

An effect of smoking on wound healing following extraction: A critical study

Dr. Kanwaldeep Singh Soodan, Dr. Pratiksha Priyadarshni, Dr. Kuljeet kaur

Abstract: Cigarette smoking has long been suspected to adversely affect wound healing but in Asian history tobacco was attributed as a medicinal plant. It was often used to avert hunger during long hours of work. But in reality, it causes various ill effects including pre-malignant lesions and cancers. Tobacco affects postoperative wound healing following surgical and non-surgical tooth extractions, routine maxillofacial surgeries, implants and periodontal therapies. Smoking tobacco is also associated with catecholamines release resulting in vasoconstriction and decreased tissue perfusion. Smoking is believed to suppress the innate and host-immune responses, affecting the function of neutrophils, the prime line of defence against infection. Thus, the association between smoking and delayed healing of oral tissues following surgeries is evident.

Key words: Tobacco, healing effects, dry socket, dental extractions.

I. Introduction

Dental extractions are routine dental procedures that are carried out in dental department. Removal of tooth removal depends on the various factors including the post extraction instructions followed by patients. A favourable architecture of alveolar ridge with sufficient alveolar bone volume is necessary to obtain functional and esthetic prosthetic rehabilitation. Knowledge about healing process at extraction site is essential to avoid insufficient bone volume.

Tobacco was introduced in India by Portuguese in 16th century. Today, use and production of tobacco has increased to such an extent that it has become the second largest production in the world [1]. Nicotine is a vasoconstrictor that decreases blood flow to the tissue, results in tissue ischemia and impairs healing of injured tissue. Nicotine also decreases platelet adhesion, raising the risk of micro-vascular occlusion and tissue ischemia. In addition, nicotine has well known harmful effects related to tissue healing such as inhibition of angiogenesis, re-epithelialization and osteogenesis along with cellular healing such as inhibition of fibroblast proliferation and adhesion and collagen synthesis [2-10].

The healing events in the tooth extraction socket terminate in the form of woven bone, which ultimately remodels resulting in the restoration of defect [11]. In general, smoking exerts harmful effects on bone and diminishes the blood filling of post-extraction socket and consequently has an adverse effect on healing of extraction wound [12]. Cigarette smoking constitutes >4000 toxic contents in gas or particulate form. Toxins of more interest are nicotine and carbon-monoxide that diminishes oxygen transport whereas hydrogen cyanide inhibits the enzymes that are necessary for oxidative metabolism and oxygen transport at cellular level.

II. Smoking and its effects on Healing

Wound healing is a dynamic process that involves number of phase's i.e. inflammatory phase, proliferation phase and maturation phase. Inflammatory phase is the body's natural response to injury. After injury, clot is formed. Once the hemostasis is achieved, blood vessels dilate to allow the essential cells, antibodies, WBCs, growth factors, enzymes and nutrients to reach the injured area. Neutrophils and macrophages come into their action. During proliferative phase, fibroblast lay down the collagen to form the granulation tissue along with angiogenesis and later epithelialization occurs. Maturation phase involves remodeling of collagen. Cellular activity reduces and the number of blood cells decreases in number.

When cigarette is inhaled, the toxins can directly poison the cilia or pass the cilia barrier, undergo tissue absorption, enter into bloodstream and gain access to other parts of body. Cigarette smoke constitutes number of toxic contents [Table 1].

Gas Phase	Particulate Phase
Carbon dioxide	Particulate matter
Carbon monoxide	Nicotine
Hydrogen cyanide	Catechol
Nitrogen oxides	Phenol
Acetone	N-nitrosornicotine
Formaldehyde	Quinoline
Acrolein	Aniline
Ammonia	2-Toulidine

Pyridine	Nickle
3-Vinylpyridine	N-nitrosodiethandamine
N-Nitrosodimethylamine	Benzo[a]-Pyrene
N-Nitrosopyrrolidine	2-Naphthylamine

With each cigarette smoked, approximately 20-30ml of carbon monoxide and 2-3mg of nicotine are inhaled [13]. Carbon monoxide produced during combustion of tobacco also reduces capillary blood flow. A clinical study has shown that a single cigarette can reduce the peripheral blood velocity by 40% in 1 hour [14].

Nicotine exerts several effects that influence wound healing. First, proliferation of RBCs, fibroblasts and macrophages are diminished [13]. Second, it increases platelet adhesiveness which causes microclots formation raising the risk of micro-vascular occlusion and tissue ischemia [15]. Third, nicotine produces cutaneous vasoconstriction. This vasoconstriction results from release of catecholamines which also raise heart rate, blood pressure and oxygen demand [4]. Various studies have shown that release of catecholamines results in stimulation of chalone hormone formation that reduces wound healing by decreasing the rate of epithelialisation [4].

The affinity of binding of carbon monoxide for hemoglobin is 200 times than that of oxygen. Resulting, carbon monoxide inhibits binding of oxygen, reduces the oxygen carrying capacity of hemoglobin which ultimately reduces the amount of oxygen to reach the periphery [13]. In addition, when carboxyhemoglobin levels rise in blood, the oxygen dissociates curve shifts to the left that means oxygen is less able to dissociate from RBCs and diffuse into the tissues, so the decrease in the levels of oxygen available for tissue perfusion results into cellular hypoxia and diminished wound healing [16, 17]. Wound healing also requires enzymes. Hydrogen cyanide inhibits enzyme system that is required for oxidative metabolism and oxygen transport at cellular level [18]. All together, the ill effects of toxic substances of smoking have potential to diminish the conditions that are required for proper wound repair and healthy scar formation.

III. Clinical side effects of smoking

1) Dry socket

Cryer et al stated that smoking is associated with endogenous release of catecholamines resulting in vasoconstriction and tissue perfusion [19]. Information on number of cigarettes smoked per day and the post-operative smoking habit of each patient were recorded. According to them, heat released from burning tobacco and tobacco along with its byproducts may act as contaminant in the surgical site together with the suction applied to the cigarette that might dislodge the clot from the alveolus interfering healing of the socket. Larsen evaluated the risk factors associated with development of localized osteitis after the extraction of 138 third molars. He found use of tobacco is associated with increased incidence of dry socket compared to other factors like age, sex, usage of oral contraceptives and increased surgical time [20]. According to Meechan et al, fibrinolytic activity caused by smoking decreases the blood supply to the surgical site after extraction and dry socket was found common amongst these smoker patients [12]. Extractions were performed in 2417 patients and incidence of painful socket was analyzed. It was observed that post-operatively poor filling of blood in socket, were found more likely to develop painful socket ($p > 0.002$). Post-operative socket filling with blood was greatly reduced in smokers compared with non-smokers ($p > 0.001$). Incidence of painful socket in heavy smokers (who smokes 20 or more cigarettes per day) was higher compared with non-smokers (> 0.005). Al-belasy et al evaluated the risk of developing localized osteitis in water pipe (shisha) smokers [19]. They found that cigarette and shisha smokers were 3-4 times more prone to develop dry socket than non-smokers. They found that smoking on the day of surgery and increased frequencies of smoking significantly increase the incidence of dry socket. According to Lopez Carriches et al, after extraction of third molar, smokers were more prone to develop trismus than non-smokers. However, they didn't observe significant difference in relation of pain [21].

According to Sweet et al, the suction associated with cigarette might dislodge the blood clot from alveolus socket and interrupt the healing. However, Alxender denies the fact that suction during smoking cause physical dislodgement of the clot [22]. Al-belasy et al believed that dry socket is caused by destruction of clot rather than physical dislodgement [19]. Though the exact mechanism by which smoking predisposes the socket become painful remains unclear, smoking seems to be strictly associated with the occurrence of dry socket.

Effect of smoking upon healing following routine oral surgical procedures

Smoking is reported to be important factor responsible for post-operative infections leading to hindrance in bone healing. A meta-analysis by Ward KD et al reported the magnitude of the association between cigarette smoking and bone mass and showed that smokers presented reduce bone mass, compared with non-smoker [23]. Saldanha et al in six months study reported that the smoking may affect remodeling process following tooth extraction. In their study, alveolar bone height lost significantly more (1.5mm) in smokers as compared to non-smokers (1mm). They also reported that radiographic bone density was more pronounced in smokers than non-smokers. They believed that smoking increases the bone resorption at the fracture bone ends,

interfering with the osteoblastic function [24]. Cheynet et al in their study of infections complications of 60 mandibular osteotomies, smoking was observed as important risk factor responsible for post-operative infections [25]. Levin et al observed greater complications following surgeries in smokers. They suggested that heat released from cigarette smoke and toxic by-products of tobacco such as nicotine, hydrogen cyanide and carbon monoxide could be risk factors affecting the success of dental procedures [26].

Interference of smoking on periodontal therapy

Cigarette smoking is significant risk factor for periodontal diseases and impairs healing after periodontal surgeries [27]. Unlike usage of smokeless tobacco that causes gingival recession at the site of placement, the usage of smoking tobacco causes widespread periodontal destruction. Tomar et al and Beck et al conducted two population based epidemiological studies in which they found periodontitis is more common in smokers than non-smokers [28, 29]. Number of clinical studies have been performed to compare the response of smokers and non-smokers to different types of surgical and non-surgical periodontal therapies [29-33] and it was found that smoking has a strong negative impact on regenerative therapy including osseous grafting [31], guided tissue regeneration [34-37] or combination of these treatments [38] and 80% failure rate in the treatment of furcation involvement defects. The majority studies found that gingival grafting for root coverage procedure is less successful than non-smokers [39-41].

IV. Discussion

Cigarette smoking affects the oral cavity in various ways ranging from staining of the teeth to more serious diseases such as oral cancer. According to lots of data reviewed, smoking has various risk factors including impaired wound healing. Treatment complications and failures in smokers inspired them for investigation of relative risks associated with smoking and the mechanism for compromised wound healing.

Nadler reported that smoking reduced urinary levels of prostacyclin (PGI₂), a prostaglandin that causes vasodilatation and decrease platelet aggregation [42]. Reus demonstrated that smoking causes vasoconstriction and diminished blood flow in ears of nude mice exposed to tobacco smoke [43]. Mosely noticed that nicotine impair's wound healing from 6th-10th day in the rabbit ear [4]. Harmful effects of nicotine were believed to damage erythrocyte precursors as well as vasoconstriction and inhibition of epithelization. In 1976 Cryer, reported that smoking is associated with epinephrine and nor-epinephrine release, resulting in vasoconstriction and decreased tissue perfusion [23]. Rief Kohl noticed accelerated irreversible histological changes of endarteritis obliterans in microvasculature of chronic smoker [44]. In animal studies, using controlled skin flaps, exposure to cigarette smoke significantly raised the risk for skin slough and ultimately necrosis. Lawrence et al investigated the survival of skin flap in rats exposed to cigarette smoke post-operatively [45]. They observed impaired wound healing and decreased rate of flap survival as they attributed to vasoconstriction due to nicotine as well as endogenous release of catecholamines, increased platelet aggregation leading to diminished flow, increased hemoglobin and fibrinogen levels with resultant increased viscosity and increased levels of carboxyhemoglobin resulting in reduced oxygen transport and changes in vascular endothelium of endarteritis.

Prevalence of ulcerative gingivitis, acute necrotizing ulcerative gingivitis and periodontitis is also increased in smokers [46-48]. Clarke et al observed tissue ischemia as a etiology for these diseases based on gingival vascular anatomy and the lack of collateral circulation to the papillary gingival [49, 50]. By using thermal diffusion principle to measure gingival blood flow in rabbits, injection of epinephrine and nicotine as well as their combinations resulted in significantly impaired gingival blood flow with some tendency for tachyphylaxis to the effect of epinephrine but little to nicotine.

V. Conclusion

The components of cigarette smoke clearly have an inhibitory effect on wound healing. Combined effects of nicotine, carbon monoxide and hydrogen cyanide are tissue ischemia, cellular hypoxia, inhibition of proliferation of epithelial cells, vasoconstriction, poisoning of enzymes and a decrease in oxygen carrying capacity of blood cells required for wound healing. All the clinicians should take these complicating factors into account and advise the patient to quit habit and inform them about prognosis of treatment.

References

- [1]. Reddy KS, Gupta PC, editors. Report on Tobacco control in India. Ministry of Health and Family Welfare, New Delhi: Government of India; 2004.
- [2]. Daftari Tk, Whitesides jr Te, Heller Jg, Goodrich Ac, Mccarey Be, Hutton Wc. Nicotine on the revascularization of bone graft. An experimental study in rabbits. Spine 1994; 19: 904-911.
- [3]. Peacock EE, Van Winkle W. Wound repair. 2nd ed. Philadelphia: WB Saunders; 1976.
- [4]. Mosely LH, Finseth F, Goody M. Nicotine and its effect in wound healing. Plast Reconstruction Surgery 1978; 61:570-575.
- [5]. Sheveleva GA, Kiryuschenkov AP, Sheina NI, Silantyeva IV. Effects of nicotine on the mother embryo system under exposure throughout the entire pregnancy. Farmacologiiani Toksikologiiia 1984; 47:78-83.

- [6]. Paulson RB, Shanfeld J, Mullet B, Cole J, Paulson JO. Prenatal smokeless tobacco effects on rat fetus. *J Craniofac Genet Develop* 1994; 14:16-25.
- [7]. Fang Ma, Frost Pj, Iida-Klein A, Hahn Tj. Effects of nicotine on cellular function in UMR 106-01 osteoblast like cells. *Bone* 1991; 12:283-286.
- [8]. Peacock ME, Sutherland DE, Schuster GS, Brennan WAO, O'Neal RB, Strong SL, Van dyke TE. The effect of nicotine on reproduction and attachment of human gingival fibroblasts in vitro. *J Periodontol* 1993; 64:658-665.
- [9]. Galvin Rj, Ramp Wk, Lenz Lg. Smokeless tobacco contains a non-nicotine inhibitor of bone metabolism. *Toxicol Appl Pharmacol* 1988; 95:292-300.
- [10]. Ramp WK, Lenz LG, Galvin RJS. Nicotine inhibits collagen synthesis and alkaline phosphatase activity, but stimulates DNA synthesis in osteoblast-like cells. *Soc Exp Biol Med* 1991; 197:36-43.
- [11]. Evian CI, Rosenberg ES, Coselet JG, Corn H. The osteogenic activity of bone removed from healing extraction sockets in humans. *J Periodontol* 1982;53:81-85.
- [12]. Meechan JG, Macgregor ID, Rogers SN, Hobson RS, Bate JP, Dennison M. 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; 26:402-409.
- [13]. The health consequences of smoking: cardiovascular disease. A report of the surgeon general. Rockville, Maryland: U.S. Department of Health and Human Services, 1983.
- [14]. Sherwin MA, Gastwirth CM. Detrimental effects of cigarette smoking on lower extremity wound healing. *J Foot Surg.* 1990;29:84-7.
- [15]. Mayfield L, Soderholm G, Hallstorm H, Kullendorff B, Edwardsson S, Bratthall G, et al. Guided tissue regeneration for the treatment of intraosseous defects using a bioabsorbable membrane: a controlled clinical study. *J Clin. Periodontol* 1998;25:585-95
- [16]. Al-Belasy FA. The relationship of "shisha" (water pipe) smoking to postextraction dry socket. *J Oral Maxillofac Surg* 2004; 62:10-4.
- [17]. Nolan J, Jenkins RA, Kurihara K, Schultz RC. The acute effects of cigarette smoke exposure on experimental skin flaps. *Plast Reconstr Surg* 1985; 75:544-9.
- [18]. Rees TD. The acute effects of cigarette smoke exposure on experimental skin flaps: a discussion. *Plast Reconstr Surg* 1985; 75:550-1.
- [19]. Mosely LH, Finseth F. Cigarette smoking: impairment of digital blood flow and wound healing in the hand. 1977; 9:97-101.
- [20]. Cryer PE, Haymond MW, Santiago JV, Shah SD. Norepinephrine and epinephrine release and adrenergic medication of smoking-associated hemodynamic and metabolic events. *N Engl. J Med* 1976; 295:573-7.
- [21]. Sweet JB, Butler DP. The relationship of smoking to localized osteitis. *J Oral Surg* 1979; 37:732-5.
- [22]. Larsen PE. Alveolar osteitis after surgical removal of impacted third molars: Identification of the patient at risk. *Oral Surg Oral Med Oral Pathol.* 1992; 73:393-7.
- [23]. Lo'pez-Carriches C, Go'mez-Font R, Martinez-Gonzalez JM, Donado-Rodriguez M. Influence of smoking upon the postoperative course of lower third molar surgery. *Med Oral Patol Oral Cir Bucal* 2006; 11:E56-60.
- [24]. Ward KD, Klesges RC. A meta-analysis of the effects of cigarette smoking on bone mineral density. *Calcify Tissue Int* 2001; 68:259-270.
- [25]. Saldanha JB, Casati MZ, Neto FH, Sallum EA, Nociti FH Jr. Smoking may affect the alveolar process dimensions and radiographic bone density in maxillary extraction sites: A prospective study in humans. *J Oral Maxillofac Surg* 2006; 64:1359-65.
- [26]. Cheynet F, Chossegros C, Richard O, Ferrara JJ, Blanc JL. Infectious complications of mandibular osteotomy. *Rev Stomatol Chir Maxillofac* 2001; 102:26-33.
- [27]. Levin L, Schwartz-Arad D. The effects of cigarette smoking on dental implants and related surgery. *Implant Dent* 2005; 14:357-61.
- [28]. Winn DM. Tobacco use and oral disease. *J Dent Educ.* 2001; 65:306-12.
- [29]. Tomar SL, Asma S. Smoking- attributable periodontitis in the united states: Findings from NHANES III: National Health and Nutrition Examination Survey. *J Periodontol* 2000; 71:743-51.
- [30]. Beck JD, Cusmano L, Green-Helms W, Koch GG, Offenbacher S. A five year old study of attachment loss in community- dwelling older adults: incidence density. *J Periodontol Res* 1997; 32:506-15.
- [31]. Ah MK, Johnson GK, Kaldahl WB, Patil KD, Kalkwarf KL. The effect of smoking on the response to periodontal therapy. *J Clin periodontal* 1994; 21:91-7.
- [32]. Preber H, Bergstrom J. Effect of non surgical treatment on gingival bleeding in smokers and non smokers. *Acta Odontol Scand* 1986; 44:85-9.
- [33]. Grossi SG, Zambon J, Machtei EE, Schifferle R, Andreana S, Genco RJ, et al. Diabetics and smokers. *J Periodontol* 1996; 67:1094-102.
- [34]. Grossi SG, Zambon J, Machtei EE, Schifferle R, Andreana S, Genco RJ, et al. Effects of smoking and smoking cessation on healing after mechanical periodontal therapy. *J Am. Dent Assoc* 1997; 128:599-607.
- [35]. Rosen PS, Marks MH, Reynolds MA. Influence of smoking on long-term clinical results of intrabony defects treated with regenerative therapy. *J Periodontol* 1996; 67:1159-63.
- [36]. Rosenberg ES, Cutler SA. The effect of cigarette smoking on the longterm success of guided tissue regeneration: A preliminary study. *Ann R Australas Coll Dent Surg* 1994; 12:89-93.
- [37]. Kaldahl WB, Johnson GK, Patil KD, Kalkwarf KL. Levels of cigarette consumption and response to periodontal therapy. *J Periodontol* 1996;67:675-81
- [38]. Trombelli L, Kim CK, Zimmerman GJ, Wikesjo UM. Retrospective analysis of factors related to clinical outcome of guided tissue regeneration procedures in intrabony defects. *J Clin Periodontol* 1997; 24:366-71.
- [39]. Luepke PG, Mellonig JT, Brunsvold MA. A clinical evaluation of a bioresorbable barrier with and without decalcified freeze-dried bone allograft in the treatment of molar furcations. *J Clin Periodontol* 1997; 24:440-6.
- [40]. Miller PD Jr. Root coverage with the free gingival graft: Factors associated with incomplete coverage. *J Periodontol* 1987; 58:674-81.
- [41]. Muller HP, Eger T, Schorb A. Gingival dimensions after root coverage with free connective tissue grafts. *J Clin Periodontol* 1998; 25: 424-30.
- [42]. Zucchelli G, Clauser C, De Sanctis M, Calandriello M. Mucogingival versus guided tissue regeneration procedures in the treatment of deep recession type defects. *J Periodontol* 1998; 69:138-45.
- [43]. Nadler JL, Velasco JS, Horton R: Cigarette smoking inhibits prostacyclin formation. *Lancet* 1: 1248, 1983.
- [44]. Reus WF, Robson MC, Zachary L, et al: Acute effects of tobacco smoking on blood flow in the cutaneous microcirculation. *Br J Plast Surg* 37:213, 1984.

- [45]. Riefkohl R, Wolfe JA, Cox EB, et al: Association between cutaneous occlusive vascular disease, cigarette smoking, and skin slough after rhytidectomy. *Plast Reconstr Surg* 77:592, 1986.
- [46]. Lawrence WT, Murphy RC, Robson MC, et al: The detrimental effect of cigarette smoking on flap survival; An experimental study in the rat. *Br J Plast Surg*. 37:2 16. 1984
- [47]. Rees TD, Liverett DM, Guy CL: The effect of cigarette smoking on skin-flap survival in the face-lift patient. *Plast Reconstr Surg* 73:911, 1984
- [48]. Craig S, Rees TD: The effects of smoking on experimental skin flaps in hamsters. *Plast Reconstr Surg* 75:842, 1985
- [49]. Pindborg JJ: Tobacco and gingivitis I; Statistical examination of the significance of tobacco in the development of ulceromembranous gingivitis and in the formation of calculus. *J Dent Res* 26:261. 1947
- [50]. Pindborg JJ: Tobacco and gingivitis II; Correlation between consumption of tobacco, ulceromembranous gingivitis, and calculus. *J Dent Res* 28:460, 1949