

## **DIABETES REVERSAL - TYPE 2**

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**Abstract:** This review article proposes a study on the possibility of reversing type 2 diabetes in which, when the reversal occurs, the patient reaches a “post-diabetes” state, which in some cases resembles the “post-diabetes” state. prediabetes”, but with lower cardiovascular risk. Diabetes is a non-communicable chronic disease, responsible for the emergence of comorbidities in patients, if there is no proper glycemic control and treatment follow-up. Thus, this article presents a brief discussion on the possibility of reversing type 2 diabetes based on results presented in studies published in the database in the last five years. It appears that updated methods of treating obesity, such as bariatric surgery or restrictive diets, can be recommended for reversing type 2 diabetes.

**Keywords:** Diabetes, diabetes reversal, bariatric surgery, very low calories, low carb.

## INTRODUCTION

Diabetes Mellitus (DM) is characterized as a metabolic disorder that causes chronic hyperglycemia and changes in carbohydrate, protein and fat metabolism, resulting from defects in insulin secretion and/or action. DM has high morbidity and mortality related to acute complications, such as hypoglycemia, and chronic complications, such as nephropathy, in addition to a higher risk for heart and cerebrovascular diseases, being a public health priority (FLOR; CAMPOS, 2017).

It is important for pharmacological therapy to highlight the difference between the main types of DM: 1 (DM1) and 2 (DM2); in which type 1 diabetes usually appears unexpectedly, which can cause severe hyperglycemia and ketoacidosis, with prevalence mainly in children and adolescents; type 2 diabetes is the most prevalent, reaching about 90 to 95% of cases (PAHO, 2016), occurring more in adults who are overweight and who have a family history of DM2, presenting milder

symptoms (WINKELMANN; FONTELA, 2014).

Much of the population has been diagnosed with diabetes. According to epidemiological data provided by the Brazilian Society of Diabetes (SBD, 2019), between the years 2000 and 2018, there was an increase in the prevalence of DM of 54% for men and 28% for women, considering the population of equal age and above. of 18 years.

In 2017, diabetes was the third leading cause of death in Brazil. The World Health Organization (WHO) pointed out that, in 2016, there were a total of 422 million people with diabetes and about 1.5 million died from the disease (WHO, 2017).

Data from the International Diabetes Federation (IDF) indicate that in 2017 the world already had 424 million people with DM, and of these, more than 12 million were Brazilians. It is estimated that in 2040 there will be 640 million individuals with the disease in the world, and in Brazil there will be 20 million diabetics (IDF, 2017), which raises an alert for the severity of comorbidities associated with the disease, such as metabolic syndrome and arterial hypertension, which worsen the clinical picture.

In view of the above, the possibility of reversing type 2 diabetes is questioned. It starts from the hypothesis that, as diabetes has no cure, reversal would be a clinical condition where the individual starts to present, during or after a treatment, controlled blood sugar levels, which may even be normal levels.

Thus, this review article is justified by the need to clarify the possibility of reversing type 2 diabetes, emphasizing that it is not a cure, but a state of glycemic control through changing habits for the treatment of diabetes, which includes diet, physical activity, and possibly drug treatment.

The objective of this article is to carry out a brief discussion around the results presented

in studies published in the database in the last five years, presenting theoretical foundations related to the topic under study.

## **THEORETICAL FOUNDATION**

According to the World Health Organization (WHO), the increase in blood glucose in the body is the third leading cause of death, behind only high blood pressure and tobacco use. Due to the aging and sedentary lifestyle of the population, not practicing physical activity and maintaining unhealthy eating habits, the incidence of obesity increases, one of the main causes that can trigger diabetes (SBD, 2019).

DM is a syndrome of multiple etiology, characterized by a chronic hyperglycemic condition and disorders associated with lipid and protein metabolism. Type 2 diabetes mellitus (DM2), the most common among the types, is characterized by a deficiency in insulin secretion and a reduction in peripheral sensitivity to this hormone, causing biological implications (DANTAS, 2019).

However, it is possible to prevent the onset of DM or, in confirmed diagnoses, improve the prognosis and quality of life of the patient, behaviors that are related to Primary Health Care, which is the first contact with the prevention and treatment of this disease (TORTORELLA et al., 2017).

Factors such as overweight, high blood pressure, dyslipidemias (changes in lipids and/or lipoproteins in the blood) and chronic complications such as microangiopathy and peripheral and autosomal neuropathies are associated with the onset of diabetes (ANDRADE; ROCHA; CRESPO, 2017).

Given these arguments, it is questioned whether reversing or remission of type 2 diabetes is possible. It seems to be possible, but this is not a cure, however, only a control of the glycemic rate. It is important to highlight the use of the terms reversion or remission for

the association with the possible “cure” of the disease.

Within the reversal and remission, the methods used in studies on the subject were: bariatric surgery, low-calorie diet (DBC) and carbohydrate restriction, the first two methods having extremely harmful side effects to health, therefore, they are not advisable methods. In order to reverse the disease (SCHUTZ et al., 2012).

DM2 can be reversed in many cases, even in most of them, especially if treatment starts early, as the return to glucose control for the diabetic depends on the ability of  $\beta$  (beta) cells to recover. Although the exact criteria are still debated, studies show that a glycated hemoglobin (HbA1c), below the diabetes threshold of 6.5%, for a long period, without the use of glycemic control drugs, qualifies for partial reversal (FONSECA, 2018).

Similarly, terms such as “partial remission” (HbA1c < 6.5% without glycemic control medication for 1 year or “complete remission” (HbA1c < 5.7% without glycemic control medication for 1 year) were defined by a panel of experts as more evidence points to the possibility of avoiding the presumably progressive nature of Type 2 Diabetes Mellitus. It is important to note that the term “cure” has not been applied to DM 2 as there is a potential for recurrence, which is well documented in the literature (DANTAS, 2019).

According to Sarah Hallberg, Medical Director and Founder of the Medically Supervised Weight Loss Program and Indiana University Health, the minimum daily carbohydrate requirement is zero, as there are essential amino acids, essential fatty acids, but no essential carbohydrates (BRUNK, 2020). ), so the recommendation for a low-energy diet (LCD) may be a viable and acceptable way to reverse type 2 diabetes.

The doctor warns that a nutrient is essential if it is necessary for survival and that it

cannot be produced any other way. From this perspective, the human organism is capable of producing a lot of glucose through the process of gluconeogenesis, therefore, there is no need for carbohydrates. Excessive consumption of carbohydrates leads to comorbidities. When patients decrease their carbohydrate intake, their glucose level drops and therefore they do not need as much insulin.

Besides, Sarah Hallberg argues that the standard ketogenic diet with 20 to 50g of net carbohydrates per day and healthy fat increase promotes rapid weight loss and body mass reduction, helps to reduce blood pressure, insulin resistance, providing the reduction in the rate of cardiovascular problems, improves blood glucose levels and, consequently, contributes to the reversal of type 2 diabetes mellitus (BRUNK, 2020).

## RESULTS AND DISCUSSION

In 2016, the World Health Organization (WHO) admitted that type 2 diabetes mellitus can be reversed through methods aimed at weight loss or caloric restriction, admitting that the dietary lifestyle will make a difference to the possibility of reversing the disease. Weight loss can occur through eating lifestyle or physical exercise, but the practice of physical activity without adequate nutrition will not be able to reverse diabetes; it is necessary to associate the two methods to obtain a satisfactory result.

Based on this finding, an analysis is made of the results presented in five articles published in the database between 2017 and 2021, which deal with the possible reversal of type 2 diabetes.

Gow et al. (2017) in a clinical trial sought to investigate whether a low-energy diet (LCD) would be a viable and acceptable treatment option for type 2 diabetes in children and adolescents, and whether adherence to this type of diet would result in rapid weight loss,

reversal of type 2 diabetes and reduction of liver fat, as had already been observed in studies with adults.

Participated in the study 8 volunteers with type 2 diabetes and obesity, aged 7 to 16 years, not medicated or treated with metformin or insulin, who started to adhere to the LCD diet for 8 weeks, and after that period they made the transition to a hypocaloric diet for 34 weeks. Among the 8 participants, 5 adhered to the study and 3 did not, who had a median weight loss of 7.5% (adherent) and 0.5% (non-adherent). None of the participants met the NAFLD criteria and four did not meet the American Diabetes Association (ADA) criteria for type 2 diabetes (GOW et al., 2017).

Liver fat was also significantly reduced by 14.7%. Only three volunteers met the criteria for Non-Alcoholic Fatty Liver Disease (NAFLD) ( $\geq 5.5\%$ ) at 8 weeks. The three participants on insulin therapy at baseline were able to stop therapy during the 8-week LCD (GOW et al., 2017).

Gow et al. (2017) concluded that an LCD is a viable treatment option for some young people with type 2 diabetes on metformin therapy, based on the assumption that among the eight participants, those who adhered to the diet achieved rapid weight loss, significant reductions in body fat, liver and reversal of type 2 diabetes, which “[...] highlights the ability of an LCD to be used as a first-line treatment option in newly diagnosed young people.” (GOW et al., 2017, p. 22). The researchers said that a change from standard care would require a study with a larger control group and longer follow-up.

Initially, such a change was attempted with rats in a clinical trial developed by Perry et al. (2018) when analyzing the mechanisms by which a very low-calorie diet reverses hyperglycemia with type 2 diabetes. correction of plasma glucose and insulin without altering

the body weight of rodents with an LCD (1/4 of their typical intake).

Lower plasma glucose was found to be associated with a 30% reduction in hepatic glucose production due to suppression of both gluconeogenesis, which is the formation of glucose from muscle lactate, glycerol from adipose tissue, and amino acids such as glutamine, by reducing the hepatic content of acetyl-CoA, and net hepatic glycogenolysis, which is the breakdown of hepatic glycogen (PERRY et al., 2018).

In addition, a short-term (3 days) low-calorie diet was used to record a reduction in hepatic triglycerides (TAG) and diacylglycerol (DAG) rates and in PKC $\epsilon$  translocation (PKCepsilon activity), associated with an improvement in hepatic insulin sensitivity, resulting in improved glucose metabolism prior to weight loss. Through this study mechanism, it was possible to track beneficial metabolic effects to improve liver metabolism due to reductions in hepatic glycogenolysis, acetyl-CoA-driven pyruvate carboxylase flux, and TAG-DAG-PKC $\epsilon$ -mediated insulin resistance (PERRY et al, 2018).

Hallberg et al. (2019) developed a study to describe methods recently included in the guidelines for reversing type 2 diabetes, claiming that traditional methods define this disease only as chronic incurable. This study resulted from a bibliographic search that selected 99 articles published in a database, such as PubMed, in the time frame between the years 1970 to 2018 with the objective of seeking evidence on the possibility of reversing type 2 diabetes.

Current methods for weight loss are bariatric surgery, recommended since 2016 by an international diabetes consensus group; low-calorie (LCD) or carbohydrate-restricted (CL) diets, which are advised by institutions such as the ADA and the European Association for the Study of Diabetes (EASD).

Hallberg et al. (2019) described the advantages and disadvantages of each current method for disease reversal. With regard to bariatric surgery, there is a unilateral improvement in blood glucose after the operation, quickly and weight loss. In addition, it allows the reduction of oral hypoglycemic medications and insulin use, reversing diabetes in up to 80% of patients in the short term. However, this procedure can have significant complications such as hemorrhage, postoperative hypoglycemia, worsening acid reflux, and micronutrient deficiencies.

Non-invasive procedures, such as LCD, are supported by several studies that report successful weight loss with decreased insulin resistance, plasma glucose and medication use, however, severe energy restriction may have some effect. deleterious effect on body composition and physiology (HALLBERG et al., 2019).

Low-carbohydrate (LC) or ketogenic diets were the most frequently prescribed treatment for diabetes until the development of exogenous insulin and, later, with the emergence of the low-fat diet. Over the past decade, clinical studies have revived research around the effectiveness of LC by pointing to new evidence on the effectiveness of carbohydrate restriction, which has recently been endorsed as a dietary pattern by the ADA and EASD. LC diets are based on macronutrient changes rather than focusing on calorie restriction. Although it shows promising short-term results, further long-term studies are needed to determine the sustainability of metabolic improvements (HALLBERG et al., 2019).

Hallberg et al. (2019) argue that health professionals need to be oriented and clarified about the methods for reversing type 2 diabetes, aiming at the proper counseling of patients who wish to reverse

the disease. The authors' approach is based on the research by Taylor (2019), who, in an article on remission of type 2 diabetes, based on a systematic review, clarified that excess fat in the liver and pancreas leads to the diagnosis of type 2 diabetes, and that remission or reversal of the condition can occur with substantial weight loss, leading to a post-diabetes state that can be long-term, as long as weight regain is avoided.

Liver insulin resistance is associated with liver fat, and the higher the level of fat, the greater this resistance, causing fasting hyperglycemia. The development of type 2 diabetes is also found to be related to beta cell defect (TAYLOR, 2019).

Taylor (2019) concluded that for weight loss by individuals with type 2 diabetes, it is essential to define a short period for low-calorie intake, motivation on the part of the individual to achieve their goal and support from family and friends. However, during this period of low calorie intake it is recommended that there is no increase in physical exercise until weight loss and maintenance begins. The author extended his research and, together with other researchers, developed an observational study to prove that weight loss is related to reversal of type 2 diabetes.

Thus, Taylor et al. (2021) in a randomized controlled trial in primary care of a low-calorie diet with structured follow-up compared to conventional management as per best practice guidelines, explain the reversal of type 2 diabetes associated with weight loss, preventing return of weight loss, based on the evidence that food restriction can contribute to the return to normal functioning of individuals with type 2 diabetes. The explanation is based on the clinical trial and on previous studies.

Results of studies show that half of the people in the first 10 years of diagnosis of type

2 diabetes, who are able to adapt to energy restriction from food, have the possibility of suspending all drugs to treat the disease and controlling glucose levels, reaching the necessary weight loss and its maintenance for type 2 diabetes remission, which occurs "[...] when hemoglobin A1c concentrations of 48 mmol/mol are recorded after weight loss and at least six months later, without any antidiabetic drugs." (TAYLOR et al., 2021, p.1).

In this trial, 30% of the 149 volunteers achieved an average weight loss of 14.5 kg in eight weeks, and 36% achieved remission for two years, with nutritional monitoring, in which they adopted, among other restrictions, a low-fat liquid diet. calorie for a planned short period. Elevated liver and pancreas fat levels of the volunteers in the trial were found to drop to normal levels, with reduced hepatic glucose production and improved  $\beta$ -cell function (TAYLOR et al., 2021).

Thus, based on the results presented by the analyzed studies, it appears that an LC diet seems to be the most viable treatment option to try to reverse type 2 diabetes, given the potential of LCD in terms of rapid weight loss and reductions in fat. liver.

## CONCLUSION

From the analyzed studies, it is confirmed that type 2 diabetes is a state of carbohydrate toxicity, as blood glucose does not reach the cells and this causes problems in a short time. Based on current methods for reversal, the LCD diet is a viable and acceptable recommendation, as carbohydrate intake is crucial for the rise in blood sugar levels that result in the need for medication.

The reversal or remission of type 2 diabetes is not a cure, but an effective control of glycemic levels in the body through a change in habits that include physical

activity and diet with restrictions, mainly in carbohydrates, which favors a return to the normal state. normality of rates, bringing quality of life to the patient and the possibility of not using medication.

## REFERENCES

ANDRADE, A. L.; ROCHA, J. M.; CRESPO, S. Avaliação do tratamento farmacológico utilizado por idosos diabéticos e hipertensos do município de Vieiras (MG). **Revista Científica da Faminas**, v. 12, n. 1, p. 37-43, 2017.

BRUNK, Doug. A restrição de carboidratos é uma opção viável para reverter o diabetes tipo 2? **Medscape**, 2020. Disponível em: <https://portugues.medscape.com/verartigo/6504372>. Acesso em: 20 ago. 2021.

DANTAS, P. de A. **Interação fármaco x alimento na doença diabetes mellitus tipo 2 em idosos**. 2019. 57 f. Monografia (Curso de Graduação em Farmácia) – Centro de Educação e Saúde / UFCG, 2019.

FLOR, L. S.; CAMPOS, M. R. Prevalência de diabetes *mellitus* e fatores associados na população adulta brasileira: evidências de um inquérito de base populacional. **Rev. bras. epidemiol.** 20 (01) Jan-Mar 2017.

FONSECA, A. D. G. et al. Fatores associados à dependência entre idosos com diabetes mellitus tipo 2. **Revista Brasileira de Enfermagem**, v. 71, s. 2, p. 922-930, 2018.

GOW, M.L.; et al. Reversão do diabetes tipo 2 em jovens que aderem a uma dieta de muito baixo teor calórico: um estudo piloto. **Diabetologia**; 60(3):406-415, 2017.

HALLBERG, S.J.; et al. Improving the scientific rigour of nutritional recommendations for adults with type 2 diabetes: A comprehensive review of the American Diabetes Association guideline-recommended eating patterns. **Diabetes Obes. Metab.**, 21, 1769–1779, 2019.

IDF. International Diabetes Federation. **IDF Diabetes Atlas – 8th edition**. 2017. Disponível em: <http://diabetesatlas.org/across-the-globe.html>. Acesso em: 18 set. 2020.

PERRY, R. J.; et al. Mechanisms by which a Very-Low-Calorie Diet Reverses Hyperglycemia in a Rat Model of Type 2 Diabetes. **Cell Metab.**, 9;27(1):210-217, 2018.

SCHUTZ, R.; et al. Reversão do diabetes mellitus tipo 2 através da cirurgia bariátrica. **Rev. bras. anal. clin.**;44(1):5-9, 2012.

SDB. Dados Epidemiológicos do diabetes mellitus no Brasil. **Departamento de Epidemiologia, Economia e Saúde Pública SBD 2018 – 2019**. 2019. Disponível em: [https://www.diabetes.org.br/profissionais/images/SBD-\\_Dados\\_Epidemiologicos\\_do\\_Diabetes\\_-\\_High\\_Fidelity.pdf](https://www.diabetes.org.br/profissionais/images/SBD-_Dados_Epidemiologicos_do_Diabetes_-_High_Fidelity.pdf). Acesso em 18 set. 2021.

TAYLOR, R. Restrição de calorias para remissão de diabetes tipo 2 em longo prazo. **Clin Med (Lond)**; 19: 37–42, 2019.

TAYLOR, R.; et al. Base nutricional da remissão do diabetes tipo 2. **BMJ**; 374: n1449, 2021.

TORTORELLA, Catiuscie Cabreira da Silva; et al. Tendência temporal da prevalência de hipertensão arterial sistêmica e diabetes *mellitus* entre adultos cadastrados no Sistema Único de Saúde em Florianópolis, Santa Catarina, 2004-2011. **Epidemiol. Serv. Saúde**, Brasília, 26(3):469-480, jul-set 2017.

WINKELMANN, E. R.; FONTELA, P. C. Condições de saúde de pacientes com diabetes *mellitus* tipo 2 cadastrados na Estratégia Saúde da Família, em Ijuí, Rio Grande do Sul, 2010-2013. **Epidemiol. Serv. Saúde**, v.23 n.4 Brasília dez. 2014.

WHO - World Health Organization. **Diabetes**. 2017. Disponível em: <http://www.who.int/mediacentre/factsheets/fs312/en/>. Acesso em: 18 set. 2021.