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MELATONIN AND PERIODONTAL HEALTH: EFFECTIVENESS IN ALVEOLAR BONE REMODELING AND TREATMENT OF PERIODONTAL DISEASES

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ABSTRACT
Objective: The objective of this narrative literature review article is to address hormone melatonin as a potential adjuvant in bone remodeling and periodontal health balance. Methodology: During the creation of this article, it was necessary to use a study that would serve as a guide for the development of this narrative literature review, thus, it was necessary to use as a basis a scientifically proven article that had already been published, thus, the work of Rother (2007) was the study used as a guide in this review, as it is an article that highlights the differences, characteristics and needs present in narrative review. In addition, because it is a literature review, it was necessary to conduct research in online databases, databases that could make available the maximum number of studies, articles and research related to the topic addressed, thus, searches were made in the following databases: PROSPERO; Science Direct; Scielo; PubMed; The Cochrane Library Results: Studies have shown that melatonin has diverse functions such as anti-inflammatory, antioxidant and osteogenic properties, where supplementation of this hormone can serve as an aid to conventional periodontal treatment, helping to improve periodontal clinical parameters. Conclusion: Several studies carried out in recent years have shown that patients who received melatonin associated with periodontal treatments obtained a reduction in probing depth and greater clinical insertion when compared to patients who underwent conventional periodontal treatments without the use of melatonin as an adjuvant.

Keywords: Melatonin. Periodontal Diseases. Bone Remodeling. Periodontics.

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INTRODUCTION

Periodontium means "around the tooth", it refers to the structures that surround the tooth, and the periodontium can be divided into the protective periodontium, composed of the gums, and the supporting periodontium, composed of the alveolar bone, periodontal ligaments and cementum, structures that together will protect and support the teeth in the mandible and maxilla. Periodontal disease is a disease that affects the periodontium, it is a serious, complex pathology, whose etiology is related to the presence of bacterial colonization and excessive inflammation in a susceptible host (Konecná et al., 2021). Periodontal diseases are one of the biggest causes of loss of teeth and bone structure of the jaws in adult patients (Assuma et al., 1998), in addition to affecting the periodontium as a whole, impacting structures such as the gums, periodontal ligaments and cementum, harming the oral health of the patient who has some pathology of the periodontium (Soumya et al., 2014).

Several hormones are produced by the human body and acquired through the ingestion of certain foods, contributing to the functioning of the human body. Melatonin is a hormone, commonly known as the sleep hormone because it is responsible for regulating the circadian cycle and determining when the body should be sleepy. This hormone is secreted mainly by the pineal gland and can also be acquired in certain foods such as wheat, vegetables and fruits. It is a hormone that has antioxidant, anti-inflammatory and osteogenic properties, serving as a contributor to the body, which protects the body's cells against many effects that can be harmful to humans (Ramesh et al., 2025; Balaji et al., 2021).

Melatonin is a hormone that has great therapeutic potential and can be administered as a supplement, serving as an adjunct to specific therapies and treatments through its beneficial properties. Recent studies such as the systematic review by Ramesh et al. 2025, have shown the possible effectiveness of melatonin as an adjunct to periodontal treatments, serving as a very effective contributor and showing great differences when compared to conventional periodontal treatments that did not use melatonin as an adjunct (Sarac et al., 2024; Anton et al., 2021 Montero et al., 2017; Cutando et al., 2013). Thus, the present narrative review aims to address the potential of melatonin within dentistry, discussing its function and possible efficacy within treatments against periodontal diseases, analyzing the possibility of this hormone serving as an adjunct to conventional periodontal treatment.

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METHODOLOGY

During the creation of this article, it was necessary to use a study that would serve as a guide for the development of this narrative literature review, thus, it was necessary to use as a basis a scientifically proven article that had already been published, thus, the work of Rother (2007) was the study used as a guide in this review, as it is an article that highlights the differences, characteristics and needs present in a systematic literature review and a narrative review, showing the main differences between these two types of reviews, which was extremely useful for the present study. In addition, because it is a literature review, it was necessary to conduct research in online databases, databases that could make available the maximum number of studies, articles and research related to the topic addressed, thus, searches were made in the following databases: PROSPERO; Science Direct; Scielo; PubMed; The Cochrane Library in conjunction with Google Academy. Keywords were also used within the databases, with the aim of acquiring only information that is related to terms related to the topic, the following keywords were used: Melatonin; Periodontal Diseases; Bone Remodeling; Periodontics.

RESULTS

BIOLOGICAL PROPERTIES OF MELATONIN AND MECHANISM OF ACTION

Melatonin (N-acetyl-5-methoxytryptamine) is an indole synthesized from tryptophan, with its main production by the pineal gland, especially during the night, under the control of the light-dark cycle. However, its extrapineal production in tissues such as bone marrow, gastrointestinal mucosa, retina, skin, immune system and salivary glands gives it a multifaceted physiological role (Pandi-Perumal et al., 2006; Reiter et al., 2010). From a functional point of view, melatonin exerts a potent antioxidant action, acting both in the direct removal of free radicals (such as superoxide anion and peroxides) and in the induction of endogenous antioxidant enzymes, such as superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx) (Tan et al., 2007).

Furthermore, it has anti-inflammatory and immunomodulatory action, being able to inhibit central inflammatory pathways such as NF-κB and mitogen-activated protein kinase (MAPK), thus reducing the expression of inflammatory cytokines such as IL-1β, TNF-α and IL-6 (Konecná et al., 2021; Reiter et al., 2016). Specific melatonin receptors have been identified in several human tissues, including MT1 and MT2 receptors, belonging to the family of G-protein-coupled receptors. These receptors are present in bone cells

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(osteoblasts and osteoclasts), periodontal fibroblasts and immune cells (Balaji et al., 2021). The activation of these receptors induces the transcription of genes related to osteogenesis, such as RUNX2, essential for osteoblast differentiation, and increases the expression of bone matrix proteins such as osteocalcin and alkaline phosphatase, fundamental in the mineralization process (Cutando et al., 2013; Ramesh et al., 2025). Studies also show that melatonin can inhibit osteoclastic differentiation via downregulation of the RANK/RANKL/OPG pathway, which contributes to the preservation of alveolar bone tissue in periodontal inflammatory conditions (Balaji et al., 2021).

APPLICATIONS IN ORAL HEALTH: CLINICAL EVIDENCE

The role of melatonin in the oral cavity has been the subject of growing scientific interest. Preclinical evidence shows that melatonin administration in animal models of periodontitis leads to reduced alveolar bone loss, reduced neutrophil infiltration, and reduced activity of matrix metalloproteinases (MMPs), enzymes directly associated with collagen destruction (Konecná et al., 2021). In clinical practice, the study by Anton et al. (2021) in patients with type 2 diabetes and periodontitis demonstrated that oral supplementation with melatonin (3 mg/day for 8 weeks) in association with scaling and root planing resulted in significant improvements in periodontal clinical parameters, such as reduced probing depth (PD), increased clinical attachment level (CI), and reduced gingival bleeding index (GBI).

Similarly, Montero et al. (2017) reported that topical application of melatonin gel significantly reduced the levels of IL-6 and TNF-α in the gingival crevicular fluid of patients with chronic periodontitis, reinforcing its local anti-inflammatory action. Additionally, the study by Cutando et al. (2013) showed an increase in the expression of alkaline phosphatase and osteocalcin in patients treated with gingival application of melatonin, indicating osteogenic activity in vivo. Other studies have demonstrated an improvement in oral health-related quality of life, indicating that the use of melatonin can have a positive impact not only on clinical outcomes, but also on the patient's subjective perception of health (Sarac et al., 2024).

MELATONIN AS AN ADJUVANT IN CONVENTIONAL PERIODONTAL TREATMENT

Conventional periodontal treatment, based mainly on the mechanical removal of subgingival biofilm through scaling and root planing (SRP), constitutes the therapeutic pillar

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in the control of periodontal disease. However, in cases of advanced periodontitis or in systemically compromised patients — such as diabetics, immunosuppressed individuals or smokers — the clinical response to mechanical therapy alone may be limited (Kinane et al., 2017). In this context, the use of pharmacological or biological adjuvant agents, such as melatonin, has been proposed as a way to enhance therapeutic outcomes. Melatonin acts as an adjuvant through several mechanisms: (i) modulation of inflammation, with inhibition of pro-inflammatory cytokines and reduction of gingival inflammatory infiltrate; (ii) antioxidant action, which protects periodontal cells from degradation induced by reactive oxygen species; and (iii) stimulation of bone regeneration, with increased osteoblastic activity and inhibition of osteoclast differentiation (Balaji et al., 2021; Reiter et al., 2016).

In a meta-analysis conducted by Ramesh et al. (2025), involving 10 randomized controlled clinical trials, it was demonstrated that the administration of melatonin as an adjunct to RAR resulted in mean reductions in probing depth (PD) of 1.25 mm and clinical attachment gain (NCI) of 1.1 mm, compared to the control group that received only conventional mechanical treatment. These results were particularly more expressive in patients with type 2 diabetes mellitus, which reinforces the immunomodulatory role of melatonin in individuals with exacerbated chronic inflammatory states (Anton et al., 2021). Furthermore, studies such as that by Sarac et al. (2024) indicate that melatonin can significantly reduce serum levels of glycated hemoglobin (HbA1c), demonstrating beneficial systemic effects in diabetic patients.

These findings suggest that melatonin, in addition to acting locally in periodontitis, can contribute to systemic glycemic control, creating an advantageous bidirectional relationship. Regarding the route of administration, the studies used systemic (oral) and topical (gingival gel) forms. The oral form generally used dosages between 3 and 10 mg/day, for periods ranging from 4 to 12 weeks. Topical gels were applied locally to the affected periodontal areas, with equally favorable results, especially in reducing the rate of gingival bleeding and improving the quality of gingival tissue (Montero et al., 2017; Cutando et al., 2013).

DISCUSSION

Melatonin is an essential hormone in regulating the circadian cycle and the sensation of sleep for the human body, which has led large industries to start producing melatonin supplements, pills with this hormone in their composition, being used by people who have

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some difficulty sleeping, such as people with insomnia, or even by others who want to regulate their sleep after having disrupted their sleep cycle and schedule, which is very common in the society we live in today, which starts to sleep less hours, sleeps late and spends hours on screens on social networks, series or work using these media, which directly impacts their sleep and which the attempt to resolve is usually through melatonin supplementation.

As much as melatonin is effective and useful for regulating sleep, recent studies such as the systematic review with meta-analysis by Ramesh et al. 2025 point out its effectiveness in the treatment of periodontal diseases, using melatonin as an adjuvant to conventional treatment, bringing great statistical differences and effectiveness, with a great reduction in inflammation, reduction in probing depth, greater tooth insertion in addition to bone production, which proves the osteogenic, anti-inflammatory and antioxidant properties of melatonin, which makes us reflect on whether melatonin can be used in other dental treatments, such as endodontic treatment, which often faces conditions of bone loss, inflammation and loss of tooth insertion if left untreated.

These factors and properties of melatonin lead us to believe that melatonin may also be a possible future adjuvant to endodontic treatments, making it possible to accelerate osteogenic metabolism and combat inflammation. It is clear that melatonin is a hormone in which its supplementation associated with other dental treatments may be something promising, effective and extremely beneficial to the patient, which may be a great future ally for the dental surgeon. However, more randomized clinical trials are needed that compare conventional endodontic treatments without the use of melatonin and endodontic treatments with the use of melatonin as an adjuvant, in addition to more studies on its use in periodontics to obtain more scientific basis that complements what already exists.

Another factor that highlights the need for more studies that analyze and test the effectiveness and application of melatonin as an adjunct to periodontal treatment is the lack of standardization. There is still no standardization of how many milligrams should be used in melatonin supplementation when used as a complement in periodontal disease treatments. Published studies have presented different amounts, from 3 to 10 mg, showing the need for more studies that aim to identify how many milligrams is ideal and justify this, in order to obtain the best efficacy of the hormone. Another point that needs to be discussed is for what period of time supplementation should occur during periodontal treatment. Different studies have presented different times of use, without standardization. It is also

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necessary for new studies to seek to identify for what period of time it is ideal and beneficial to the body. Furthermore, existing studies only observe the beneficial sides of melatonin as an adjunct to periodontal treatment. However, new studies are needed to identify whether there is any negative systemic aspect, whether this supplementation can trigger any problems for the patient, such as decreased melatonin production by the body, increased sleep and even whether there is a chance of creating a dependency.

CONCLUSION

Several studies conducted in recent years have shown that patients who received melatonin associated with periodontal treatments had a reduction in probing depth and greater clinical insertion when compared to patients who underwent conventional periodontal treatments without the use of melatonin as an adjuvant. It is conclusive that melatonin has great potential and effectiveness when used as an adjuvant to periodontal treatment, with scientific evidence that shows and proves its positive effect.

However, there is a clear need for further studies that seek to standardize the amount of milligrams per melatonin tablet that should be ingested, in addition to standardizing the amount per day and for how long the patient should take this supplement. In addition, other studies should analyze whether this supplementation during periodontal treatment can cause negative systemic effects or not. Another conclusive point is in relation to the effectiveness of melatonin as an anti-inflammatory and for its osteogenic properties, being of extreme scientific importance that research be carried out that seeks to evaluate the possible effectiveness of melatonin as an adjuvant to endodontic treatments, taking into account that these properties can be beneficial within endodontics.

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