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CARBOHYDRATE RESTRICTION IN THE AID FOR TREATMENT OF DIABETES MELLITUS 2

A RESTRIÇÃO DE CARBOIDRATO NO AUXÍLIO AO TRATAMENTO DE DIABETES MELLITUS 2

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ABSTRACT

Several studies have shown a relationship between carbohydrate restriction and the improvement of biomarkers related to Diabetes Mellitus 2. This article deals with a reflective review on carbohydrate restriction in the treatment of Diabetes Mellitus 2 to analyze the impacts of a carbohydrate-restricted diet on disease control and its complications. For data collection, it was performed a bibliographic search of articles in national and international journals, published between 2009 and 2019 in three languages and four electronic scientific databases. As result, it was noted that a small reduction in carbohydrate intake in the diet is an effective strategy to improve the biomarkers related to Diabetes Mellitus 2 and their complications and to significantly reduce the use of antidiabetic drugs. It was concluded, therefore, that carbohydrate restriction may be a possible strategy to be used as adjunctive therapy for the treatment of Diabetes Mellitus 2, although this theme should be better evaluated by prospective, randomized, and long-term studies.

Keywords: diabetes mellitus; insulin; glucose; carbohydrate; diet.

RESUMO

Diversos estudos têm mostrado uma relação entre a restrição de carboidrato e a melhora dos biomarcadores relacionados ao Diabetes Mellitus 2. O presente artigo trata de uma revisão bibliográfica sobre a restrição de carboidrato no auxílio ao tratamento de Diabetes Mellitus 2 com o objetivo de analisar os impactos de uma dieta restrita em carboidrato no controle da patologia e suas complicações. Para a coleta de dados, foi realizada uma pesquisa bibliográfica de artigos em periódicos nacionais e internacionais, publicados entre 2009 e 2019 em três idiomas e em quatro bases de dados eletrônico-científicos. Como resultado, notou-se que uma pequena redução do consumo de carboidratos na dieta é uma estratégia eficaz para a melhoria dos biomarcadores relacionados ao Diabetes Mellitus 2 e suas complicações, bem como para redução significativa do uso de medicamentos antidiabéticos. Concluiu-se, portanto, que a restrição de carboidrato pode ser uma possível estratégia a ser utilizada como terapia coadjuvante para o tratamento do Diabetes Mellitus 2, embora essa temática deva ser mais bem avaliada por estudos prospectivos, randomizados e de longo prazo.

Palavras-chave: diabetes mellitus; insulina; glicemia; carboidrato; dieta.

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INTRODUCTION

Type 2 Diabetes Mellitus (DM2) is a chronic disease arising from the ineffective use of insulin by the body that causes a condition of high concentrations of glucose in the blood, i.e. hyperglycemia[1].

According to the latest Vigitel data, 7.7% of the Brazilian adult population was diagnosed with diabetes in 2018. When compared to 2006, there was a significant increase compared to 2006, with 5.5% of[2].

This significant increase can be attributed to population growth and aging, increased urbanization, the increasing prevalence of obesity and sedentary lifestyle, as well as changes in dietary patterns that include increased consumption of sugary foods and beverages[3,4].

The treatment of DM2 aims to keep blood glucose on a healthy scale and has as tools food adaptation, increased physical activity, and, in some cases, the use of medications[5]. When medication is required, pharmacological agents such as metformin, sulphonylureas, and GLP-1 agonists are also chosen, and insulin replacement is often also chosen[6].

According to the Brazilian Diabetes Society[7], sulphonylureas are medicines that act in increasing pancreatic insulin secretion, developing prolonged hypoglycemic action throughout the day, and consequently decreased glycated hemoglobin (HbA_{1c}).

In the case of food adaptation, the restriction of carbohydrate intake (CHI) is an effective strategy for the treatment of DM2, because, in addition to ensuring better blood glucose control, it has greater support for individuals affected by the disease when compared to diets with fat restriction, since this strategy reduces appetite and ensures greater satiety[8,9].

This restriction is characterized by the intake of a maximum of 45% CHI of the individual's daily energy in addition to a reduced intake of processed foods and sugary beverages, as suggested by reviews and evidence-based recommendations about the subject[10-12].

Recent randomized, controlled trials in the short and long term – considered the gold standard of the research – have shown that carbohydrate-restricted diets (CHRD) work better than fat-restricted diets (FRD) for weight loss and glucose and insulin response. These studies used both normal individuals and individuals with metabolic syndromes and another health-related disorder[13-16].

Regarding the relevance of DM2, it is estimated that spending on its prevention and treatment can reach up to 15% of a country's annual health budget[17]. This expense is relevant if considered that the disease can generate complications of the most diverse orders, such as neuropathies, heart attack, stroke, vision loss, kidney disease, nerve injury, and gangrene of lower limbs that could lead to amputation[18]. Also, the disease is associated with premature death from various types of cancer, infectious diseases, external causes, and degenerative disorders[19].

Considering the severity of the disease and the financial tax that DM2 entails, effective strategies for the prevention and control of this pathology become indispensable. Furthermore, studies suggest that dietary supplementation with restriction in CHO by affected people may be a relevant strategy to combat the disease.

Because there are still few studies on the subject, an in-depth review is needed to understand the relevance of the association of CKD as an aid to the treatment of DM2 because it has great potential in reducing DM2 biomarkers such as HbA_{1c}, glycemia, besides great potential in reducing indirect biomarkers to DM2 such as HDL-c, LDL-c, body weight, and waist circumference. It is noted, therefore, that CKD is an alternative of extremely low cost; however, of remarkably high competence for the improvement of the condition of this disease.

Because of the above, the present study aimed to analyze the impacts of a restricted carbohydrate diet on the control of DM2 and its complications.

METHODOLOGY

The present study is a bibliographic review. For data collection, bibliographical research of articles was conducted in national and international journals, published between 2009 and 2019 in English, Spanish and Portuguese. The search was conducted in four scientific electronic databases - Scielo, LILACS, PubMed, and Medline.

The following descriptors were used: Diabetes Mellitus, Insulin, Blood Glucose/Glycemia, Carbohydrate and Low-carbohydrate Diet/Low Diet in Carbohydrates/Carbohydrate Restricted Diet to perform the search in the databases. These terminologies are registered in the Descriptors in Health Science (DeCS) created by the Virtual Health Library.

Data analysis

After the searches in each database, 553 articles were found in total. After excluding duplicate references and review articles, the analysis of the collected articles was performed by reading the titles and abstracts to exclude studies that did not meet the scope of the research, such as animal research, in vitro cells and studies that targeted pregnant women, participants with other pathologies without DM2 or children in their sample. In addition, articles with a classification lower than B3 were excluded, according to the Qualis Journal Classification 2015. Therefore, 10 articles remained that were used in this review.

It is noteworthy that only articles with experimental design (randomized or not clinical essays) were included and the general outcomes found in the studies with the use of diets were evaluated, that is, both variables related to biomarkers for DM2 and its complications, as well as variables associated with body structure such as weight, body mass index (BMI) and waist circumference.

Then, a thorough and critical reading of the articles was carried out in full to identify the meaning nuclei of each text and subsequent grouping of subthemes that synthesized the productions.

LITERATURE REVIEW

Pathophysiology of DM2

According to Alberti and Zimmet[20], DM2 can be characterized by four metabolic imbalances – obesity, insulin action, insulin-secreting dysfunction, and increased endogenous glucose production, and the first three imbalances may be present even before the onset of the pathology.

The Brazilian Diabetes Society[21] characterizes DM2 by combining two abnormalities: resistance to insulin action and the inability of beta-cell to keep adequate insulin secretion; abnormalities similar to those cited by Alberti and Zimmet[20] when it refers to the secretory action and dysfunction of this hormone.

The pancreas produces two hormones essential for the regulation of blood glucose, specifically in the islets of *Langerhans*: insulin, produced by β cells, and glucagon, produced by the A. Physiologically, glucagon is responsible for stimulating glucose production by the liver and insulin is responsible for blocking this production and increasing glucose uptake by peripheral tissues[22-24].

After the meal of a healthy person, blood glucose tends to increase within normal limits, characterizing postprandial hyperglycemia[22]. This increase in blood glucose suppresses glucagon production and increases insulin production. However, in people with DM2, pancreatic islet cell dysfunction occurs, causing inadequate insulin release by β cells and, consequently, a lack of response by cells α to the physiological suppression of glucagon, intensifying hyperglycemia[24].

Prolonged hyperglycemia increases the prevalence of chronic complications of DM2, such as cardiovascular disease, nephropathy, diabetic foot, and retinopathy [22].

Glycated hemoglobin is a biomarker that reflects the concentration of blood glucose levels in the last 3 months since blood glucose binds to hemoglobin and it has an average life period of 90 days.

The result is in the percentage of hemoglobin linked to blood glucose. The higher the blood glucose concentration, the greater the glucose bond with hemoglobin and, consequently, the higher the value of glycated hemoglobin. Therefore, the values of glycated hemoglobin will indicate whether the person is in a hyperglycemia condition, contributing to the positive or negative diagnosis of diabetes.

According to the Brazilian Diabetes Society[25], values below 5.7% of ha1bc indicate the absence of diabetes; from 5.7 to 6.4% indicates prediabetes and above or equal to 6.5%, poorly controlled diabetes.

Glycated hemoglobin is an important parameter to be used also for glycemic control in diabetic people. Also, according to BDS, people with diabetes should present ha1bc in a range of 4 to 6%. From 6 to 7% it is understood that they are in a moderately controlled diabetes condition and above 7% in a poorly controlled diabetes condition.

Obesity is characterized by excessive body weight defined through the Body Mass Index (BMI) being equal to or greater than 30kg/m², while normal weight is characterized when BMI is between 18.5 and 25kg/m$^{26.27}$ One of the complications of obesity is insulin resistance, a hormone that aids in the entry of glucose into cells. Excessive accumulation of fat induces the pancreas to increase insulin production, and consequently to develop a condition of resistance to the hormone.

Still related to weight, waist circumference is considered a predictor for the development of DM2, as it is the region that concentrates visceral fat, the fat that is directly related to the risk of diabetes, blood pressure, and high cholesterol. According to the WHO, the waist circumference of men and women should be below 94cm and 80cm, respectively.

Therefore, weight loss and waist circumference are important parameters to analyze the condition of DM2 aggravated by obesity and visceral fat.[28]

Insulin resistance, a condition known to be caused by DM2, occurs due to several factors, such as increased glucose production and hypertriglyceridemia (high triglycerides in the blood), associated with a reduction of high-density lipoprotein (HDL) and elevation in low-density lipoprotein (LDL).[29]

Both HDL and LDL are responsible for transporting cholesterol and triglycerides in the blood plasma by the water-insoluble nature of cholesterol. However, while LDL-c transports cholesterol from the liver to cells, HDL-c has an antiatherogenic effect, that is, it performs reverse transport by removing excess cholesterol, taking it back to the liver.[29,30]

According to the Dyslipidemia Guidelines of the Brazilian Society of Cardiology[31], HDL-c reference values considered within the standard are above 40mg/dL for adults over 20 years of age. On the other, LDL-c, the individual classifies the individual into risk categories of cardiovascular diseases with the value that is already the therapeutic target: below 130mg/dL (low risk), below 100mg/dL (intermediate risk), below 70mg/dL (high risk) and below 50mg/dL (very high risk).

CHO Ingestion Recommendations

According to the Brazilian Diabetes Society, traditional nutritional therapy for patients with DM2 consists of consumption of 45% to 60% CHO related to the total energy value, and should not be less than 130g per day, although the maximum depends on the person's biomarkers, in addition to a detailed analysis of his clinical history.[31]

According to Recommended Daily Intake[21], CHO's recommendation for a healthy person ranges from 45% to 65% of total daily eating. Therefore, a consumption below 45% of the total diet could be

characterized as a diet with low CHO content. As for the characterization of a CKD, this is not yet well elucidated.

However, some studies suggest the use of lower amounts of this macronutrient for this type of diet. According to a study by Davis et al.[32], participants with CKD should consume a maximum of 25g of CHO per day. Dashti et al.[33] used 20g of CHO to characterize a ketogenic diet, a subtype of the restrictive carbohydrate diet. The ketogenic diet is composed of high-fat content, moderate protein content and low carbohydrate content, giving priority in fat metabolism to energy production instead of glucose metabolism. This metabolic preference ensures energy for longer periods, in addition to reducing the body's demand for insulin.[34,35,36]

Authors of famous diets with low CHO content as "Dr. Atkins' New Diet Revolution"[37], "Protein Power"[38], and "The South Beach Diet"[39] consumption of up to 26% CHO from the daily total calorie.

Therefore, it is noted that there is still no consensus on the characterization of the amount of this macronutrient in CKD. However, it can be inferred that the reference value should not exceed the limit of 45% CHO of the total feeding.

Experimental studies on the use of CKD in the treatment of DM2.

Studies using CKD have been widely conducted, including to observe its therapeutic effects in pathologies such as DM2.

A recent study by Huhmann et al.[40] analyzed the impact of two enteral formulas with different macronutrient compositions in patients with DM2. The impact was observed through glucose concentration as primary outcome and insulin as a secondary outcome. Through a randomized clinical essay, two visits were made to 12 adults with DM2. On the first visit, one part of the participants received an experimental formula containing 37% calories of hydrolyzed whey protein and 29% of carbohydrate calories and the other part received an isocaloric control formula containing 35% protein calories and 45% of carbohydrate calories. After a period from 5 to 7 days, participants were crossed to receive the alternative formula.

As a result, it was noticed that the average glucose concentration was significantly lower with the experimental formula compared to the control formula. This result was determined after measuring at eight-time points (between 10 and 180 min) after infusion of these formulas in both groups, being $p = 0.48$ for baseline and $p < 0.05$ after 180 min. In addition, the area under the curve was also significantly smaller with the experimental formula compared to the control formula (71.99l ± 595.18 and 452.62 ± 351.38, respectively; $p = 0.025$), although there is no significant difference in insulin concentration. The area under the curve is a way of measuring the concentration of a substance in the blood plasma compared to the time that substance is absorbed.

The research conducted by Guldbrand et al.[41] compared the effects of 2 years of intervention with CKD and DRG. A randomized clinical essay involving 61 adults with DM2 (using or not hypoglycemic oral medication, incretin, or insulin) was conducted, analyzing variables such as weight, glycated hemoglobin (HbA_{1c}), Hdl-c, and LDL-c. The CKD group consisted of 30 participants, 14 men and 16 women with an average age of 61.2 ± 9.5 years old. This group consumed a diet with the following proportions: 50% fat, 30% protein, and 20% CHO. The group with DRG had 31 participants, 13 men and 18 women with an average age of 62.7 ± 11 years old, and consumed a diet containing 30% fat (less than 10% saturated fat), 10 to 15% protein and 55 to 60% CHO, a quantity recommended for the treatment of DM2 in Sweden.

The authors observed a statistically significant reduction in Hba_{1c} in the CKD group after 6 months (month 0: DRG 55.6 ± 8.0 mmol/mol) and DRC 58.5 ± 10.2 mmol/mol); month 6: DRG 58.5 ± 10.2 mmol/mol and DRC 53.7 ± 10.3 mmol/mol); $p = 0.56$ for DRG and $p = 0.004$ for CKD), although this statistical significance was not kept after 24 months ($p = 0.29$ for DRG and $p = 0.098$ for CKD). The insulin doses were not significantly reduced in the CKD group (0 months, CKD 42 ± 65 E, DRG 39 ± 51 E; 6 months CKD 30 ± 47 E, DRG 38 ± 48 E, $p = 0.046$), although HDL-c increased statistically significantly in the CKD group (from 1.13 ± 0.33 mmol/l to 1.25 ± 0.047 mmol/l, $p = 0.018$). LDL-c and weight loss were not significantly different between them (weight loss: CKD group -4.31 ± 3.6kg versus -3.99 ± 4.1kg for group with DRG; LDL-c: group with CKD 2.4mmol/l versus 2.1mmol/l for the group with DRG; $p < 0.001$). Although the CKD group presented 58.4 mmol/l at the end of 24 months and the CKD group presented 57.6 mmol/l, both were within the normal HbA1c reference value by the IFCC mmol/l method (53 to 64 mmol/l). Going further, as LDL-c was also within the normal reference value (<100mg/dL), it is suggested that CKD may be a safe alternative for the treatment of DM2 and possible cardiovascular risks.

Analyzing the effects of a CKD about a moderate diet in CHO, Saslow et al.[42] points to considerable differences. From a randomized clinical essay with 34 participants with BMI greater than 25kg/m² pre-diabetic or already diagnosed with DM2,

weight, and HbA was analyzed$_{1c}$ for 3 months. The group with moderate CHO diet (CMD) was composed of 18 participants with an average age of 55.1 ± 13.5 years old. They should ingest 45 to 55% CHO, keep protein intake, and reduce fat. The CKD group consisted of 16 participants of an average age of 64.8 ± 7.7 years and consumed a ketogenic diet with 20 to 25g of CHO per day (without the fibers), keeping the amount of protein and consuming the other calories in the form of fat.

Initially, from the selected participants, there were excluded those who used insulin or took more than three oral hypoglycemic medications. Then, 34 participants mentioned remained, whose medications were kept throughout the study.

As a result, it was observed that the Hba$_{1c}$ did not decrease in the group DMC, while in the CKD group it decreased by 0.6% (p = 0.04). Weight loss in the CKD group was 5.5kg versus 2.6kg in the group with CMD (p = 0.09). Besides, 44% of the participants in the CKD group with one or more medications for DM2, compared with 11% of the participants in the group with CMD (p = 0.03). The use of sulphonylureas decreased by 31% in the CKD group and only 5% in the group with CMD (p = 0.05). Therefore, no results were statistically significant, although the authors show a possibility of CHO restriction for the improvement of glycemic control in patients with DM2 besides allowing a decrease in the use of medications for the disease.

The research conducted by Guldbrand et al.[41] compared the effects of 2 years of intervention with CKD and DRG. A randomized clinical essay involving 61 adults with DM2 (using or not hypoglycemic oral medication, incretin, or insulin) was conducted, analyzing variables such as weight, glycated hemoglobin (HbA$_{1c}$), Hdl-c and LDL-c. The CKD group consisted of 30 participants, 14 men and 16 women with a mean age of 61.2 ± 9.5 years. This group consumed a diet with the following proportions: 50% fat, 30% protein and 20% CHO. The group with DRG had 31 participants, 13 men and 18 women with a mean age of 62.7 ± 11 years, and consumed a diet containing 30% fat (less than 10% saturated fat), 10 to 15% protein and 55 to 60% CHO, a quantity recommended for the treatment of DM2 in Sweden.

Participants in the CKD group using antidiabetic drugs had their initial dosage halved and the participants in the CKD group had the medication discontinued at the beginning of the food program.

Of the variables evaluated, weight (from DRCL 95.71 ± 9.56 and DRC 104 ± 18.89 for DRCL 89.02 ± 5.97 and CKD 91.56 ± 17.45; p <0.001), BMI (from DRCL 36.31 ± 2.63 and CKD 39.84 ± 6.40 for DRCL 33.87 ± 2.75 and DRC 35.05 ± 5.90; p <0.001) and waist circumference (from DRCL 113.92 ± 8.43 and CKD 115.27 ± 10.45 for DRCL 109.94 ± 9.07 and DRC 106.81 ± 9.36; p <0.001) decreased statistically significantly in both groups, although the CKD group obtained an even more expressive result. Glucose and HbA levels$_{1c}$ significantly reduced in diabetics of both groups, although the result was also more expressive in the CKD group (week 0: DRCL 8.2 ± 0.3 and CKD 7.8 ± 0.1; week 24: DRCL 7.9 ± 0.3 and CKD 6.7 ± 0.3; p < 0.0001). It is known that, according to the reference values mentioned in dm2 pathophysiology, the values presented as a result of this study are not yet within normal values, but the duration of the study was only 24 weeks and may have decreased more if the study lasted.

Davis et al.[32] compared the effects of CKD and CKD in 1 year of intervention, analyzing weight loss and HbA$_{1c}$. The sample contained 105 overweight adults and DM2, 82 women and 23 men. Individuals who consumed CKD ingested 20 to 25g of this nutrient per day, depending on the weight of each (as some lost weight at first, an increase of 5g of carbohydrate per week was allowed). Volunteers with DRG reduced fat consumption to 25% of energy needs based on initial weight.

As for the medications, for the CKD group, sulphonylurea was removed and insulin was reduced by 50% at the beginning of the intervention, and for the group with DRG, sulphonylurea and insulin were reduced by 50% and 25%, respectively.

The authors observed that in the first 3 months weight loss occurred more rapidly in the CKD group (1.7kg/month – 95%CI 1.4-2.0) than in the group with CKD (1.2kg/month – 95%CI 0.86-1.5), but, in 1 year, a similar reduction of 3.4% was observed in both dietary groups, due to weight gain of 0.23kg/month (95%CI 0.09-0.35) of the CKD group compared to a plateau effect with an average weight gain of 0.01kg/month (95%CI 0.13-0.14) of the group with DRG. Weight reduction was statistically significant in both groups (p=0.005). Therefore, it is important to analyze not only the initial effect of treatment for weight loss but also the maintenance of this weight after the weight loss process. As for HbA$_{1c}$, there was no statistically significant change in any of the groups in 1 year, which is explained by the conservative reduction of medications during the intervention. The authors conclude, therefore, that differences in the effects of a diet with CKD in the short term were not sustained.

When analyzing the effects of a CKD compared to a conventional diet in DM2, Haimoto et al.[10] found that a small reduction in CHO already causes significant differences. The authors performed a 2-year intervention in 133 participants with DM2 and analyzed BMI, HbA_{1c} and the dose of antidiabetic drugs. Of these 133 participants, 57 of them, 23 men and 34 women, with a mean age of 69 ± 11 years, chose the conventional diet (DCONV) with 55-60% CHO, up to 30% fat and other energy contributions from protein. The other 76 participants, 40 men and 36 women with a mean age of 64 ± 7 years, chose CKD, eliminating CHO from one or two main meals and all snacks, but consuming protein and fat in a liberated way.

As a result, the CKD group consumed 45% CHO, reducing this macronutrient by 12% when compared to the Group with DCONV. After 2 years, the levels of Hba_{1c} significantly reduced in the CKD group (baseline - CKD 10.9 ± 1.6%; 6 months - CKD 7.4 ± 1.4%; $p < 0.001$), although BMI has reduced only slightly, without statistical significance ($p = 0.057$). Sulfonylurea doses were reduced (glibenclamide: 6 to 1, reducing from 4mg to 2.5mg at the end of 6 months; glimepiride: from 1 to 0, starting with 3mg and removing the drug), although 1 participant who did not ingest any sulphonylurea had to receive tolbutamide of 500mg. There was no discussion of the article about this controversial data, however, the individual could be taking another antidiabetic medication, having changed only the class of prescribed medication.

On the other hand, Westman et al.[44] sought to test the hypothesis that CKD would lead to an improvement in glycemic control over 24 weeks in patients with obesity and DM2, through a randomized clinical trial. The study included 49 volunteers between 18 and 65 years old with BMI of 27 to 50kg/m², who were divided into two groups: those with CKD, specifically ketogenic diet with the consumption of up to 20g of CHO per day, and those with CKD, through a deficit of 500kcal per day based on the weight maintenance diet according to the weight of each. Weight loss, HbA_{1c} and the reduction of DM2 medicines. The results were expressive: the CKD group showed greater improvements in HbA_{1c} (-1.5% versus -0.5%; $p = 0.03$) and body weight (-11.1kg versus -6.9kg; $p = 0.008$) compared to the CKL group, although only the reduction in body weight was a statistically significant value. In addition, dm2 drugs were reduced or eliminated by 95.2% in the CKD group versus 62% in the CKD group.

Finally, the study conducted by Dashti et al.[33] highlights the beneficial effects of CKD in obese diabetic individuals (IDO) compared to obese individuals with normal blood glucose (INDO) levels. The study consisted of 64 participants with BMI greater than 30kg/m² divided into 2 groups: one with 30 participants with high blood glucose levels (10.5 ± 3.0 mmol/l) and another with 33 participants with normal levels (5.1 ± 0.4 mmol/l). The intervention lasted 56 weeks and weight and blood glucose levels were analyzed. All participants were instructed to consume 20g of CHO and 80 to 100g of proteins.

At the end of these 56 weeks, body weight (week 1 - IDO 108.081 ± 21.245kg and INDO 105.273 ± 15.377kg; week 56 - IDO 83,536 ± 18,030kg and INDO 74.923 ± 11.384kg; $p < 0.0001$)and blood glucose level (week 1 - IDO 10.481 ± 3.026 and INDO 5.127 ± 0.440 mmol/l; week 56 – IDO 4.874 ± 0.556 mmol/l and INDO 4.726 ± 0.529 mmol/l; $p = 0.0069$) improved statistically significantly in both groups, although these parameters were more pronounced in the IDO, which indicates greater benefits of CKD for this type of group. In addition to the therapeutic value of this diet, the study demonstrates that this is a safe approach to use for a long period in obese diabetic individuals.

It is noteworthy that although most studies have not reported side effects of diets, Westman et al[443] reported symptoms during the study with no statistically significant difference between groups, such as headaches (CKD: 53.1%, DRCL: 46.3%), constipation (CKD: 53.1%, DRCL: 39.0%), diarrhea (CKD: 40.6%, DRCL: 36.6%), insomnia (CKD: 31.2%, DRCL: 19.5%) and back pain (CKD: 34.4%, DRCL: 39.0%).

However, Saslow et al.[42] observed that the CKD group reported a greater reduction in heartburn (month 0: CKD 1.8 (1.0) and CMD 1.4 (0.6); month 3: CKD 1.1 (0.3) and CMD 1.4 (0.7)), negative mood between meals (month 0: CKD 1 8 (0.6) and CMD 1.8 (0.7); month 3: CKD 1.3 (0.5) and CMD 1.6 (0.7)) and dm2 suffering (month 0: CKD 1.8 (0.5) and CMD 2.3 (0.9); month 3 : CKD 1.3 (0.6) and CMD 2.1 (0.8)) compared to the CMD group, although only the reduction in heartburn showed a statistically significant difference. Also, within the CKD group, participants had an increase in constipation. It is necessary, therefore, a continuous follow-up by qualified professionals if specific symptomatology arises that requires adjustment or a complete change of strategy.

For a better understanding of the results presented in this article, chart 1 indicates whether the biomarkers analyzed obtained statistical significance because of the studies.

Table 1 - Results of the studies according to the statistical significance of the biomarkers analyzed in the control groups and in the impact groups, with a restrictive diet in CHO.

STUDY	BIOMARKERS	CONTROL GROUP	IMPACT GROUP
Huhmann et al.	Glucose Insulin	↓ ↓	↓↓ ↓
Guldbrand et. al	Weight BMI HbA_{1c} HDL-c LDL-c Insulin	↓ ↓ ↓ ↑ ↓ ↓	↓ ↓ ↓↓ ↑↑ ↓ ↓
Saslow et. al	BMI HbA_{1c} Weight	↓ - ↓	↓ ↓ ↓
Hussain et al.	HbA_{1c} Glucose BMI CC	↓↓ ↓↓ ↓↓ ↓↓	↓↓ ↓↓ ↓↓ ↓↓
Davis et. al	Weight HbA_{1c}	↓↓ ↓	↓↓ ↓
Haimoto et. al	BMI HbA_{1c}	↓ ↓	↓ ↓↓
Westman et al.	BMI HbA_{1c}	↓↓ ↓	↓↓ ↓↓
Dashti et. al	Weight Glucose	↓↓ ↓↓	↓↓ ↓↓

CC: waist circumference; ↓: reduced, by without significance; ↓↓: significantly reduced; -: there was no reduction in.

It is noted that the biomarkers, mostly, reduced in both groups – control and restrictive diets in CHO – demonstrating that both strategies are valid for the control of biomarkers related to DM2. However, some points are difficult to analyze since the time of the studies was short, with 2 years the study of a long time, and the reduction of carbohydrate was different between the methodologies presented.

Another important point to highlight is statistical significance. In none of the studies, the biomarkers considered had this sign in the control group without having, concomitantly, in the group with a restrictive diet in CHO. This demonstrates that, even though both strategies are valid, some points still stand out in the CHO-restricted diet.

FINAL CONSIDERATIONS

Although there is still no consensus on the characterization of CKD regarding the distribution of macronutrients, a small reduction in CHO intake in the diet has already been shown to be an effective strategy for improving biomarkers related to DM2 and its complications.

The significant reduction or even the withdrawal of antidiabetic drugs in individuals who reduced CHO consumption suggests that this is a possible strategy to be used as adjunctive therapy for DM2.

It is necessary to emphasize that, despite the positive results presented with the use of CKD in diabetics, one should always take into account the individuality of the patient and his tolerance to this type of nutritional intervention, since non-adaptation can hinder the patient's adhering to the food plan and consequently the control of the pathology.

In addition, it is extremely important to follow up with a professional nutritionist for the elaboration of a CKD given the qualitative difference of CHOs, the percentages of other macronutrients to be distributed in this diet, and the degree of insulin resistance or deficiency in the secretion of this hormone.

Although it was not the subject of inclusion in this review, several articles were found associating CKD with the practice of physical exercise[45-47], being a point of paramount importance when analyzing blood glucose with CKD and the practice of physical exercise, both for possible improvement of the associated parameter and for care when restricting CHO when the individual is practicing physical activity.

Finally, the articles that comprised this review showed some adverse results at the level of HbA_{1c}, showing the need to conduct more randomized long-term studies on the theme to elucidate and deepen the

understanding of the real effect of CKD in patients with DM2.

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