

MELATONIN AS AN ADJUVANT IN THE CONTROL OF GLYCATED HEMOGLOBIN IN PATIENTS WITH DIABETES AND PERIODONTAL DISEASE

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ABSTRACT

Objective: The objective of this narrative review article is to address the possible effectiveness of melatonin as an adjuvant in the control of glycated hemoglobin in patients with diabetes and periodontal disease.

Methodology: This article is a narrative literature review. Therefore, it was necessary to conduct online searches to obtain a set of articles related to the topic addressed in this study. The online searches were conducted in the following online databases: PubMed, Cochrane Library, EMBASE, and Google Scholar. During these searches, to obtain only results related to the present study, the following keywords were used: Melatonin, Salivary, Periodontitis, Glycated Hemoglobin. Furthermore, Boolean terms such as "AND" and "OR" were used in PubMed and Cochrane searches. After conducting the searches, the results were screened, a process divided into three phases: The first phase is the elimination of duplicate articles, eliminating duplicates through the Zotero platform. The second phase was to eliminate articles unrelated to the topic by reading their titles and abstracts. The third and final phase consisted of reading the remaining articles in full, using studies compatible with this narrative review.

Results: Studies have shown that melatonin, either in conjunction with non-surgical periodontal treatment or alone, has a positive effect on glycated hemoglobin levels in diabetic patients with periodontal disease.

Conclusion: A set of studies shows that melatonin is a viable and promising option when used in patients with diabetes and periodontal disease, providing benefits in regulating glycated hemoglobin levels. However, further studies are needed to standardize dosage, duration of use and administration.

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Keywords: Melatonin. Salivary. Periodontitis. Glycated Hemoglobin.

MELATONINA COMO ADJUVANTE NO CONTROLE DA HEMOGLOBINA GLICADA EM PACIENTES COM DIABETES E DOENÇA PERIODONTAL

RESUMO

Objetivo: O objetivo deste artigo de revisão narrativa é abordar a possível eficácia da melatonina como adjuvante no controle da hemoglobina glicada em pacientes com diabetes e doença periodontal.

Metodologia: Este artigo é uma revisão narrativa da literatura. Portanto, foi necessário realizar buscas online para obter um conjunto de artigos relacionados ao tema abordado neste estudo. As buscas online foram realizadas nas seguintes bases de dados online: PubMed, Cochrane Library, EMBASE e Google Acadêmico. Durante essas buscas, para obter apenas resultados relacionados ao presente estudo, foram utilizadas as seguintes palavras-chave: Melatonina, Salivar, Periodontite, Hemoglobina Glicada. Além disso, termos booleanos como "AND" e "OR" foram utilizados nas buscas no PubMed e Cochrane. Após a realização das buscas, os resultados foram triados, um processo dividido em três fases: A primeira fase é a eliminação de artigos duplicados, eliminando-os por meio da plataforma Zotero. A segunda fase foi a eliminação de artigos não relacionados ao tema por meio da leitura de seus títulos e resumos. A terceira e última fase consistiu na leitura integral dos artigos restantes, utilizando estudos compatíveis com esta revisão narrativa.

Resultados: Estudos demonstraram que a melatonina, seja em conjunto com o tratamento periodontal não cirúrgico ou isoladamente, apresenta efeito positivo sobre os níveis de hemoglobina glicada em pacientes diabéticos com doença periodontal.

Conclusão: Um conjunto de estudos demonstra que a melatonina é uma opção viável e promissora quando utilizada em pacientes com diabetes e doença periodontal, proporcionando benefícios na regulação dos níveis de hemoglobina glicada. No entanto, mais estudos são necessários para padronizar a dosagem, a duração do uso e a administração.

Palavras-chave: Melatonina. Salivary. Periodontitis. Hemoglobina Glicada.

MELATONINA COMO ADYUVANTE EN EL CONTROL DE LA HEMOGLOBINA GLICATADA EN PACIENTES CON DIABETES Y ENFERMEDAD PERIODONTAL

RESUMEN

Objetivo: El objetivo de esta revisión narrativa es abordar la posible eficacia de la melatonina como adyuvante en el control de la hemoglobina glucosilada en pacientes con diabetes y enfermedad periodontal.

Metodología: Este artículo es una revisión narrativa de la literatura. Por lo tanto, fue necesario realizar búsquedas en línea para obtener un conjunto de artículos relacionados con el tema abordado en este estudio. Las búsquedas se realizaron en las siguientes bases de datos: PubMed, Biblioteca Cochrane, EMBASE y Google Académico. Durante estas búsquedas, para obtener únicamente resultados relacionados con el presente estudio, se utilizaron las siguientes palabras clave: Melatonina, Salivar, Periodontitis, Hemoglobina glucosilada. Además, se utilizaron términos booleanos como "AND" y "OR" en las búsquedas en PubMed y Cochrane. Tras las búsquedas, se realizó un cribado de los resultados, un proceso dividido en tres fases: la primera fase consiste en la eliminación de artículos

duplicados a través de la plataforma Zotero. La segunda fase consistió en la eliminación de artículos no relacionados con el tema mediante la lectura de sus títulos y resúmenes. La tercera y última fase consistió en la lectura completa de los artículos restantes, utilizando estudios compatibles con esta revisión narrativa.

Resultados: Diversos estudios han demostrado que la melatonina, ya sea en combinación con un tratamiento periodontal no quirúrgico o sola, tiene un efecto positivo en los niveles de hemoglobina glucosilada en pacientes diabéticos con enfermedad periodontal.

Conclusión: Diversos estudios demuestran que la melatonina es una opción viable y prometedora cuando se utiliza en pacientes con diabetes y enfermedad periodontal, ya que proporciona beneficios en la regulación de los niveles de hemoglobina glucosilada. Sin embargo, se necesitan más estudios para estandarizar la dosis, la duración del uso y la administración.

Palabras clave: Melatonina. Salival. Periodontitis. Hemoglobina Glucosilada.

1 INTRODUCTION

Melatonin, a neurohormone primarily synthesized by the pineal gland, is best known for regulating circadian rhythms. However, its functions extend beyond sleep regulation. It has demonstrated potent antioxidant, anti-inflammatory, and immunomodulatory properties, which have made it a subject of growing interest in various chronic inflammatory conditions, including periodontitis and diabetes (Reiter et al., 2017; Hardeland, 2018).

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder characterized by insulin resistance and persistent hyperglycemia. Glycemic control, typically assessed through glycated hemoglobin (HbA1c) levels, is essential to reduce the risk of complications. Chronic low-grade inflammation and oxidative stress play key roles in the pathophysiology of diabetes, and adjuvant therapies that can mitigate these processes are actively being explored (American Diabetes Association, 2024; Forbes & Cooper, 2013). Periodontal disease is a common chronic inflammatory condition affecting the supporting structures of the teeth. A growing body of evidence supports a bidirectional relationship between periodontitis and T2DM. Periodontal inflammation may increase systemic inflammatory burden, negatively influencing insulin sensitivity and glycemic regulation. Moreover, periodontal therapy has been shown to improve glycemic outcomes in diabetic patients (El-Wakeel & Hazaa, 2015; Santos et al., 2020).

In this context, melatonin emerges as a promising adjunctive therapeutic agent due to its anti-inflammatory and antioxidant mechanisms that may benefit both periodontal and metabolic health. Recent studies suggest that melatonin supplementation, either alone or as an adjunct to nonsurgical periodontal therapy, may contribute to significant improvements in HbA1c levels in patients with T2DM and periodontitis (Bazyar et al., 2022; Anton et al., 2021; Navya et al., 2021). The objective of this narrative review article is to address the possible effectiveness of melatonin as an adjuvant in the control of glycated hemoglobin in patients with diabetes and periodontal disease.

2 METHODOLOGY

This article is a narrative literature review. Therefore, it was necessary to conduct online searches to obtain a set of articles related to the topic addressed in this study. The online searches were conducted in the following online databases: PubMed, Cochrane Library, EMBASE, and Google Scholar. During these searches, to obtain only results related to the present study, the following keywords were used: Melatonin, Salivary, Periodontitis, Glycated Hemoglobin. Furthermore, Boolean terms such as "AND" and "OR" were used in PubMed and Cochrane searches. After conducting the searches, the results underwent screening, a process divided into three phases: The first phase is the

elimination of duplicate articles, eliminating duplicates through the Zotero platform. The second phase was the elimination of articles unrelated to the topic addressed by reading their titles and abstracts. The third and final phase consisted of reading the remaining articles in full, using studies compatible with this narrative review. Furthermore, Rother's (2007) study served as a guide during the development of this study, as it addresses the differences between a systematic review and a narrative review, addressing the approaches, methodology, structure, and content of each type.

3 RESULTS

Multiple clinical studies have investigated the effects of melatonin supplementation on glycated hemoglobin (HbA1c) levels in individuals with type 2 diabetes and periodontitis, suggesting a promising role for melatonin in improving glycemic control when used as an adjunct to nonsurgical periodontal therapy. In a randomized, double-blind clinical trial, Bazzyar et al. (2022) evaluated 50 patients with type 2 diabetes and chronic periodontitis who received 6 mg of oral melatonin daily for eight weeks in conjunction with standard periodontal treatment. Their findings revealed a significant reduction in HbA1c levels compared to the placebo group, with a mean decrease of approximately 1.3 percentage points, highlighting a potentially clinically meaningful effect. The authors also noted concurrent improvements in inflammatory markers such as IL-6 and hs-CRP, supporting the systemic influence of melatonin's anti-inflammatory and antioxidant actions.

Similar results were observed in the study by Anton et al. (2021), which included 54 diabetic patients undergoing nonsurgical periodontal therapy. Participants who received 3 mg of melatonin daily for eight weeks demonstrated a greater reduction in HbA1c compared to those who received placebo. These findings suggest that even at lower doses, melatonin can exert beneficial effects on glycemic markers, particularly when combined with mechanical periodontal therapy. Additionally, this study reported parallel improvements in periodontal clinical parameters, reinforcing the bidirectional relationship between periodontal health and metabolic control.

In another randomized clinical trial, Navya et al. (2021) investigated the adjunctive use of melatonin in 60 patients with diabetes and chronic periodontitis. The group that received melatonin showed more pronounced reductions in HbA1c following eight weeks of treatment compared to controls. Notably, this trial further emphasized that improvements in glycemic markers were closely associated with reductions in periodontal inflammation, once again underscoring the systemic interplay.

Contrastingly, in a triple-blind randomized trial, Domańska-Glonek et al. (2020) administered 6 mg of melatonin at bedtime for eight weeks to 34 diabetic patients and did not observe statistically

significant differences in HbA1c compared to the placebo group. The authors suggested that variability in patient characteristics, initial HbA1c levels, and the absence of concurrent periodontal treatment may have influenced the outcome.

Despite isolated studies reporting neutral findings, the majority of available evidence supports the conclusion that melatonin, particularly when used alongside periodontal therapy, contributes to improved glycemic regulation as reflected in reduced HbA1c levels. These effects are likely mediated by melatonin's well-documented capacity to reduce oxidative stress and systemic inflammation, two key mechanisms implicated in insulin resistance and poor glycemic control in patients with chronic inflammatory diseases such as periodontitis.

Systematic reviews, such as that conducted by Aladhadh et al. (2021), have also highlighted the potential of melatonin as a therapeutic adjunct. Their meta-analysis of antioxidant agents including melatonin demonstrated significant improvements in clinical periodontal outcomes in diabetic patients, although they noted the relative scarcity of trials reporting HbA1c specifically. As such, while preliminary findings are promising, the need for further high-quality randomized trials remains, particularly those that evaluate long-term glycemic control and standardized melatonin protocols in patients with comorbid diabetes and periodontitis.

4 DISCUSSION

The interrelationship between diabetes and periodontal disease poses a major clinical challenge, as both conditions share similar pathophysiological mechanisms, such as chronic inflammation and oxidative stress. In this context, adjunctive therapies that can modulate these common pathways become highly relevant. Melatonin, due to its widely recognized biological properties, emerges as a promising candidate. The studies analyzed in this review indicate that melatonin can positively contribute to reducing glycated hemoglobin levels in patients with diabetes and periodontitis. This effect can be explained by its ability to modulate inflammatory and oxidative processes, in addition to potentially improving insulin sensitivity. The improvement in blood glucose levels observed in several clinical trials can therefore be attributed not only to the local impact of melatonin on periodontal tissue, but also to its systemic effects.

Furthermore, the use of melatonin as an adjunct to non-surgical periodontal treatment appears to enhance the effects of this type of intervention, providing additional benefits to glycemic control. This is particularly relevant in a context where glycated hemoglobin control is one of the main prognostic indicators for patients with diabetes. Considering melatonin's relatively low cost, good tolerability, and safety profile, its use may represent a low-risk and potentially high-benefit therapeutic

alternative. However, it is important to highlight that available studies still exhibit heterogeneity regarding dosage, administration method, treatment duration, and population characteristics. These differences hinder therapeutic standardization and limit the generalizability of results. Furthermore, most available studies have relatively small numbers of participants and short follow-up periods.

Consequently, the need for additional studies with more robust methodological designs, larger sample sizes, and longer follow-up periods becomes evident in order to confirm the findings observed to date and establish safe and effective clinical protocols for the use of melatonin in this population.

5 CONCLUSION

A set of studies shows that melatonin is a viable and promising option when used in patients with diabetes and periodontal disease, providing benefits in regulating glycated hemoglobin levels. However, further studies are needed to standardize dosage, duration of use and administration.

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