Journal of

Oral Science & Rehabilitation

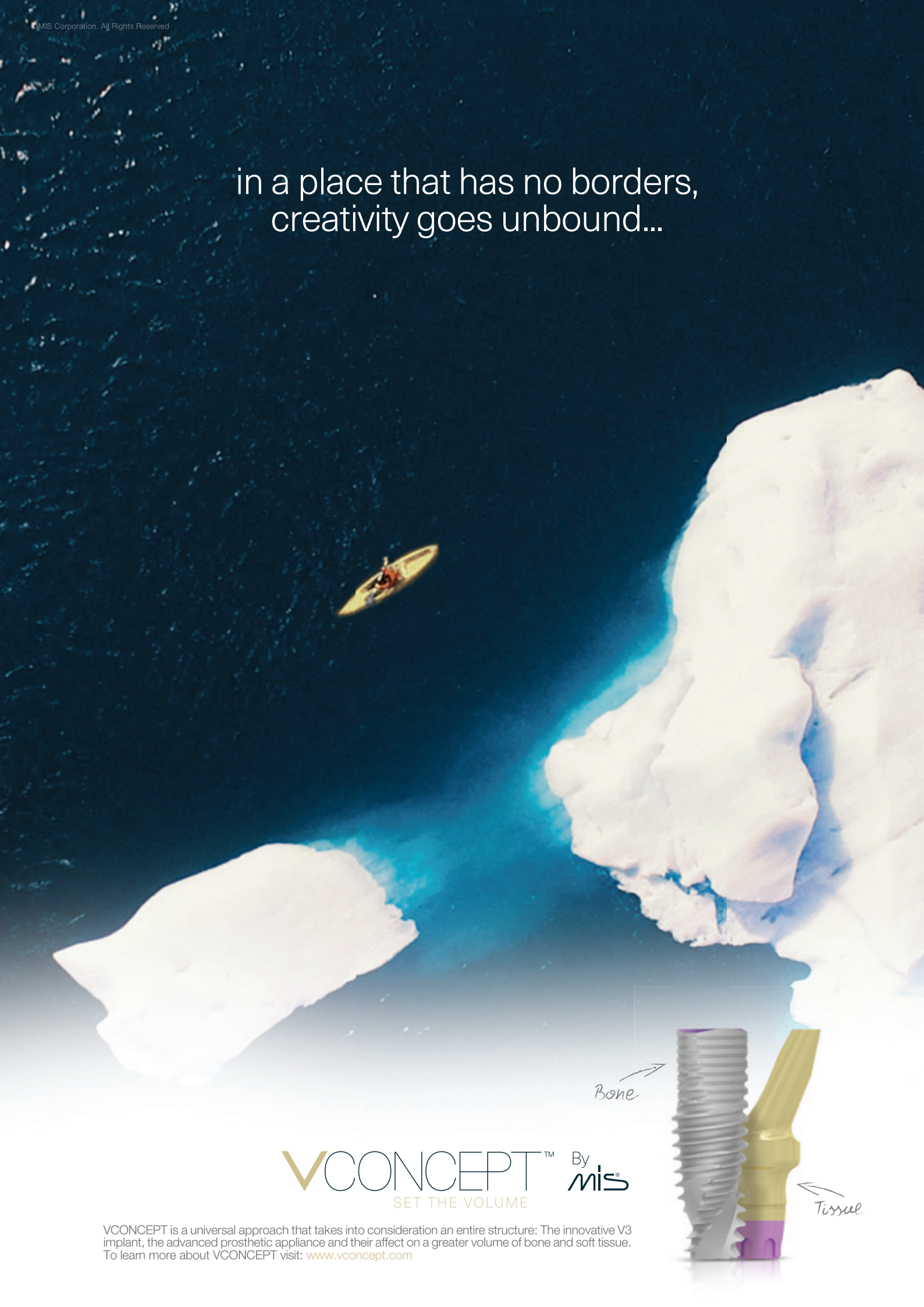
Journal for periodontology, implant dentistry, dental prosthodontics and maxillofacial surgery

ISSN 2365-6123

Volume 2 — Issue 2/2016

dti] Dental Tribune International

in a place that has no borders, creativity goes unbound...



VCONCEPT™ By MIS®

SET THE VOLUME

VCONCEPT is a universal approach that takes into consideration an entire structure: The innovative V3 implant, the advanced prosthetic appliance and their affect on a greater volume of bone and soft tissue. To learn more about VCONCEPT visit: www.vconcept.com

Journal of

Oral Science & Rehabilitation

For dentists, daily clinical work is as easy as driving a car. Their own experience provides them with the necessary confidence and skill. However, the situation changes with the introduction of a new method or product. In order to gain the requisite skill for performing a new technique, it may be enough to participate in practical courses. Using a new biomaterial for regeneration or sinus floor elevation may instead require small changes in technique. However, this may represent a substantial change in biology because biomaterials do not have the same response during healing and do not achieve the same results.

When we have doubts about the quality of a new technique or a new material, we often ask for the opinion of experts and we trust their advice. It would, however, be better to be already well prepared so that we may gain greater value from consultations with experts about the issue of interest.

Only through continued updating is it possible to gain the knowledge to help us make independent choices regarding materials and methods to be used in our daily practice and, indeed, the *Journal of Oral Science & Rehabilitation* was born out of a desire to update clinicians regarding new techniques and materials.

As said above, it is easy to drive a car. However, it may be useful to know how the car functions and how to fix it when it does not work properly.

Dr. Daniele Botticelli
Co-editor

Contents

ticare

TISSUE CARE PHILOSOPHY

Tissue care philosophy

- Implant-Prosthesis **adjustment**
- **Integrative surface**
- **Delicacy** in the **drilling** sequence
- **We care** for the **treatment,** we trace every **implant**

MOZOGRAU ticare

TISSUE CARE PHILOSOPHY

www.ticareimplants.com www.mozo-grau.com

About the *Journal of Oral Science & Rehabilitation*

The aim of the *Journal of Oral Science & Rehabilitation* is to promote rapid communication of scientific information between academia, industry and dental practitioners, thereby influencing the decision-making in clinical practice on an international level.

The *Journal of Oral Science & Rehabilitation* publishes original and high-quality research and clinical papers in the fields of periodontology, implant dentistry, prosthodontics and maxillofacial surgery. Priority is given to papers focusing on clinical techniques and with a direct impact on clinical decision-making and outcomes in the above-mentioned fields. Furthermore, book reviews, summaries and abstracts of scientific meetings are published in the journal.

Papers submitted to the *Journal of Oral Science & Rehabilitation* are subject to rigorous double-blind peer review. Papers are initially screened for relevance to the scope of the journal, as well as for scientific content and quality. Once accepted, the manuscript is sent to the relevant associate editors and reviewers of the journal for peer review. It is then returned to the author for revision and thereafter submitted for copy editing. The decision of the editor-in-chief is made after the review process and is considered final.

About Dental Tribune Science

Dental Tribune Science (DT Science) is an online open-access publishing platform (www.dtscience.com) on which the *Journal of Oral Science & Rehabilitation* is hosted and published.

DT Science is a project of the Dental Tribune International Publishing Group (DTI). DTI is composed of the leading dental trade publishers around the world. For more, visit

www.dental-tribune.com

Benefits of publishing in the journal for authors

There are numerous advantages of publishing in the *Journal of Oral Science & Rehabilitation*:

– Accepted papers are published in print and as e-papers on www.dtscience.com.

– Authors' work is granted exposure to a wide readership, ensuring increased impact of their research through open-access publishing on www.dtscience.com.

– Authors have the opportunity to present and promote their research by way of interviews and articles published on both www.dtscience.com and www.dental-tribune.com.

– Authors can also post videos relating to their research, present a webinar and blog on www.dtscience.com.

Subscription price

€50.00 per issue, including VAT and shipping costs.

Information for subscribers

The journal is published quarterly. Each issue is published as both a print version and an e-paper on www.dtscience.com.

Terms of delivery

The subscription price includes delivery of print journals to the recipient's address. The terms of delivery are delivered at place (DAP); the recipient is responsible for any import duty or taxes.

The role of melatonin in periodontal and periimplant bone homeostasis and regeneration

Pablo Galindo Moreno,[a] Gustavo Avila Ortiz,[b] Hom-Lay Wang,[c] Miguel Padial Molina,[a] Inmaculada Ortega Ollera[a] & Francisco O'Valle[d]

[a] Department of Oral Surgery and Implant Dentistry, School of Dentistry, University of Granada, Granada, Spain
[b] Department of Periodontics, College of Dentistry, University of Iowa, Iowa City, Iowa, U.S.
[c] Department of Periodontics and Oral Medicine, School of Dentistry, University of Michigan, Ann Arbor, Mich., U.S.
[d] Pathology Department, School of Medicine, and Institute of Biopathology and Regenerative Medicine, University of Granada, Granada, Spain

Corresponding author:

Dr. Pablo Galindo Moreno

C/ Recogidas, 39 5º Izq
18005 Granada
Spain

T +34 958 52 0658
F +34 958 52 0658
pgalindo@ugr.es

How to cite this article:

How to cite this article: Galindo Moreno P, Avila Ortiz G, Wang HL, Padial Molina M, Ortega Oller I, O'Valle F. The role of melatonin in periodontal and periimplant bone homeostasis and regeneration.

J Oral Science Rehabilitation. 2016 Jun;2(2):8–15.

Abstract

Background

Melatonin, a hormone produced primarily in the pineal gland, possesses a series of biological properties that appear to have an influence on bone homeostasis. Currently, little is known about how melatonin influences bone metabolism in periodontology and implantology.

Objectives

The objectives of this study are (1) to review the properties of melatonin in regulating bone homeostasis; (2) to discuss its direct and indirect effects on bone; and (3) to propose mechanisms for the use of melatonin as an agent to promote alveolar bone regeneration.

Conclusion

Melatonin positive regulation of bone formation and homeostasis, in combination with the inhibitory effects on bone resorption, highlights the potential use of melatonin as a marker of periodontal and periimplant bone-related diseases. *In vitro* and animal studies show promising results on the use of melatonin as a regenerative agent, although no clinical studies have yet been performed.

Keywords

Melatonin, osteoblasts, osteoclasts, periodontal disease, dental implant, free radicals.

Introduction

Numerous systemic hormonal changes are known to be associated with aging.[1] Some conditions linked to circadian rhythms and age may alter bone metabolism, resulting in changes in immune activity or bone-associated pathologies,[2] such as periodontal disease. These disorders may be associated with alterations in normal levels of melatonin.[3, 4]

Melatonin (*N*-acetyl-5-methoxytryptamine), a hormone that is endogenously synthesized, primarily in the pineal gland, is a molecule with intense antioxidant activity[5] and a wide range of biological actions, notably in the control of metabolism and bone development.[6] Melatonin is currently used in therapies as a coadjuvant in cancer therapy,[7] for anti-aging,[8] as an immunostimulatory agent[9] or as a sleep regulator,[10] as well as to increase bone density in menopausal patients[11] **(Fig. 1)**. It is reported that salivary melatonin is released by the acinar cells of the major salivary glands and the gingival crevicular fluid. It follows a circadian rhythm, with the highest values at night. Moreover, in the oral cavity, melatonin can act both by receptor-mediated and by receptor-independent pathways.[12] Therefore, through complex molecular pathways that have gained special interest for the research community in periodontology, it may play a role in alveolar periodontal and periimplant bone maintenance and regeneration.

Melatonin is an amphiphilic molecule that is able to cross most biological barriers. It can exert its effect by binding to G-protein-coupled membrane receptors (MT_1 and MT_2) or by penetrating the cell through a specific family of transmembrane channels,[13] subsequently initiating a nuclear or cytoplasmic molecular cascade. When it reaches the nuclei, melatonin binds to a subfamily of nuclear receptors key in regulating bone metabolism, the RZR (retinoid Z receptor)/ROR (retinoid orphan receptor) receptor.[14] It then regulates a number of cellular events, such as promotion of mitosis, induction of DNA repair,[15] or cell differentiation and proliferation.[16]

Interestingly, it is known that melatonin can be synthesized in the bone marrow, where its concentration is around 100-fold higher than in serum.[17] Furthermore, melatonin in the bone marrow protects its cells against cytotoxic agents *in vivo*.[18] However, the specific biochemical mechanisms that regulate this modulation, specifically in alveolar bone in humans, are currently not fully understood.[11] Hence, it is the purpose of this review to describe the properties of melatonin in regulating bone homeostasis, directly and indirectly, as well as to analyze different therapeutic strategies for the use of melatonin as an agent to promote periodontal and periimplant bone maintenance and regeneration **(Fig. 2)**.

Direct effects on bone

I. Melatonin and bone formation

The major organic component of bone extracellular matrix is Type I collagen, which supports the expression of bone cell phenotypes and enhances mineralization. Melatonin has been shown to regulate the synthesis of Type I collagen as a preliminary step to the expression of other bone-related proteins, such as bone sialoprotein, alkaline phosphatase and osteocalcin, during osteoblastic maturation.[16]

Bone sialoprotein (BSP) is referred to as a marker of the late stage of osteoblastic differentiation. BSP is expressed during osteoblastic cell differentiation in the extracellular matrix, where it is essential for osteoblast attachment and bone mineralization. Within this context, it has been reported that MC3T3 pre-osteoblast cells matured in 12 days in the presence of melatonin compared with 21 days without melatonin. Gene expression of BSP and related proteins of osteoblastic differentiation (e.g., osteocalcin, alkaline phosphatase) is also accelerated and increased in melatonin-treated compared with nontreated cells.[19] Furthermore, by inhibiting the interaction of BSP with osteoblastic cell lines, the activity of alkaline phosphatase, osteocalcin synthesis and cellular response to parathyroid hormone (PTH) are also inhibited[20] and, subsequently, osteoblast differentiation is impaired.[21] Thus, these findings suggest that melatonin may have an effect in regulating osteoblast proliferation and differentiation. These effects could lead to beneficial effects in the treatment of pathological processes associated with bone resorption or destruction by mediating not only in the expression of BSP but of other bone glycoproteins as well, resulting in enhanced bone apposition.

II. Melatonin and bone resorption

Melatonin also exerts an important direct biological action on the osteoclast, another key cell in