GENGIGEL®
Hyaluronic Acid

ORAL HEALTH & SMOKE
FACT FILE

HOW CAN SMOKING AFFECT ORAL HEALTH?

Oral diseases and disorders whose incidence is related to smoking include oral cancer and precancer, periodontal disease, caries and tooth loss, gingival recession and other benign mucosal disorders as well as implant failure (Warnakulasuriya, 2010). Concerning oral cancer, the differential risk analyses between nonsmokers and heavy smokers, and the steady progression of risk with increasing amount smoked both provide sufficient evidence for smoking tobacco as a major risk factor. This is due to carcinogenic compounds in tobacco smoke that induce mutagenic events causing multiple types of genetic disruption in chromosomes and genes eventually leading to cancer.

risk of periodontitis

85%

Smoking tobacco is also a major risk factor for periodontal disease. This conclusion stems from several studies that have been carried out in a variety of settings, greatly increasing the generalizability of the findings. In all the studies that have estimated the smoking associated relative risk at more than one level of periodontal disease severity, the relative risk was observed to increase as the severity level increases, suggesting an exposure gradient or a 'dose-response' relationship (Warnakulasuriya, 2010). A recent meta-analysis on the subject showed that smoking increases the risk of periodontitis by 85% (Leite, 2018). Smoking also induces tooth loss: increased rates of tooth loss among smokers have been observed in a number of longitudinal studies, some concerning data over more than a decade (Warnakulasuriya, 2010). Similarly, the negative effect of smoking on caries incidence and implant failure is well-known and established. Smoking has also been reported to cause brown/black discolouration of teeth, dental restorations and dentures, alteration of taste and smell, to be associated with a coated tongue (black hairy tongue), and to impair and delay wound healing after dentoalveolar surgical procedures such as tooth extractions (Meechan, 1998). Furthermore, smokers are more susceptible to oral candidosis (Warnakulasuriya, 2010).

taste alteration

smell alteration

HOW DOES SMOKING FAVOR THE ONSET OF PERIODONTITIS?

The association between smoking and the periodontal disease has still not been fully clarified, as it seems to be multifactorial. In smokers, the periodontal tissues are continuously exposed to nicotine and its metabolites due to deposition of nicotine on the root surface (Cuff, 1989) and cotinine levels (a metabolite of nicotine) are elevated in saliva and gingival crevicular fluid (Chen, 2001). Cigarette smoking is likely to affect the composition of the oral microflora due to a decrease in oxygen tension in periodontal pockets and may lead to a selection of anaerobic bacteria (Hanioka, 2000). Tobacco smoking affects the humoral mediated and the cell mediated immunity of the host and this may increase susceptibility to periodontal disease (Palmer, 2005; Gunsolley, 1997; Loos, 2004; Ryder, 2007; Ryder, 2002; Tangada, 1997). There is evidence for an impact of smoking on bone metabolism such as an increased secretion of the bone resorbing factors PGE2 and IL-1ß74 or a decreased intestinal uptake of calcium (Krall, 1999), and these factors may also increase susceptibility to periodontal disease in smokers. It is very likely that tobacco smoking disrupts the physiological turnover of tooth-supporting structures with the net effect being periodontal tissue breakdown (Palmer, 2005; Ryder, 2007; Johnson, 2007). Paradoxically, smokers present significantly less gingival inflammation and a lower gingival crevicular fluid volume compared with nonsmokers: smoking may decrease gingival bleeding and crevicular fluid volume as a result of changes in the proportion of blood vessels and vascular alterations in periodontal tissues, a condition again favoring periodontium disrupting (Nociti, 2015). Similar multifactorial mechanisms seem to be at the root of impaired or delayed wound healing (Nociti, 2015).

HOW DO SMOKERS RESPOND TO PERIODONTAL TREATMENT?

Clinical studies have long compared the response of smokers and nonsmokers to various types of periodontal treatments, including nonsurgical and surgical therapies (Johnson, 2004). In general, the results have shown that smoking promotes an unfavorable clinical response (i.e. worse reductions in probing depth and lower gains in clinical attachment) to nonsurgical and surgical periodontal therapies, as well as to regenerative and plastic periodontal procedures (Andia, 2008; Bowers, 2003; Dannewitz, 2006; Heasman, 2006; Martins, 2004; Patel, 2012; Preber, 1986; Silva, 2006; Soder, 1999). Smoking is also a major risk factor for poor response to initial treatment in subjects with generalized aggressive periodontitis and treated with nonsurgical periodontal therapy (Hughes, 2006). Previous data revealed that approximately 90% of cases of refractory periodontitis are observed in smokers (MacFarlane, 1992; Magnusson, 1996) and that heavy smoking is a risk factor for disease progression after active periodontal therapy (Matuliene, 2008). Studies have shown that smokers present a worse clinical response to scaling and root planing than do nonsmokers (Grossi, 2007; Heasman, 2006; Wan, 2009). Although the adverse effects of smoking on health may persist for many years, such effects may be reversible after quitting the smoking habit. Therefore, smoking cessation seems to be a relevant approach to reduce the risk of periodontitis and improve the response to periodontal therapies in smokers.

WHY RESORTING TO NON-DRUG TREATMENTS?

As the smoking habit reduces the effect of scaling and root planing, several studies have proposed the use of adjunctive therapeutic approaches (i.e. local/systemic antimicrobials and anti-inflammatory agents) to improve the effects of basic periodontal therapy in smokers. With regard to antimicrobial therapies, a systematic review has revealed that the evidence for an additional benefit of adjunctive antimicrobial therapy in smokers with chronic periodontitis is lacking and questionable. Regarding anti-inflammatory drugs, it has been proposed that a subantimicrobial dose of doxycycline, as an adjunct to scaling and root planing, may contribute to the reduction of the degradation of connective periodontal tissue collagen and the severity of inflammation in periodontitis (Caton, 2011). Preshaw et al. (Preshaw, 2005) demonstrated that both smokers and nonsmokers could benefit from a systemic subantimicrobial dose of doxycycline; however, nonsmokers receiving this doxycycline therapy demonstrated the greatest clinical attachment level gains and probing depth reductions. Needleman et al. (Needleman, 2007) also evaluated the effects of low-dose doxycycline or placebo administration, associated with nonsurgical periodontal therapy, in smokers. However, the authors did not observe any benefit from the use of doxycycline as an adjunct to nonsurgical periodontal therapy in smokers after 3 months. Kurtis et al. (Kurtis, 2007) evaluated the effects of scaling and root planing and adjunctive flurbiprofen, a nonsteroidal anti-inflammatory agent, on the levels of prostaglandin and thiobarbituric acid-reactive substance in gingival crevicular fluid from smokers and nonsmokers with chronic periodontitis. Administration of flurbiprofen, as an adjunct to scaling and root planing, had an increased inhibitory effect on the levels of such mediators in smokers, compared with nonsmokers. Evidence concerning drug treatment is, accordingly, still limited and this is still a field of active clinical research (Nociti, 2015).

WHY HIGH MOLECULAR WEIGHT HYALURONIC ACID?

Hyaluronic acid (HA), or hyaluronan, is a naturally occurring non-sulphated, linear polymer composed of repeating units of glucuronic acid and N-acetylglucosamine (Chen, 1999; Kavasi, 2017). HA levels are particularly high in the extracellular matrix of tissues undergoing rapid turnover, where regeneration and repair are occurring, such as the oral mucosa (Valachová, 2016). HA has many different functions, including maintenance of tissue homeostasis and cell surface protection, but is also involved in many physiological processes, such as cell attachment, migration and proliferation, embryogenesis, wound healing, and regulation of immune response and inflammation (Kavasi, 2017). High molecular weight hyaluronic acid (HMWHA) is deposited in normal tissues and interacts with other components of the ECM to control the structural organization of ECM and signalling. In general, endogenous HMWHA possesses enhanced anti-angiogenic, anti-inflammatory and immunosuppressive properties (Kavasi, 2017). High molecular weight hyaluronic acid (HMWHA) is a linear molecule with a highly complex secondary and tertiary structure in aqueous solution; its amphophilic nature allows this molecule to trap large quantities of water and, at the same time, to bond to hydrophobic molecules such as the lipidic substances of cell membranes (Scott, 1998). This property is relevant in controlling hydration and contributes to retardation of viral and bacterial passage through the hyaluronan-rich pericellular zone, as well as during periods of change when HA levels are elevated, during inflammatory processes (Chen, 1999). Clinical studies have shown that HA accelerates the healing of various types of wounds, including burns, epithelial surgical wounds, and chronic wounds (Shaharudin, 2016).

Why Gengigel®?

The devices belonging to the Gengigel® family achieve their expected performance due to the action of its principal component, high molecular weight hyaluronic acid, (HMWHA), which makes Gengigel® strongly bioadhesive, an effect that may be enhanced by using a calibrated mixture of some ancillary glycopolymers. In this way Gengigel® adheres to the oral mucosa for long enough to promote the activation of the physiological tissue repair process, improving the healing response and reducing healing time. Further, by maintaining the balance of extracellular fluids, again because of the presence of high molecular weight hyaluronic acid, it promotes resorption of oedema in inflammatory states, rapidly reducing the associated pain. Last but not least, it protects the oral mucosa from harmful agents, preserving the micro-environment of the mucosal surface, and regularizing the growth of bacterial flora.

Clinical evidence concerning Gengigel® includes clinical data from prospective, comparative studies, which can thus be considered to be of high quality. Furthermore, several studies had a split-mouth design, which facilitated their interpretation by minimizing the effects of inter-patient variability. The studies covered different Gengigel® indications, including management of clinical signs associated with periodontal disease or gingival inflammation following surgical periodontal therapy. In all cases, the patients were treated with the gel formulation, either in a single application given at the time of surgery, or with multiple applications following the initial periodontal surgery/treatment. Depending on the study, the follow-up period varied between 7 days and 6 months, providing sound clinical data on the effectiveness of long-term treatment with Gengigel®.

REFERENCES

Andia DC, Martins AG, Casati MZ, Sallum EA, Nociti FH. Root coverage outcome may be affected by heavy smoking: a 2-year follow-up study. J Periodontol 2008: 79: 647–653.

Bowers GM, Schallhorn RG, McClain PK, Morrison GM, Morgan R, Reynolds MA. Factors influencing the outcome of regenerative therapy in mandibular Class II furcations: Part I. J Periodontol 2003: 74: 1255–1268.

Caton J, Ryan ME. Clinical studies on the management of periodontal diseases utilizing subantimicrobial dose doxycycline (SDD). Pharmacol Res 2011: 63: 114–120.

Chen WY, Abatangelo G. Functions of hyaluronan in wound repair. Wound Repair Regen. 1999 Mar-Apr;7(2):79-89.

Chen X, Wolff L, Aeppli D et al. Cigarette smoking, salivary/gingival crevicular fluid cotinine and periodontal status. A 10-year longitudinal study. J Clin Periodontol 2001 28 4: 331-339.

Cuff MJ, McQuade MJ, Scheidt MJ et al. The presence of nicotine on root surfaces of periodontally diseased teeth in smokers. J Periodontol 1989 60 10: 564-569.

Dannewitz B, Krieger JK, Husing J, Eickholz P. Loss of molars in periodontally treated patients: a retrospective analysis five years or more after active periodontal treatment. J Clin Periodontol 2006: 33: 53–61.

Grossi SG, Goodson JM, Gunsolley JC, Otomo-Corgel J, Bland PS, Doherty F, Comiskey J. Mechanical therapy with adjunctive minocycline microspheres reduces red-complex bacteria in smokers. J Periodontol 2007: 78: 1741– 1750.

Gunsolley JC, Pandey JP, Quinn SM et al. The effect of race, smoking and immunoglobulin allotypes on IgG subclass concentrations. J Periodontal Res 1997 32 4: 381-387.

Hanioka T, Tanaka M, Takaya K et al. Pocket oxygen tension in smokers and non-smokers with periodontal disease. J Periodontol 2000 71 4: 550-554.

Heasman L, Stacey F, Preshaw PM, McCracken GI, Hepburn S, Heasman PA. The effect of smoking on periodontal treatment response: a review of clinical evidence. J Clin Periodontol 2006: 33: 241–253.

Hughes FJ, Syed M, Koshy B, Bostanci N, McKay IJ, Curtis MA, Marcenes W, Croucher RE. Prognostic factors in the treatment of generalized aggressive periodontitis: II. Effects of smoking on initial outcome. J Clin Periodontol 2006: 33: 671–676.

Johnson GK, Hill M. Cigarette smoking and the periodontal patient. J Periodontol 2004: 75: 196–209.

Kavasi RM, Berdiaki A, Spyridaki I, Corsini E, Tsatsakis A, Tzanakakis G, Nikitovic D. HA metabolism in skin homeostasis and inflammatory disease. Food Chem Toxicol. 2017 Mar; 101:128-138.

Krall EA, Dawson-Hughes B. Smoking increases bone loss and decreases intestinal calcium absorption. J Bone Miner Res 1999 14 2: 215-220. Johnson GK, Guthmiller JM. The impact of cigarette smoking on periodontal disease and treatment. Periodontology 2000 2007 44: 178-194.

Kurtis B, Teuter G, Serdar M, Pinar S, Demirel I, Toyman U. Gingival crevicular fluid prostaglandin E(2) and thiobarbituric acid reactive substance levels in smokers and non-smokers with chronic periodontitis following phase I periodontal therapy and adjunctive use of flurbiprofen. J Periodontol 2007: 78: 104–111.

Leite FRM, Nascimento GG, Scheutz F, López R. Effect of Smoking on Periodontitis: A Systematic Review and Meta-regression. Am J Prev Med. 2018 Jun;54(6):831-841.

Loos BG, Roos MT, Schellekens PT et al. Lymphocyte numbers and function in relation to periodontitis and smoking. J Periodontol 2004 75 4: 557-564.

MacFarlane GD, Herzberg MC, Wolff LF, Hardie NA. Refractory periodontitis associated with abnormal polymorphonuclear leukocyte phagocytosis and cigarette smoking. J Periodontol 1992: 63: 908–913.

Magnusson I, Walker CB. Refractory periodontitis or recurrence of disease. J Clin Periodontol 1996: 23: 289–292.

Martins AG, Andia DC, Sallum AW, Sallum EA, Casati MZ, Nociti FH Jr. Smoking may affect root coverage outcome: a prospective clinical study in humans. J Periodontol 2004: 75: 586–591.

Matuliene G, Pjetursson BE, Salvi GE, Schmidlin K, Bragger U, Zwahlen M, Lang NP. Influence of residual pockets on progression of periodontitis and tooth loss: results after 11 years of maintenance. J Clin Periodontol 2008: 35: 685–695.

Meechan JG, Macgregor ID, Rogers SN et al. The effect of smoking on immediate post-extraction socket filling with blood and on the incidence of painful socket. Br J Oral Maxillofac Surg 1988 26 5: 402-409.

Needleman I, Suvan J, Gilthorpe MS, Tucker R, St George G, Giannobile W, Tonetti M, Jarvis M. A randomized-controlled trial of low-dose doxycycline for periodontitis in smokers. J Clin Periodontol 2007: 34: 325–333.

Nociti FH Jr, Casati MZ, Duarte PM. Current perspective of the impact of smoking on the progression and treatment of periodontitis. Periodontol 2000. 2015 Feb;67(1):187-210.

Palmer RM, Wilson RF, Hasan AS et al. Mechanisms of action of environmental factors--tobacco smoking. J Clin Periodontol 2005 32 Suppl 6: 180-195.

Patel RA, Wilson RF, Palmer RM. The effect of smoking on periodontal bone regeneration: a systematic review and meta-analysis. J Periodontol 2012: 83: 143–155.

REFERENCES

Preber H, Bergstrom J. Cigarette smoking in patients referred for periodontal treatment. Scand J Dent Res 1986: 94: 102–108.

Preshaw PM, Hefti AF, Bradsha MH. Adjunctive subantimicrobial dose doxycycline in smokers and non-smokers with chronic periodontitis. J Clin Periodontol 2005: 32: 610–616.

Ryder MI, Wu TC, Kallaos SS et al. Alterations of neutrophil f-actin kinetics by tobacco smoke: implications for periodontal diseases. J Periodontal Res 2002 37 4: 286-292.

Ryder MI. The influence of smoking on host responses in periodontal infections. Periodontol 2000 2007 43: 267-277.

Shaharudin A, Aziz Z. Effectiveness of hyaluronic acid and its derivatives on chronic wounds: a systematic review. J Wound Care. 2016 Oct 2;25(10):585-592.

Silva CO, Sallum AW, de Lima AF, Tatakis DN. Coronally positioned flap for root coverage: poorer outcomes in smokers. J Periodontol 2006: 77: 81–87.

Soder B, Nedlich U, Jin LJ. Longitudinal effect of non-surgical treatment and systemic metronidazole for 1 week in smokers and non-smokers with refractory periodontitis: a 5-year study. J Periodontol 1999: 70: 761–771.

Tangada SD, Califano JV, Nakashima K et al. The effect of smoking on serum IgG2 reactive with Actinobacillus actinomycetemcomitans in early-onset periodontitis patients. J Periodontol 1997 68 9: 842-850

Valachová K, Volpi N, Stern R, Soltes L. Hyaluronan in Medical Practice. Curr Med Chem. 2016;23(31):3607-3617.

Wan CP, Leung WK, Wong MC, Wong RM, Wan P, Lo EC, Corbet EF. Effects of smoking on healing response to non-surgical periodontal therapy: a multilevel modelling analysis. J Clin Periodontol 2009: 36: 229–239.

Warnakulasuriya S, Dietrich T, Bornstein MM, Casals Peidró E, Preshaw PM, Walter C, Wennström JL, Bergström J. Oral health risks of tobacco use and effects of cessation. Int Dent J. 2010 Feb;60(1):7-30.

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Via Egadi, 7 - 20144 Milano – Italy
info@ricerfarma.com