Effects of cigarette smoking on cutaneous wound healing

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Abstract

Cigarette smoking is one of the leading and most preventable health problems of Western society. Unfortunately, smokers provide a challenge for wound care practitioners as smoking is associated with impaired tissue restoration, increased risk of surgical wound infections and pressure ulcers and is a deleterious factor in the repair of post-surgical flaps and grafts.

Smoking inhibits healing through the effects of anoxia, hypoxia, impaired epithelialisation, vasoconstriction and enzymatic system toxicity. Individuals undergoing elective surgery may require additional assistance involving a multidisciplinary approach to cease smoking preoperatively. Managing patients' wounds that include an arterial component necessitates a holistic approach involving client education, regular dressing changes and liaison with the physician.

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Introduction

Cigarette smoking is one of the leading and most preventable health problems of Western society [1]. Smoke from cigarettes comprises of over 1500 components that have extensive pharmacological consequences on body tissues [2]. The detrimental effects of smoking significantly increases the risk of non-malignant respiratory diseases, myocardial infarction, strokes, lung cancer, and oropharyngeal, oesophageal, stomach, cervical and bladder cancer [1, 3].

Smoking impairs normal arterial endothelial function, is a predisposing factor in the development of atherosclerosis and contributes to peripheral vascular disease and angina [4]. Regrettably, smokers provide a challenge for wound care practitioners, as smoking is associated with impaired tissue restoration, increased risk of surgical wound infections and pressure ulcers, and is a deleterious factor in the repair of post-surgical flaps and grafts [5-8].

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Regardless of recognised health hazards associated with smoking, 47% of men and 12% of women smoke worldwide [9]. Cessation of smoking improves the walking distance of 85% of patients with intermittent claudication by 50-75% [10]. Research demonstrates that smokers of one cigarette pack per day have a 3 times increased risk of tissue necrosis, while two packs per day have a 6 times greater risk than non-smokers [7].

A review of the literature comparing smokers with non-smokers demonstrates that smoking impairs wound healing from trauma, disease or surgery [2, 11]. Smokers demonstrate a higher incidence of unsatisfactory healing and complications such as infection, necrosis and epidermolysis following plastic, reconstructive and breast surgery than non-smokers [12-14]. Smokers are more susceptible to developing intra and postoperative complications, with increased morbidity, mortality, extended length of hospital stay and delayed recovery [15, 16].

While anaesthetics and surgical procedures place additional stress upon the pulmonary, cardiac and circulatory system, when combined with smoking, vital organs are further deprived of oxygen. Previous studies have advised smokers to quit for at least 1 week before and after surgical intervention to minimise complications [2, 11]. However, more recent research indicates smokers should refrain from smoking for much longer, with patients undergoing reconstructive head and neck surgery having reduced incidence of impaired wound healing when smoking was ceased for more than 3 weeks [17].

Effects of smoking on wound healing

The observed deleterious effects of smoking and delayed healing are evident in clinical practice, yet few controlled studies are available to support the relationship [5]. Evidence indicates that the compounds of smoking, which include nicotine, tar, nitric oxide, hydrogen cyanide, carbon monoxide and aromatic amines, inhibit healing through the effects of anoxia, hypoxia, impaired epithelialisation, vasoconstriction and enzymatic system toxicity [18-20]. Smoking promotes the formation of chalones by catecholamines that reduce epithelialisation [2, 11].

Nicotine is a ganglionic cholinergic receptor agonist whose pharmacologically response is dosage dependent [3]. Nicotine and cotinine stimulate central and peripheral release of epinephrine, which increases smooth muscle vasoconstriction through the production of thromboxane A2 and decreasing the vasodilator prostacyclin [19, 21]. Cutaneous blood flow decreases as much as 40% to produce ischaemia and impair healing [19].

Smoking a single cigarette creates a vasoconstrictive effect for up to 90 minutes, while smoking a packet results in tissue hypoxic that lasts an entire day [7]. Moreover, nicotine decreases erythrocytes' proliferation and oxygen transportation, with carboxyhaemoglobin levels increasing to deplete cells of vital oxygen [11, 20]. Carbon monoxide further impairs oxygen transport and metabolism, while hydrogen cyanide inhibits enzymatic oxidative metabolism and oxygen transportation [15].

Nicotine increases platelet adhesiveness, blood viscosity and the risk of microvascular thrombi to increase ischaemia and reduce perfusion [11]. Basement membrane injury and swelling exacerbates platelet aggregation through the release of adenosine diphosphate [15]. Studies show that smokers have impaired fibrinolysis, which increases blood viscosity and reduces micro-perfusion from elevated plasma-plasminogen-activator-inhibitor, and reduced platelet-anti-aggregator-agent prostacyclin [5, 15]. Smokers are potentially at increased risk of infection, as nicotine depresses the immune response by reducing the growth and viability of lymphocytes and decreasing immunoglobulin-G, which provides resistance against microorganisms [15, 22].

Research demonstrates that, in similar environments, a smoker's skin temperature is more than 1^0C lower than a non-smoker's, possibly from reduced local thermo-regulatory blood flow and decreased nitric oxide (vasodilator) bioactivity [6]. Decreased vasodilator reaction reduces the pressure-induced reactive hyperaemia response, an early sign of potential tissue breakdown [6].

Impact of smoking on collagen and vitamin C

The role of fibroblasts in skin repair includes formation of fibronectin, collagen, elastin and glycosaminoglycans [15]. Fibroblasts produce fibroblast growth factor (FGF) to stimulate angiogenesis and epithelialisation. Additionally, FGF have chemotactic and mitogenic properties for fibroblasts and keratinocytes [23]. Both smoking and passive smoking change fibroblast morphology to make them more adhesive and elongated, with reduced capacity to migrate [2]. These changes impair fibroblast proliferation and reduce the production and quality of granulating tissue [2, 15].

Microscopically, fibroblastic microtubules are less organised, the centrosomes impaired, and the Golgi apparatus and endoplasmic reticulum network demonstrate damage with clustering around the nucleus [20]. These changes increase fibre stress by forming focal adhesions, where cells congregate at the wound edge and delay contraction through the inability of fibroblasts to migrate into the wound [20, 24].

In high concentrations, passive smoking destroys chicken embryonic fibroblasts, whereas lower concentrations activate stress response proteins that increase cellular survival [20]. The increase in cell survival, together with reduced cellular migration, produces excessive connective tissue that results in fibrosis and excess scarring in wounds of both smokers and passive smokers [20]. Recent research in the effects of cigarette smoke on cell culture show smoking considerably decreases immune responses which impair wound healing [24]. Smoking also reduces interleukin-1 production, impairs B-cell transduction pathways, diminishes the effect of natural killer cells and causes T-cells to have diminished reactivity to specific antigens [24].

Smoking has a depleting affect on the body's vitamin C reserves and increases metabolic turnover of vitamin C by free radical oxidation [25, 26]. Collagen requires vitamin C, oxygen and iron to produce hydroxylysine and hydroxyproline that form strong cross-linkages [5, 25]. Smoking and arterial disease reduces oxygen and vitamin C levels to produce collagen that is incapable of forming strong cross-links and readily breaks down [25]. Smokers require a minimum of 140mg of vitamin C daily to maintain a total body pool that is similar to non-smokers consuming 100mg per day [26].

Smoking also reduces synthesis of type I and III collagen [9]. Type I collagen is predominant in mature wounds, and is synthesised within 72 hours of injury to give permanent tensile strength and adhesive sites for cellular growth [27, 28]. Impaired type I collagen synthesis increases tissue dehiscence and reduces wound tensile strength [19]. Type III is synthesised post-injury and is responsible for matrix formation, fibroblast

migration and proliferation. A deficiency in type III collagen impairs granulation formation. During scar formation, type III collagen is replaced by type I collagen until the normal skin ratio 4:1 of type 1 collagen to type III collagen is achieved [29]. Tissue-inhibitor-matrix-metalloproteinase-1 is 14% lower in smokers than non-smokers, which may explain the increased extracellular matrix turnover in smokers [9].

Smoking cessation strategies

Regrettably, smoking is addictive and the success of established smokers quitting is approximately 4% without assistance [10]. Accordingly, individuals may require additional support. However, the success of smoking intervention strategies differs, with chronic smokers showing negligible responses to billboards and cigarette packets warnings, while the efficacy of physician advice, self-help approaches and nicotine replacement therapy (NRT) is only 20% [10, 30, 31].

A literature review identified the preoperative period as the most appropriate period for suggesting smoking cessation measures, as individuals are more likely comply if they believe their health is at risk [16, 30]. The Expected Utility Model which examines quality of life expectations in relation to smoke cessation, found that individuals were more likely to quit when confronted with the risk of a lower limb amputation than a shorter life expectancy [30].

Albeit there is minimal evidence to identify the most appropriate strategy to undertake for ceasing smoking preoperatively, a multi-strategic client-centred approach involving behavioural and pharmacological intervention, delivered at the time an individual shows readiness, is believed to be the most effective option [16, 30, 32, 33]. The approach encompasses the medical team, wound clinician and health educators to establish client rapport and ensure advice, psychosocial support, skills building and pharmacology strategies are successful [3, 34, 35].

Smoking cessation strategies include:

- Discussing the types and suitability of pharmacological agents [7].
- Establishing steps to initiate the programme:
  - Setting a date to quit [36].
  - Developing skills to increase chance of quitting:
    - Identifying and avoiding activities or settings that encourage smoking [36].
    - Establishing smoke free areas such as the home and car [3].
    - Identifying substitute activities, for instance walking or chewing gum [36].
- Psychosocial support:
  - Encouraging the support of family and friends [36].
  - Recognising the need for encouragement/feedback [34].

Researchers have found that implementing an 8 week programme of NRT in conjunction with advice and behaviour support demonstrates a positive outcome for heavy smokers (> 15 cigarettes per day) who are motivated to quit [10, 37]. The success rate for quitting and reducing intermittent claudication increases when NRT is used [31]. Nicotine replacement preparations include patches, gum and sprays, which have few side effects and are equally effective at relieving nicotine withdrawal symptoms [31, 38]. The various preparations mean that if one route is unsuccessful, another option or a combination of delivery profiles is available.

Where NRT proves unsuccessful and the individual remains motivated to quit, then the antidepressant Bupropion may be prescribed to lessen withdrawal symptoms [38]. To date, little is known about its pharmacotherapy in relation to smoking cessation, although studies advocate that it be given with behavioural support [37, 39]. Bupropion is contraindicated in patients taking antidepressants or who have epilepsy as known side effects include insomnia and seizures [37].

Wound management

Regardless of whether an individual smokes or not, they have the right to receive high quality wound care. However, smokers with arterial disease need to appreciate that conservative management is unpredictable where circulation is compromised [40]. Therefore, client education, regular dressing changes and liaison with the physician is essential. The goal of management is to maintain blood flow and address any changes that may occur.

In the event of an infection, a wound swab is required to identify aerobic and anaerobic microflora, and ensure appropriate broad-spectrum antibiotic therapy are prescribed [41, 42]. Slough needs to be autolytically debrided to minimise the risk of infection, while local antibacterial dressings containing povidone-iodine or silver may return the wound to bacterial balance [42, 43]. Maceration needs to be avoided to prevent tissue degradation and reduce the risk of infection [40].

An array of dressing products is available to manage arterial wounds. Occlusive dressings promote the growth of anaerobic organisms and traumatise the skin [44]. The choice of dressing therefore needs to:

- Be non-restricted and pressure off-loading so not to impair circulation.

- Maintain thermo-regulation with moisture balanced.
- Control exudate, odour and infection through bacterial balance.
- Autolytic debride and fill dead space.
- Be comfortable and protect the wound and peri-wound from trauma.

Conclusion

Health care practitioners face a challenging goal to assist patients to quit smoking and to promote wound healing. The multiplicity effects of smoking impair all phases of wound healing; this necessitates providers to adopt a holistic multidisciplinary approach to patient management.

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