



STRICT GLYCEMIC CONTROL: A LITERATURE REVIEW

REVIEW ARTICLE

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ABSTRACT

Diabetes mellitus is a disease that is difficult to control worldwide. Since the better understanding of the pathophysiology of the disease by modern medicine, several ways to control the evolution of the pathology in question have been proposed. As an example, we can mention a study published in 1993 by the Diabetes Control and Complications Trial (DCCT) and, later, in 1998, validated by the United Kingdom Prospective Diabetes Study (UKPDS), which established glycated hemoglobin as one of the main markers evolution and prognosis of the disease. Since the publication of these studies, goals such as: strict glycemic control (corresponding to glycated hemoglobin goals less than or equal to 6.5 mg/dL), have been accepted by the world medical community as references in the control and follow-up of the disease. In this context, the present article has as its guiding question: should strict glycemic control be desired for all patients? Aiming to find out, through literature review, whether glycemic control should be required for all patients. Therefore, a literature review was carried out on published articles on the subject in question, aiming to focus on quaternary prevention and the importance of good clinical practice

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collaborated by evidence-based medicine. The results indicate that, in the case of strict glycemic control, there is no evidence of benefits in general in its use, being reported in the literature that, in certain populations, especially those over 80 years of age, its use is linked to increased effects. adverse effects and morbidity caused by the disease.

Keywords: Glycated Hemoglobin, Glycemic Control, Rigorous Glycemic Control, Evidence Based Medicine.

INTRODUCTION

Sun *et al.* (2021), portray that diabetes, only in the year 2021, proved to be one of the most difficult diseases to control in the world. According to the tenth edition of the Diabetes Atlas, 537 million adults (from 20 to 79 years of age) are carriers of this pathology, which corresponds to approximately 01 in 10 adults worldwide. Regarding mortality from the disease, the Atlas estimates that there were 6.7 million deaths in 2021, totaling 01 death every 05 seconds (SUN *et al.*, 2021).

Due to the increase in these numbers, the statistical projections for the coming years are not favorable. An increase of approximately 46% in the absolute number of carriers of the disease worldwide is predicted between 2021 and 2045 (from 537 to 783 million). In this context, forecasts indicate an increase of 13% in Europe (from 61 to 69 million). In Latin and Central America, the expected increase reaches 50% (from 32 to 49 million) and, in Africa, to 134% (from 24 to 55 million). It is also verified that in underdeveloped countries, there is an important historical-social relationship for the spread of this disease (SUN *et al.*, 2021).

For the control of diabetes mellitus (DM), it was essential to create a monitoring test to monitor the disease, aiming to prevent its main complications, such as: renal, micro and macrovascular sequelae and organ failure (SUMITA; ANDRIOLO, 2006).).

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The first study to argue that the control of glycated hemoglobin levels implied a reduction in disease morbidity and mortality, published by the Diabetes Control and Complications Trial (DCCT), became a landmark for a better understanding of the pathophysiology of the disease and for the prevention of its complications. Following 1441 people over an eleven-year period (1982-1993), the study was able to prove that controlling hemoglobin levels below 7 mg/dL reduced the early stages of disease and microvascular complications of diabetes mellitus by 35-76% of patients, after a mean follow-up of 6.5 years. The main criticisms of the study are related to the eligibility criteria, as only patients aged between 13 and 39 were included, thus making it difficult to establish better goals for other age groups. In addition to this factor, when delimiting, mainly, patients with type I diabetes mellitus and already dependent on the use of insulin therapy, the study adopted a population with greater chances of evolution to micro and macrovascular complications (DCCT RESEARCH GROUP, 1993).

Another study, later published by the United Kingdom Prospective Diabetes Study (UKPDS), demonstrated the importance of glycemic control in patients with type II diabetes mellitus. The study in question, carried out in some countries of the former United Kingdom (Scotland, England and Northern Ireland), over a period of fourteen years (1977-1991), with patients diagnosed with type II diabetes and ages ranging from 25 to 65 years. of age, could show a significant relative risk decrease of 25% ($p=0.0099$) for microvascular diseases, but failed to show a significant relative risk decrease for macrovascular events (UK PROSPECTIVE DIABETES STUDY GROUP, 1998).

Based on the importance of controlling the chronic disease in question, increasingly stringent goals of glycemic control have been assigned by specialists in the field. The performance of glycated hemoglobin every 03 months, at the beginning of treatment and after medication adjustment, and every 06 months, after stabilization of the condition, has become common in medical practice (MISER, 2007).

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However, the question about the need to establish a consensus on the values and goals of glycemic control remains, especially when it is evident that increasingly stringent goals of glycemic control have been established (MISER, 2007). In this context, the present article has as its guiding question: Should strict glycemic control be desired for all patients? Aiming to find out, through literature review, whether glycemic control should be required for all patients. Therefore, a literature review was carried out on published articles on the subject in question, aiming to focus on quaternary prevention and the importance of good clinical practice collaborated by evidence-based medicine.

DEVELOPMENT

Although diabetes control is always desired, several evidences show that intensive therapy and stricter goals may not generate benefits and cause unfavorable complications. Despite this, entities and publications still try to standardize restricted goals for different age groups (YAU *et al.*, 2012).

In 2004, in an attempt to standardize the control of glycated hemoglobin, goals were established, and later reassessed, for adults, children and the elderly, by the Interdisciplinary Group for Standardization of Glycated Hemoglobin (A1C). Therefore, for effective control, goals were established: for adults, below 7 mg/dL; for prepubertal children, up to 8 mg/dL; pubescent, up to 8.5 mg/dL; and elderly, up to 8 mg/dL. Despite being criticized, especially the control values for the elderly and patients with special needs, these goals are still the main ones addressed in the literature in the area (ANDRIOLO; VIEIRA, 2008).

With regard to intensive glycemic control (corresponding to glycated hemoglobin targets less than or equal to 6.5 mg/dL), mainly with cardiovascular correlations and complications, randomized studies were performed. Among them, we can mention an article, published in 2014, which evaluated 8494 patients, following them for an average of 5, 4-5, 9 years. At the end of follow-up, the researchers concluded that

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intensive glycemic control showed no evidence of long-term benefits, reduction of mortality or cardiovascular events. However, the author reports that most clinicians, at that time, still adopted strict glycemic control as best clinical practice (ZOUNGAS *et al.*, 2014).

In 2012, in a study with 185 patients, 50% of whom were insulin dependent, whose mean age was 80 years and taking into account confounding factors, it was observed that a glycated hemoglobin between 8 mg/dL and 8.9 mg/dL was related to better markers and functional prognosis after two years of follow-up. However, it appears that there is still resistance in joining the work for quaternary prevention by specialists in the area (YAU *et al.*, 2012).

The hospital experience is strongly intertwined with the interventionist idea. The literature shows that it is necessary to better stratify the populations treated and that the treatment is appropriate to the person, and not the person to the treatment. Therefore, it is evident that strict glycemic control does not show benefits for the population in general, with the exception of some rare cases in specific populations, contraindicated for recurrent use (VALLADÃO JÚNIOR; GUSSO; OLMOS, 2017).

FINAL CONSIDERATIONS

Diabetes is increasingly a challenge for modern medicine. Being linked not only to biological factors, the disease follows statistical progression patterns globally, which reflect its historical and social dynamics, especially in relation to the country's culture and economy. In this context, evidence-based medicine and good clinical practice are fundamental tools to counter the spread of the disease and the increase in the number of cases worldwide.

With regard to glycemic control, glycated hemoglobin has already proved to be one of the most important weapons against the progression of the disease to worse prognoses, but its practical implementation still shows divergences in the literature.

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Therefore, returning to the guiding question of this study, which aimed to answer whether strict glycemic control should be aimed at all patients, it was found that there is no evidence for benefits in general in its use, and it is clear that in certain populations, especially over 80 years of age, its use is linked to an increase in adverse effects and disease morbidity. In line with this finding, the current literature shows a consensus on contraindicating its recurrent use. Finally, it was found that doctors need to know how to better stratify their patients and indicate different glycemic targets according to age, complications and side effects observed during the treatment of diabetes.

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