognitive function and mental health, in addition to being related to some types of cancer.⁵³

Little attention has been paid to the global trends in DM complications and to how morbidity characteristics associated with this pathology have changed. Morbidity data related to diseases secondary to DM sometimes mask the real problem and the great need for improvements in therapeutic efforts aimed at this pathology.⁵³

Corroborating these findings, Feinman and colleagues⁵⁴ present 12 points of evidence that support the use of diets low in carbohydrates as the first approach in the treatment of DM 2, and as the most effective adjunct to pharmacology in DM 1. Among them, the authors show that as hyperglycemia is the most striking feature of DM, the restriction of carbohydrates in the diet has a greater effect in decreasing blood glucose concentrations. They also state that during the obesity and DM 2 epidemics, the caloric increases that cause these two conditions are almost entirely related to the increase in carbohydrates in the diet. The authors also point to literary evidence of the benefits and safety of LCHP diets, as well as the lack of evidence that correlates the consumption of total and saturated fats with risk of cardiovascular disease.⁵⁵⁻⁵⁸

Despite this, there are still questions about the possibility of side effects of these diets, as in the case of strategies in which the proportion of proteins in the diet is increased in relation to the recommendations and other macronutrients.

The main criticisms of some authors arise in view of their possible kidney damage, caused by excess nitrogen excretion during protein metabolism, and which can cause an increase in glomerular pressure and hyperfiltration.⁵⁹ According to the same authors, despite this, there are still many studies that point to a morphological adaptation of the organism of individuals with normal renal function, considering the increase in protein consumption without any negative effect.⁵⁹ Among the studies gathered by the present study, no types of renal alterations were mentioned as side effect of LCHP diets.

There are authors in the literature who drew attention to another possible adverse effect of LC diets, regarding the risks of increasing the proportion of lipids in the diet in diets such as LCHF.⁶⁰⁻⁶² Such risk would come from the fact that, when fat becomes the main source of energy in the diet, this can result in a much higher proportion of saturated fat, and lead to an unfavorable change in the lipid profile, with consequent increase in cardiovascular risk. However, in this study, there are articles that demonstrate the opposite in their results, in which a carbohydrate-restricted diet resulted in improvement in the lipid profile.^{17,19,27} These authors claim that in a balanced and well-oriented diet, the consumption of lipids will follow a healthy profile and there will be a balance between the consumption of saturated, monounsaturated and polyunsaturated fats, as well as increased consumption of omega 3.

The evidence presented by the studies selected for this review mostly point to benefits in the use of carbohydrate-restricted diets for the management of DM, or at least an equivalence when compared to other strategies (without adverse effects). Although all selected studies were randomized, an item that although important was not verified in any of the studies is blinding, or masking.

This fact can be justified by the type of study chosen to integrate this review, which has as an essential part of its methodology that researchers receive training in the application of the intervention and, therefore, have knowledge about the experimental condition. Therefore, double-blind intervention is not feasible. Even so, it can be observed in some of the selected studies that the participants could be blinded as to the group in which they would be allocated – intervention or control –, which reduces the risk of bias in the results.

CONCLUSION

In general, what can be inferred from most studies in which dietary interventions were proposed using diets with low carbohydrates and high levels of other macronutrients, either fats or proteins, is that this nutritional approach tends to guarantee better control of DM, both in type 1 and type 2. And yet, in most cases, interventions did not present unmanageable adverse events.

Such deductions are plausible, considering the dominant effects of dietary carbohydrates on postprandial blood glucose, overall glycemic control and Hb1Ac concentrations, as well as the consequent reductions in insulin doses and medications required in an LC diet. The results, confirmed in many clinical trials, indicate improvements in parameters capable of preventing chronic complications of DM.

However, in light of the limitations of the studies, which are not yet numerous – in the case of DM 1 – and need to have their hypotheses verified in the long term, these discoveries alone have not yet been sufficient to configure an official strategy for DM control, recommended by the main guidelines in this area. Additional research should continue to be carried out to determine the degree of carbohydrate restriction (and other aspects of the diet) needed to achieve these benefits, an optimal insulin regimen and / or medication to accompany this strategy (specifically, to avoid severe hypoglycemia), and to ensure safety and efficacy in treatment, preventing complications and decreasing DM morbidity.

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Contributors

Campos LP and Lobo LMC participated in all stages, from the conception of the study to the revision of the final version of the article.

Conflict of interest: the authors declare that there is no conflict of interest.

Received: June 25, 2019

Approved: January 5, 2020