

Bölüm 2

ANTİOKSIDANLARIN PERİODONTOLOJİDE KULLANIMI

Alper KIZILDAĞ¹

Periodontitis bakteriyel enfeksiyon sonucu başlayan ve konak dokunun bu enfeksiyona cevabı ile doku yıkımının ilerlediği bir hastalık olarak kabul görmektedir (1). Periodontitisin neden olduğu destek dokulardaki kemik kaybına bağlı olarak dişin kaybı meydana gelebilmektedir. Bununla birlikte periodontitisin kariyovasküler hastalıklar ve diyabet gibi çeşitli metabolik rahatsızlıklar ile ilişkili olduğu belirtilmiştir (2).

Reaktif oksijen türleri (ROT) birçok enflamatuvar hastalığın ilerlemesinde önemli rol oynadığından dolayı son yıllarda üzerinde durulan bir konu haline gelmiştir (3). ROT hücreler tarafından üretilmektedir ve normal hücresel aktiviteler için gereklidir. Bununla birlikte ROT antioksidan aktivitesi tarafından dengelenmekte ve dokular üzerindeki zararlı etkileri engellenmektedir. Herhangi bir sebepten dolayı ROT üretimi arttığında veya antioksidan aktivitesi azaldığında oksidatif stres ortaya çıkar ve periodontal dokularda yıkım meydana gelir (4). ROT lipit peroksidasyonuna, DNA ve protein hasarına, çeşitli enzimlerin oksidasyonuna ve enflamatuvar sitokinlerin artışına neden olabilmektedir (5). Ayrıca nükleer faktör kappa B reseptör aktivatör ligandi (RANKL) üzerinde de rol oynayarak osteoklast hücrelerinin formasyonunda ve hayatı kalmasında etkili olur (6).

Bu sebepten dolayı ROT'un neden olduğu periodontal harabiyeti engellemek amacıyla çeşitli antioksidanlar kullanılmaktadır. Bu kitap bölümünde periodontolojide kullanılan bir kısım antioksidanlardan ve bu antioksidanların etkilerinden bahsedilecektir.

ANTİOKSIDANLAR

Antioksidanların Periodontal Sağlık Üzerine Etkileri

Antioksidanlar dişeti ve periodontal iyileşme süresince fibroblast göçünü ve çoğalmasını düzenleyerek fonksiyonel mekanizmalar üzerinde rol oynarlar. Antioksidanlar etkilerini 3 mekanizma ile göstermektedirler.

1. Dokuların yıkımından sorumlu olan sitokinlerin, kemokinlerin ve proenflamatuvar proteinlerin üretimini azaltır.

¹ Dr. Öğretim Üyesi, Pamukkale Üniversitesi, Diş Hekimliği Fakültesi Periodontoloji Anabilim Dalı, alperkizildag@pau.edu.tr

liseminin neden olduğu oksidatif stresi ve alveolar kemik kaybını anti-diyabetik ve anti-oksidatif özellikleri sayesinde azalttığı gösterilmiştir (75). İmplant ile ilgili yapılan çalışmalarda ise topikal melatonin uygulamasının implant etrafındaki yeni kemik oluşumunu uyardığı tespit edilmiştir (76,77).

KAYNAKÇA

- 1 Bartold PM, Van Dyke TE. Periodontitis: a host-mediated disruption of microbial homeostasis. Unlearning learned concepts. *Periodontol* 2000. 2013;62(1):203-217.
- 2 Nazir MA. Prevalence of periodontal disease, its association with systemic diseases and prevention. *Int J Health Sci.* 2017;11(2):72-80.
- 3 Mittal M, Siddiqui MR, Tran K, et al. Reactive oxygen species in inflammation and tissue injury. *Antioxid Redox Signal.* 2014;20(7):1126-1167.
- 4 Chapple IL, Matthews JB. The role of reactive oxygen and antioxidant species in periodontal tissue destruction. *Periodontol* 2000. 2007;43(1):160-232.
- 5 Wei PF, Ho KY, Ho YP, et al. The investigation of glutathione peroxidase, lactoferrin, myeloperoxidase and interleukin-1 β in gingival crevicular fluid: implications for oxidative stress in human periodontal diseases. *J Periodontal Res.* 2004;39(5):287-293.
- 6 Galli C, Passeri G, Macaluso G. FoxOs, Wnts and oxidative stress-induced bone loss: new players in the periodontitis arena? *J Periodontal Res.* 2011;46(4):397-406.
- 7 Battino M, Bullon P, Wilson M, et al. Oxidative injury and inflammatory periodontal diseases: the challenge of anti-oxidants to free radicals and reactive oxygen species. *Crit Rev Oral Biol Med.* 1999;10(4):458-476.
- 8 Kaklamanos E, Tsalikis L. A review on peri-implant crevicular fluid assays potential in monitoring and predicting peri-implant tissue responses. *J Int Acad Periodontol.* 2002;4(2):49-59.
- 9 Patel K, Srinivasan K. Bioavailability of micronutrients from plant foods: an update. *Crit Rev Food Sci Nutr.* 2016;56(10):1608-1619.
- 10 Bohlooli S, Barmaki S, Khoshkhahesh F, et al. The effect of spinach supplementation on exercise-induced oxidative stress. *J Sports Med Phys Fitness.* 2015;55(6):609-614.
- 11 Zhao M, Liu X, Luo Y, et al. Evaluation of protective effect of freeze-dried strawberry, grape, and blueberry powder on acrylamide toxicity in mice. *J Food Sci.* 2015;80(4):869-874.
- 12 Mates J. Effects of antioxidant enzymes in the molecular control of reactive oxygen species toxicology. *Toxicology.* 2000;153(1-3):83-104.
- 13 Sukhtankar L, Kulloli A, Kathariya R, et al. Effect of non-surgical periodontal therapy on superoxide dismutase levels in gingival tissues of chronic periodontitis patients: A clinical and spectrophotometric analysis. *Dis Markers* 2013;34(5):305-311.
- 14 Akalin FA, Toklu E, Renda N, et al. Analysis of superoxide dismutase activity levels in gingiva and gingival crevicular fluid in patients with chronic periodontitis and periodontally healthy controls. *J Clin Periodontol.* 2005;32(3):238-243.
- 15 Kim SC, Kim OS, Kim OJ, et al. Antioxidant profile of whole saliva after scaling and root planning in periodontal disease. *J Periodontal Implan.* 2010;40(4):164-171.
- 16 Scandalios J. Oxidative stress: molecular perception and transduction of signals triggering antioxidant gene defenses. *Braz J Med Biol Res.* 2005;38(7):995-1014.
- 17 Chapple I, Brock G, Eftimidi C, et al. Glutathione in gingival crevicular fluid and its relation to local antioxidant capacity in periodontal health and disease. *Mol Pathol.* 2002;55(6):367-373.
- 18 Daiya S, Sharma RK, Tewari S, et al. Micronutrients and superoxide dismutase in postmenopausal women with chronic periodontitis: a pilot interventional study. *J Periodontal Implan.* 2014;44(4):207-213.
- 19 Trivedi S, Lal N, Mahdi AA, et al. Association of salivary lipid peroxidation levels, antioxidant enzymes, and chronic periodontitis. *Int J Periodontics Restorative Dent.* 2015;35(2):14-19.

- 20 Ellis S, Tucci M, Serio F, et al. Factors for progression of periodontal diseases. *J Oral Pathol Med.* 1998;27(3):101-105.
- 21 Panjamurthy K, Manoharan S, Ramachandran CR, et al. Lipid peroxidation and antioxidant status in patients with periodontitis. *Cell Mol Biol Lett.* 2005;10(2):255-264.
- 22 Maxwell SR, Dietrich T, Chapple IL. Prediction of serum total antioxidant activity from the concentration of individual serum antioxidants. *Clin Chim Acta.* 2006;372(1-2):188-194.
- 23 Akalin FA, Işıksal E, Baltacıoğlu E, et al. Superoxide dismutase activity in gingiva in type-2 diabetes mellitus patients with chronic periodontitis. *Arch Oral Biol.* 2008;53(1):44-52.
- 24 Akalin FA, Baltacıoğlu E, Alver A, et al. Total antioxidant capacity and superoxide dismutase activity levels in serum and gingival crevicular fluid in pregnant women with chronic periodontitis. *J Periodontol.* 2009;80(3):457-467.
- 25 Tonguç MÖ, Öztürk Ö, Sütçü R, et al. The impact of smoking status on antioxidant enzyme activity and malondialdehyde levels in chronic periodontitis. *J Periodontol.* 2011;82(9):1320-1328.
- 26 Agnihotri R, Pandurang P, Kamath SU, et al. Association of cigarette smoking with superoxide dismutase enzyme levels in subjects with chronic periodontitis. *J Periodontol.* 2009;80(4):657-662.
- 27 Duarte PM, Napimoga MH, Fagnani EC, et al. The expression of antioxidant enzymes in the gingivae of type 2 diabetics with chronic periodontitis. *Arch Oral Biol.* 2012;57(2):161-168.
- 28 Trivedi S, Lal N, Mahdi AA, et al. Evaluation of antioxidant enzymes activity and malondialdehyde levels in patients with chronic periodontitis and diabetes mellitus. *J Periodontol.* 2014;85(5):713-720.
- 29 Schwager J, Schulze J, et al.. Modulation of interleukin production by ascorbic acid. *Vet Immunol Immunopathol.* 1998;64(1):45-57.
- 30 Campbell JD, Cole M, Bunditrutavorn B, et al. Ascorbic acid is a potent inhibitor of various forms of T cell apoptosis. *Cell Immunol.* 1999;194(1):1-5.
- 31 Field CJ, Johnson IR, Schley PD. Nutrients and their role in host resistance to infection. *J Leukoc Biol.* 2002;71(1):16-32.
- 32 Geesin JC, Darr D, Kaufman R, et al. Ascorbic acid specifically increases type I and type III pro-collagen messenger RNA levels in human skin fibroblasts. *J Invest Dermatol.* 1988;90(4):420-424.
- 33 Shiga M, Kapila YL, Zhang Q, et al. Ascorbic acid induces collagenase-1 in human periodontal ligament cells but not in MC3T3-E1 osteoblast-like cells: potential association between collagenase expression and changes in alkaline phosphatase phenotype. *J Bone Miner Res.* 2003;18(1):67-77.
- 34 Boxer LA, Vanderbilt B, Bonsib S, et al. Enhancement of chemotactic response and microtubule assembly in human leukocytes by ascorbic acid. *J Cell Physiol.* 1979;100(1):119-126.
- 35 Melnick SL, Roseman JM, Engel D, et al. Epidemiology of acute necrotizing ulcerative gingivitis. *Epidemiol Rev.* 1988;10:191-211.
- 36 Vogel R, Wechsler S. Nutritional survey of patients with moderate to severe periodontitis. *Clin Prev Dent.* 1979;1(5):35-38.
- 37 Blignaut J, Grobler S. High fruit consumption and the periodontal status of farm workers. *Clin Prev Dent.* 1992;14(2):25-28.
- 38 Cohen M, Meyer D. Effect of dietary vitamin E supplementation and rotational stress on alveolar bone loss in rice rats. *Arch Oral Biol.* 1993;38(7):601-606.
- 39 Beck MA, Kolbeck PC, Rohr LH, et al. Vitamin E deficiency intensifies the myocardial injury of coxsackievirus B3 infection of mice. *J Nutr.* 1994;124(3):345-358.
- 40 Singh N, Narula SC, Sharma RK, et al. Vitamin E supplementation, superoxide dismutase status, and outcome of scaling and root planing in patients with chronic periodontitis: a randomized clinical trial. *J Periodontol.* 2014;85(2):242-249.
- 41 Nizam N, Discioglu F, Saygun I, et al. The effect of α -tocopherol and selenium on human gingival fibroblasts and periodontal ligament fibroblasts in vitro. *J Periodontol.* 2014;85(4):636-644.

- 42 Kim JE, Shklar G. The effect of vitamin E on the healing of gingival wounds in rats. *J Periodontol.* 1983;54(5):305-308.
- 43 Slade JE, Bartuska D, Rose LF, et al. Vitamin E and periodontal disease. *J Periodontol.* 1976;47(6):352-354.
- 44 Vinson JA, Jang J. In vitro and in vivo lipoprotein antioxidant effect of a citrus extract and ascorbic acid on normal and hypercholesterolemic human subjects. *J Med Food.* 2001;4(4):187-192.
- 45 Hirasawa M, Takada K, Makimura M, et al. Improvement of periodontal status by green tea catechin using a local delivery system: a clinical pilot study. *J Periodontal Res.* 2002;37(6):433-438.
- 46 Kushiyama M, Shimazaki Y, Murakami M, et al. Relationship between intake of green tea and periodontal disease. *J Periodontol.* 2009;80(3):372-377.
- 47 Nakamura H, Ukai T, Yoshimura A, et al. Green tea catechin inhibits lipopolysaccharide-induced bone resorption in vivo. *J Periodontal Res.* 2010;45(1):23-30.
- 48 Linden GJ, McClean KM, Woodside JV, et al. Antioxidants and periodontitis in 60–70-year-old men. *J Clin Periodontol.* 2009;36(10):843-849.
- 49 Walston J, Xue Q, Semba RD, et al. Serum antioxidants, inflammation, and total mortality in older women. *Am J Epidemiol.* 2005;163(1):18-26.
- 50 Yamaguchi M, Uchiyama S. β -Crytoxanthin stimulates bone formation and inhibits bone resorption in tissue culture in vitro. *Mol Cell Biochem.* 2004;258(1-2):137-144.
- 51 Wood N, Johnson RB. The relationship between tomato intake and congestive heart failure risk in periodontitis subjects. *J Clin Periodontol.* 2004;31(7):574-580.
- 52 Velazquez C, Navarro M, Acosta A, et al. Antibacterial and free-radical scavenging activities of Sonoran propolis. *J Appl Microbiol.* 2007;103(5):1747-1756.
- 53 Park YK, Alencar SM, Aguiar CL, et al. Botanical origin and chemical composition of Brazilian propolis. *J Agric Food Chem.* 2002;50(9):2502-2506.
- 54 Orsi R, Sforcin J, Rall V, et al. Susceptibility profile of *Salmonella* against the antibacterial activity of propolis produced in two regions of Brazil. *J Venom Anim Toxins Incl Trop Dis.* 2005;11(2):109-116.
- 55 Seidel V, Peyfoon E, Watson DG, et al. Comparative study of the antibacterial activity of propolis from different geographical and climatic zones. *Phytother Res.* 2008;22(9):1256-1263.
- 56 Kujumgiev A, Tsvetkova I, Serkedjieva Y, et al. Antibacterial, antifungal and antiviral activity of propolis of different geographic origin. *Journal of ethnopharmacology.* 1999;64(3):235-240.
- 57 Murray M, Worthington H, Blinkhorn A, et al. A study to investigate the effect of a propolis-containing mouthrinse on the inhibition of de novo plaque formation. *J Clin Periodontol.* 1997;24(11):796-798.
- 58 Aral CA, Kesim S, Greenwell H, et al. Alveolar bone protective and hypoglycemic effects of systemic propolis treatment in experimental periodontitis and diabetes mellitus. *J Med Food.* 2015;18(2):195-201.
- 59 El-Sharkawy HM, Anees MM, Van Dyke TE. Propolis improves periodontal status and glycemic control in patients with type 2 diabetes mellitus and chronic periodontitis: a randomized clinical trial. *J Periodontol.* 2016;87(12):1418-1426.
- 60 Michaluart P, Masferrer JL, Carothers AM, et al. Inhibitory effects of caffeic acid phenethyl ester on the activity and expression of cyclooxygenase-2 in human oral epithelial cells and in a rat model of inflammation. *Cancer Res.* 1999;59(10):2347-2352.
- 61 Park EH, Kahng JH. Suppressive effects of propolis in rat adjuvant arthritis. *Arch Pharm Res.* 1999;22(6):554.
- 62 Chen YJ, Shiao MS, Wang SY, et al. The antioxidant caffeic acid phenethyl ester induces apoptosis associated with selective scavenging of hydrogen peroxide in human leukemic HL-60 cells. *Anticancer Drugs.* 2001;12(2):143-149.
- 63 Koltuksuz U, Mutuş HM, Kutlu R, et al. Effects of caffeic acid phenethyl ester and epidermal growth factor on the development of caustic esophageal stricture in rats. *J Pediatr Surg.* 2001;36(10):1504-1509.

- 64 Celik S, Gorur S, Aslantas O, et al. Caffeic acid phenethyl ester suppresses oxidative stress in Escherichia coli-induced pyelonephritis in rats. *Mol Cell Biochem.* 2007;297(1-2):131-138.
- 65 Ha J, Choi HS, Lee Y, et al. Caffeic acid phenethyl ester inhibits osteoclastogenesis by suppressing NF κ B and downregulating NFATc1 and c-Fos. *Int Immunopharmacol.* 2009;9(6):774-780.
- 66 Ucan M, Koparal M, Ağaçayak S, et al. Influence of caffeic acid phenethyl ester on bone healing in a rat model. *J Int Med Res.* 2013;41(5):1648-1654.
- 67 Kazancioglu HO, Bereket MC, Ezirganli S, et al. Effects of caffeic acid phenethyl ester on wound healing in calvarial defects. *Acta Odontol Scand.* 2015;73(1):21-27.
- 68 Yiğit U, Kirzioğlu FY, Uğuz AC, et al. Is caffeic acid phenethyl ester more protective than doxycycline in experimental periodontitis? *Arch Oral Biol.* 2017;81:61-68.
- 69 Redman JR. Circadian entrainment and phase shifting in mammals with melatonin. *J Biol Rhythms.* 1997;12(6):581-587.
- 70 Cajochen C, Kräuchi K, Wirz-Justice A. Role of melatonin in the regulation of human circadian rhythms and sleep. *J Neuroendocrinol.* 2003;15(4):432-437.
- 71 Park KH, Kang JW, Lee EM, et al. Melatonin promotes osteoblastic differentiation through the BMP/ERK/Wnt signaling pathways. *J Pineal Res.* 2011;51(2):187-194.
- 72 Bartold PM, Wiebkin OW, Thonard JC, et al. The effect of oxygen-derived free radicals on gingival proteoglycans and hyaluronic acid. *J Periodontal Res.* 1984;19(4):390-400.
- 73 Diab-Ladki R, Pellat B, Chahine R, et al. Decrease in the total antioxidant activity of saliva in patients with periodontal diseases. *Clin Oral Investig.* 2003;7(2):103-107.
- 74 Arabaci T, Kermen E, Özkanlar S, et al. Therapeutic effects of melatonin on alveolar bone resorption after experimental periodontitis in rats: A biochemical and immunohistochemical study. *J Periodontol.* 2015;86(7):874-881.
- 75 Kose O, Arabaci T, Kara A, et al. Effects of melatonin on oxidative stress index and alveolar bone loss in diabetic rats with periodontitis. *J Periodontol.* 2016;87(5):e82-e90.
- 76 Guardia J, Gómez-Moreno G, Ferrera MJ, et al. Evaluation of effects of topical melatonin on implant surface at 5 and 8 weeks in Beagle dogs. *Clin Implant Dent Relat Res.* 2011;13(4):262-268.
- 77 Muñoz F, López-Peña M, Miño N, et al. Topical application of melatonin and growth hormone accelerates bone healing around dental implants in dogs. *Clin Implant Dent Relat Res.* 2012;14(2):226-235.