What are the effects of smoking on wound healing?

Annemarie Brown

Wound healing is complex and there are many factors that can interfere with the normal healing process, which can result in an acute wound becoming a chronic, non-healing one. Cigarette smoking is frequently listed as one of the factors which can interfere with wound healing. However, it is one of the potentially modifiable lifestyle behaviours that can reduce the risk of developing a non-healing wound (Ellis, 2018). Although the precise mechanisms as to how smoking delays healing are currently not clear (Sorensen et al, 2010a, b; Sorensen, 2012), this paper explores the literature on how smoking interferes with the wound healing process at a pathophysiological level, together with how it may be responsible for increased infection rates and delayed healing. In addition, it also discusses how smoking can contribute to infection and wound dehiscence in surgical wounds and delay healing in chronic wounds, resulting in a prolonged recovery time for the patient.

KEYWORDS:
- Smoking
- Wound healing
- Infection
- Wound dehiscence
- E-cigarettes
- Smoking cessation

Cigarette smoke contains over 4,000 different toxins and while it is difficult to identify which specific toxins are harmful to wound healing, nicotine, tar, carbon monoxide and hydrogen cyanide appear to be the most deleterious (Campanile et al, 1998; Rayner, 2006). These are considered to be the key elements which contribute to an environment for poor wound healing.

POOR OXYGENATION

Wounds need an adequate blood supply to receive the necessary nutrients, chemicals and cells for healing. Smoking leads to wound hypoxia as a result of reduced blood flow to the skin/wound and also a decreased concentration of oxyhaemoglobin, as the carbon monoxide molecules from the cigarette smoke compete with the haem molecules to bind to the red blood cells (Campanile et al, 1998; Leow and Maibach, 1998). Furthermore, these harmful compounds are thought to disrupt the inflammatory and proliferative cell functions and result in wound hypoxia, which is a contributory factor for wound infection (Bishop, 2008 in Ellis, 201; Table 1).

Myers et al (2011) in a systematic review and meta-analysis found that one of the leading causes of poor wound oxygenation in postoperative surgical wounds is smoking. Van Adrichem et al (1992a) measured the oxygen levels in the microcirculation of the thumb in healthy volunteers before and after smoking one cigarette and found that oxygen levels had only returned to half the normal pre-cigarette levels after 10 minutes. In a further study on patients who had required surgical revascularisation of digits, the researchers found that after 10 minutes post-cigarette, the oxygen levels had not recovered to normal limits at all and they warned about the negative effects of smoking on oxygenation, particularly in this already vulnerable group of patients (Van Adrichem et al, 1992b). A further study demonstrated that smoking a cigarette for 10 minutes reduces tissue oxygenation for up to one hour and the researchers therefore hypothesised that a 20-cigarette per day smoker will have persistent low oxygenation levels throughout their smoking life (Jensen et al, 1991).

NICOTINE

Nicotine causes vasoconstriction of the blood vessels resulting in very low oxygen levels, together with increased platelet adhesion and a reduced level of keratinocytes, fibroblasts, macrophages and red blood cells, all of which are essential components of the wound healing process (Campanile et al, 1998; Grose et al, 2002).

Keratinocytes are particularly important in the proliferative phase of wound healing, as they are responsible for re-epithelisation through their migration and proliferation within the wound (Manassa et al, 2003). A reduced number of less mobile keratinocytes will result in an extended re-epithelisation time, and, as the wound remains open for longer, this may lead to further bacterial contamination and local infection (Zia et al, 2000; Bikhchandani et al, 2007; Sorensen et al, 2012). Sorensen et al (2012) suggested that this may be the cause of post-surgical wound infection in smokers, a hypothesis with which other researchers concur (Jensen et al 1991; Morecraft et al, 1994; Sorensen et al, 2010a, b), and Holscher et al (2018) found that smoking was associated with more frequent 30-day hospital readmission rates due to wound healing complications.
Interestingly, Morimoto et al (2008) studied different strengths of nicotine and their impact on wound healing. The researchers applied different concentrations to surgically created, full-thickness wounds on mice daily for seven days, with 8mm diameter silicone sheeting sutured over the wounds. They found that the high solutions of nicotine impaired wound healing, however low concentrations of nicotine applied topically actually improved healing by promoting improved capillary growth. Despite this finding, the researchers do not advocate applying nicotine topically to wounds due to concerns over potential toxicity levels (Morimoto et al, 2008).

E-CIGARETTES

The increase in the usage of electronic cigarettes (e-cigarettes), which are believed to be less harmful than traditional cigarettes, has prompted researchers to study the effects of e-cigarettes on wound healing. Fracol et al (2017) reported on a case where an e-cigarette user underwent breast reconstruction following breast cancer surgery and developed a necrotic skin flap. Although marketed as ‘healthier’ than traditional cigarettes, they contain nicotine in addition to propylene glycol, glycerol and flavouring and, according to Fracol et al (2017), the amount of nicotine they deliver will vary according to the user’s frequency of use and type of device/cartridge used, and may even be higher than traditional cigarettes. The researchers concluded that the vapour produced by e-cigarettes is cytotoxic to endothelial cells, whether or not nicotine is present, and that e-cigarettes may have as much of a detrimental effect on tissue oxygenation as traditional cigarettes because a reduced subcutaneous blood flow was found in the e-cigarette users studied (Page et al, 2016).

Sorensen et al (2009) studied the correlation between skin blood flow levels and nicotine replacement aids and found that, initially, there was a very small increase in blood flow to the skin, followed by a significantly reduced subcutaneous blood flow. However, there was no effect on the aerobic metabolism in tissues when an intravenous dose of 1mg of nicotine was administered, which is like the dose used in nicotine replacement aids.

Their findings are supported by other studies which have demonstrated no adverse effects on wound healing with the use of nicotine replacement aids, unless taken in toxic doses (Falcone and Ruberg, 1980). These inconclusive findings demonstrate that the real effects of nicotine on wound healing are still not fully understood (Ortiz and Grando, 2012; McDaniel and Browning, 2014).

Research into the effects of e-cigarettes is ongoing however, and in the current absence of robust evidence that e-cigarettes are detrimental to health, Public Health England (PHE) recommends them as a smoking cessation aid or an alternative to traditional cigarette smoking (McNeill et al, 2018). Healthcare professionals, however, should bear the use of these in mind when trying to establish the cause of non-healing wounds and consider recommending patients use lower concentrations of nicotine in their e-liquids.

Table 1: What is hypoxia and how does it affect wound healing (Tandara and Mustoe, 2004)?

<table>
<thead>
<tr>
<th>Event Description</th>
<th>Hypoxia Impact</th>
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<tr>
<td>Immediately after injury, the wound environment is devoid of oxygen as a result of the trauma to the tissues, resulting in a hypoxic wound bed.</td>
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<tr>
<td>Within days, oxygen levels return to normal as a result of new blood supply from newly formed granulation tissue.</td>
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<tr>
<td>It is suggested that hypoxia is beneficial in the early stages of wound healing, as it stimulates the development of blood vessels in granulation tissue.</td>
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<tr>
<td>Oxygen is necessary in wound healing to provide the energy required for cell metabolism.</td>
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<td>It is necessary for all cells involved in the repair process and the formation of collagen.</td>
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<tr>
<td>The cells required to fight infection are heavily dependent on high oxygen levels, particularly in the inflammatory phase.</td>
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<tr>
<td>If wound infection develops, oxygen levels reduce, and the strength of the newly developed collagen will be impaired.</td>
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<tr>
<td>Transcutaneous tissue oxygen levels have been measured at 5–20mmHg in non-healing chronic wounds, compared to 30–50mmHg in healing wounds.</td>
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Increased Risk of Wound Infection in Smokers

In a normal healing wound, during the inflammatory phase, leucocytes are attracted into the wound via a cascade of chemical messengers and cell interactions (Hart, 2002). Other cells, such as neutrophils, monocytes and T-lymphocytes also appear in the wound during this phase and are responsible for clearing up any cellular debris and removing any microorganisms which may cause infection (Sorensen et al, 2004). These cells are responsible for creating an ideal environment for new tissue growth to develop in the wound. Sorensen et al (2010a) studied the levels of neutrophil and monocyte activity between two groups (smokers and non-smokers), and found that activity levels of these two cells were 50% and 68% less in the smokers’ group (Sorensen et al, 2010a). The researchers found that these levels returned to normal following 20 days of smoking abstinence (Sorensen et al, 2003; Sorensen et al, 2010a).

Fibroblasts and Collagen Production

During the next proliferative phase of healing, the tissue lost by the wounding/injury must be replaced to repair the defect. This occurs as fibroblasts migrate into the wound, an extracellular matrix is deposited, granulation tissue forms and a new layer of skin develops (epithelialisation) (Enoch and Leaper, 2005). Wong and Martins-Green (2004) and Wong et al (2004) found that the structure and function of fibroblasts are affected by exposure to even very small concentration levels of cigarette smoke, meaning that...
second-hand exposure to cigarette smoke may impede healing.

COLLAGEN STRENGTH

Collagen develops in the final phase of healing and is the primary component required for remodelling of the new tissue and tensile strength of the resultant scar (Martin, 2013). Smoking has been associated with diminished tensile strength, particularly in surgical wounds (Jorgensen et al, 1998). As a result, smoking has been associated with:

- Wound dehiscence (Manassa et al, 2003; Abbas and Hill, 2009)
- Tissue flap necrosis (Campos et al, 2008; Little et al, 2009)
- Anastomotic leakage (Sorensen et al, 1999)
- Decreased wound tensile strength (Sorensen, 2006)
- Infection (Myles et al, 2002; Sorensen et al, 2002; Sorensen et al, 2003).

Sievert et al (2013) suggested that smoking combined with a high body mass index (BMI) may even result in more frequent recurrence of pilonidal sinus development. Sorensen et al (2010b) assert that smoking in combination with a reduced level of vitamin C seen in smokers, contributes to weaker collagen formation in surgical wounds. They demonstrated a two to three-fold decrease in vitamin C levels in smokers, which is an important antioxidant in addition to its role in fibroblast function and collagen synthesis (Sorensen et al, 2009).

CHRONIC WOUNDS AND SMOKING

All wounds pass through the same wound healing trajectory. However, the focus of most studies is on the detrimental impact of smoking on the healing of post-surgery wounds (McDaniel and Browning, 2014). There is a growing body of research which links smoking with poorer healing outcomes, but less research on the effects of smoking on chronic wounds (Lefrancois et al, 2017).

Alvaro-Afonso et al (2018) and Xue-Lei et al (2018) conducted systematic reviews and meta-analyses to study the effects of smoking on diabetic foot ulcer healing and concluded that healing rates were consistently lower among smokers than non-smokers. This is an area that requires further research. However, until proven otherwise, it must be assumed that the negative effects of smoking also apply to chronic wounds.

IMPLICATIONS FOR PRACTICE

Smoking cessation advice

Although smoking has been identified as a risk for non-healing surgical wounds, it is unclear precisely how smoking cessation may affect the cellular mechanisms involved in wound healing. Patients are frequently advised to refrain from smoking before surgery, and some surgical procedures may be withheld if they refuse to do so (Bikhchandani et al, 2007; Fallat and Chahal, 2013). What is currently unclear is how long patients should cease to smoke preoperatively to ensure better outcomes.

Wong et al (2012) found that abstinence of smoking for at least four weeks reduced respiratory complications, and at least three to four weeks abstinence reduced wound healing complications. They also concluded that smoking cessation for less than four weeks had no positive or negative impact on postoperative respiratory complications.

Sorensen et al (2009) found that the inflammatory phase of healing was delayed in smokers, but this returned to normal after four weeks...
of abstinence. They also found that the proliferative phase was impaired in smokers, however this was not reversed even after three months of smoking cessation.

Sorensen (2012) conducted a systematic review and meta-analysis to compare the outcomes of surgery on smokers and non-smokers/ex-smokers and concluded that former smokers had fewer healing complications compared with current smokers. He also proposed that smoking cessation for four to eight weeks before surgery significantly reduced surgical site infection (SSI) and should be encouraged. However, he found no benefit in smoking cessation for four weeks preoperatively in terms of wound healing. His study found that former smokers continued to have a lifelong higher risk of healing complications compared to non-smokers. However, he stated that his findings needed to be treated with caution due to methodological differences in the studies included in the review (Sorensen, 2012).

CONCLUSION

This article has reviewed the evidence on the detrimental effects of smoking on the wound healing process and when smokers should be encouraged to quit smoking before surgery. The literature demonstrates that smoking is harmful and will increase the risk of wound healing complications, such as wound infection, although the precise effects of nicotine on wound healing are still unclear. There is currently no consensus as to when smokers should refrain from smoking preoperatively to avoid wound complications and most of the literature focuses on surgical wounds, rather than chronic wounds, although both wound types share the same phases of healing.

Despite the lack of evidence, therefore, it must be assumed that the detrimental effects of smoking affect both surgical and chronic wounds. Community nurses are in an ideal position to counsel patients with regards to smoking cessation before undergoing surgical procedures, or to discuss smoking status with patients who have non-healing wounds.

The damage to overall health as a result of smoking cigarettes is well known. Thus, community nurses have an important health promotion role in encouraging their patients to quit.

REFERENCES


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Having read this article, reflect on:

- How smoking can delay wound healing
- Why smokers have an increased risk of wound infection
- The smoking cessation advice and support you give your patients.

Then, upload the article to the free JCN revalidation e-portfolio as evidence of your continued learning: www.jcn.co.uk/revalidation

KEY POINTS

- Wounds need an adequate blood supply to receive the necessary nutrients, chemicals and cells for healing.

- Smoking leads to wound hypoxia, as a result of reduced blood flow to the skin and wound and also a decreased concentration of oxyhaemoglobin.

- Nicotine causes vasocostriction of the blood vessels resulting in very low oxygen levels.

- The literature demonstrates that smoking is harmful and will increase the risk of wound healing complications, such as wound infection, although the precise effects of nicotine on wound healing are still unclear.


