Effects of Melatonin on Periodontitis and Alveolar Bone Loss : a Review

〔REVIEW〕

Effects of Melatonin on Periodontitis and Alveolar Bone Loss : a Review

Nazmus SHALEHIN[1], Md Riasat HASAN[1,2], Kazuharu IRIE[1]

[1] Division of Histology, Department of Oral Growth and Development, Health Sciences University of Hokkaido, Japan
[2] Division of Clinical Cariology and Endodontology, Department of Oral Rehabilitation, Health Sciences University of Hokkaido, Japan

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Abstract

Alveolar bone loss is a very common phenomenon in periodontal disease. Previous studies have suggested that melatonin decreases aggressive inflammation and alveolar bone loss in periodontitis. This article will review the advanced effects of melatonin that might be clinically beneficial for the treatment of diabetic or non–diabetic periodontitis.

Introduction :

Periodontitis is a term that describes a group of inflammatory diseases affecting the periodontium. In cases of periodontitis, alveolar bone loss is very common and recent papers have suggested that melatonin (chemical name : N–acetyl–5–methoxy tryptamine) decreases aggressive inflammation and alveolar bone loss in periodontitis. Melatonin is a pineal gland indoleamine hormone with anti–inflammatory and immunomodulatory effects (Kara et al., 2013 ; Arabaci et al., 2015). Melatonin possesses antimicrobial properties against a variety of bacteria and viruses (Tekbas et al., 2008 ; Boga et al., 2012) and its lipophilic nature allows the easy and rapid contact with cells and cellular components (Menendez–Pelaez et al., 1993). Melatonin is present in some foods including cherries, bananas, grapes, rice, cereal, herbs, plums, olive oil, wine, beer, orange, and pineapple (Hattori et al., 1995 ; Catherine, 2011). It is medically used in sleep disorders, jet lag, headaches, cancer, gallstones, protection from radiation, tinnitus, and psychiatric disorders (Srinivasan et al., 2009). It causes very few side effects, including dizziness and drowsiness (Buscemi et al., 2005).

Antioxidant effects :

Melatonin is a wide–spectrum antioxidant and a powerful scavenger of free–radical oxygen and nitrogen species (Arnao and Hernandez–Ruiz , 2006 ; Tan et al., 1993). Melatonin is an antioxidant that easily crosses cell membranes and the blood–brain barrier (Poeggeler et al., 1994). Melatonin was reported to be twice as active as vitamin E, which was thought to be the most effective lipophilic antioxidant (Lowes et al., 2013). An important characteristic of melatonin that distinguishes it from other classic radical scavengers is that its metabolites are also scavengers ; this is termed “the cascade reaction” (Tan et al., 2007). Another study indicated that melatonin also protects against mitochondrial oxidative stress (Carrillo–Vico et al., 205). In addition to its scavenger effects, melatonin indirectly stimulates various antioxidant enzymes (Kara et al., 2013 ; Arabaci et al., 2015 ;). Furthermore, melatonin is superior to other antioxidants because it does not become pro–oxidative when it loses an electron during interactions with free radicals (Czesnikiewicz– Guzik et al., 2007).

Antidiabetic effects :

Many studies have also highlighted the potent antidiabetic properties of melatonin (Golbidi et al., 2011 ; Zephy and Ahmad, 2015 ; Muhlbauer et al., 2007 ; Picinato et al., 2002) . Melatonin administration significantly reduced plasma glucose levels in rats with diabetes mellitus (DM), providing evidence that melatonin is a potent antidiabetic (Limson et al., 1998 ; Dubocovich et al., 2010). It directly affects insulin release by interacting with MT1 and MT2 receptors located on the surface of pancreatic beta cells (Muhlbauer et al., 2007). Melatonin inhibits adenylate cyclase–cy-

clic adenosine monophosphate (MT1 and MT2) and guanylate cyclase–cyclic guanosine monophosphate systems (MT2) via a Gi–protein signaling cascade to reduce the release of insulin (Limson et al., 1998 ;). In addition, melatonin synthesis was decreased when insulin release was increased (Kemp et al., 2002) and insulin release was decreased after melatonin administration (Picinato et al., 2002). This close relationship between insulin and melatonin levels indicates that melatonin supplementation might be beneficial for controlling insulin levels and preventing diabetic complications (Kose et al., 2016).

Immunomodulatory effects :

Melatonin interacts with the immune system (Arusanian and Beier, 2002). However, the details of these interactions are unclear. The anti–inflammatory effects of melatonin seem to be the most relevant and most documented in the literature to date. However, there have been few trials designed to judge the effectiveness of melatonin in disease treatment. Most existing data are based on small, incomplete clinical trials. Another study suggested melatonin might be useful against infectious diseases (Limson et al., 1998) including viral disease such as HIV, bacterial infections, and cancer.

Effects on Periodontitis and Alveolar Bone Loss

A recent study evaluated the potential effects of melatonin administration on myeloperoxidase (MPO) activity and alveolar bone destruction. MPO activities, osteoclasts, the RANKL/osteoprotegerin (OPG) ratio and neutrophil densities were increased in periodontitis, which might be responsible for alveolar bone loss (Kose et al., 2016). Melatonin administration significantly reduced gingival tissue MPO levels and stimulated the proliferation of osteoblasts to promote bone formation (Roth et al.,1999). Gingival tissue neutrophil density, RANKL–positive osteoclast density, and the cemento–enamel junction/alveolar bone rest distance were significantly higher in cases of periodontitis with and without DM, but were significantly reduced following melatonin administration. Although melatonin is a popular antioxidant and antidiabetic agent, a limited number of studies have investigated the influence of melatonin on periodontitis (Kose et al., 2016). Recent studies showed that melatonin decreased inflammation and alveolar bone loss in rats with periodontitis through its immunomodulatory and antioxidant effects (Kara et al., 2013 ; Arabaci et al., 2015). Following the treatment of mice with melatonin, the mineral apposition rate and osteoid volume were increased, indicating that melatonin predominantly increases bone mass, and suppresses osteoclast number and bone resorption ; however, it did not increase the histomorphometric bone formation parameters (Koyama et al., 2002).

Topical use of Melatonin :

Cudanto et al. evaluated the effects of topical melatonin (1% orabase cream formula) administered to the surface of attached gingiva for 20 days in cases of periodontitis with DM or healthy individuals (Cutando et al., 2014). The topical melatonin administration significantly decreased clinical periodontal parameters (gingival index and probing depth), alkaline and acid phosphatase enzyme levels, and RANKL levels while increasing OPG levels (Cutando et al., 2013).

Systemic administration of Melatonin :

Kose et al. evaluated the effects of systemic melatonin treatment on hyperglycemia–induced oxidative stress and alveolar bone loss (Kose et al., 2016). The study showed that melatonin administration decreased neutrophil density and MPO activity in cases of periodontitis with and without DM. These effects might be associated with the ability of melatonin to decrease neutrophil counts and phagocytic activity in the periodontal field during the inflammatory activity of periodontitis, which might prevent alveolar bone loss (Kose et al., 2016). Furthermore, melatonin regulates the number and activities of osteoblasts and osteoclasts (Kose et al., 2016). A significant reduction in alveolar bone loss after melatonin administration might be related to its regulation of oxidative and inflammatory balances via its antioxidant, immunomodulatory, and antidiabetic effects (Kose et al., 2016).

Summary :

Melatonin might be clinically beneficial for the treatment of diabetic or non–diabetic periodontitis. However, additional studies are required to explain the effectiveness of melatonin for the treatment of periodontitis and bone loss.

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Nazmus SHALEHIN

Education

2013 *Bachelor of Dental Surgery* (BDS) from City Dental College, under Dhaka University

Professional Experiences

2015 to 2016 Medical Officer (OPD), City Dental College, Dhaka, Bangladesh.

2016–Present Division of Histology, Department of Oral Growth and Development, Health Sciences University of Hokkaido, Japan