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Honey in The Management of Diabetic Foot : A Review of The Literature

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Abstract

"Honey is healing for man" is mentioned in the Holy Quran (Surah An-Nahl 16:69). Honey has many therapeutic properties such as anti-acteria, anti-inflammatory, anti-oxidant, immune booster, and cell growth stimulator. It also promotes wound healing. Diabetic patients are at increased risk of having infection over the foot (diabetic foot) due to presence of peripheral neuropathy and peripheral vascular disease. Management of diabetic foot revolves around surgery and wound dressing. Wound healing in diabetic patient is unpredictable. Delayed wound-healing results in higher chance of secondary infection. This paper illustrates the therapeutic properties of honey in relation to management of diabetic foot. Studies showed that honey reduces inflammation and kills bacteria thus accelerates wound healing. Honey confers less side effect compare to other chemical medicine such as antibiotics. It also soothes the pain, non-irritating, gives no secondary reactions and its allergy is rare. It is a cost-effective method of dressing that can be used in underdeveloped countries. This paper was prepared for Special Study of Module, Year 4 Medical Student, Faculty of Medicine and Health Science, Universiti Sains Islam Malaysia.

Keywords: honey, diabetic foot, wound healing.

INTRODUCTION

Worldwide, 387 million people are living with diabetes, that accounted for 8.3% prevalence (IDF, 2014). In Malaysia, the prevalence of diabetes among adults has increased significantly from 6.3% in 1986 and 14.9% in 2006 to 22.6% in 2013. In other words, at least 2.6 million adults in the country already have diabetes (Wan Nazaimoon et al., 2013). The World Health Organization has projected that Malaysia will have 2.48 million people with diabetes by 2030 (WHO, 2014). Apparently, the target has been achieved prematurely.

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Diabetes is a systemic disease with a wide array of complications; from head to toes. The most distressing complication is diabetic foot ulcer that affects 15% of diabetic patients (Pendsey 2010). A small benign looking wound on the diabetic patient's foot often ends up in amputation.

DIABETIC FOOT INFECTION

Complex interplay between these factors; trauma in the presence of neuropathy and/or peripheral vascular disease with infection occurring as a secondary phenomenon following disruption of protective epidermis results in foot ulceration in diabetic patients (Colledge et al., 2010). Several recent studies have found that poor glycaemic control, duration of diabetes, hyperlipidaemia, elevated albumin excretion rates and obesity as risk factors for the development of diabetic peripheral neuropathy (Solomon & Selvarajah, 2012).

Major metabolic abnormality in diabetic nerve is the accumulation of sorbitol due to increased flux of sorbitol secondary to hyperglycaemia. This accumulation of sorbitol causes nerve damage. This nerve damage affects peripheral sensation, nerve innervations of the muscles and fine vasomotor control that causes symmetrical sensory and motor polyneuropathy. These neuropathies cause loss of protective sensation and foot deformities, which alters the distribution of plantar pressure forces during walking correspondingly. Loss of protective sensation results in inadvertent injuries, for example heat injury after applying hot water.

There may be also increased risk of pedal ulceration due to unperceived repetitive pressure and shear stress in persons of lacking protective sensation (Rieber et al. 1999). The abnormality of plantar pressure distribution causes the reactive thickening of skin (callus) at the sites of abnormal load. Beneath the callus, the ischemic necrosis of tissue occurs. Then, it causes the breakdown of skin and subcutaneous tissue showing the neuropathic ulcer with a punched –out appearance (Jeffcoate & Harding, 2003).

In addition, diabetic vasculopathy can lead to poor circulation that impairs wound healing (Apcofamerica, 2013). The vascular disease involves microvascular and macrovascular components. The microvascular disease consists of thickening of capillary basement membrane and arterio-vascular shunting. Macrovascular disease results in atherosclerosis in the vessels that leads to occlusion or narrowing of vessels and eventually ischaemia. Both of these vascular diseases contribute to the decrease of nutrient capillary blood flow to the wound and lead to poor healing (Frykberg et al., 2006).

Diabetic patient often considered as immunocompromised. Their immune system function is much weaker than healthy persons. Thus, infection from even non-virulent organisms might turn to life–threatening event. Apart from immunopathies, compromised blood supply and hyperglycaemic state predispose diabetic persons to foot infections (Bronze, 2013). The foot infection span from superficial cellulitis, deep-skin and soft tissue infections worsen to acute and chronic osteomyelitis.

MANAGEMENT OF DIABETIC FOOT INFECTION

The aim of the treatment of foot ulcer is to obtain wound closure as soon as possible and to prevent recurrence (Lotfy et al. 2006). If there is adequate blood supply to the foot, dead tissue can be debrided in the expectation that healing will occur, provided the infection is controlled and the feet are off-loaded adequately. If there is ischaemia as well, the priority is to revascularise the foot (Garden et al., 2012).

Wounds without evidence of soft tissue or bone infection do not require antibiotic therapy. For infected wounds, tissue specimen from debridement should be cultured. Staphylococcus spp is the most common cause of skin infection. Therefore, empiric antibiotic therapy can be narrowly targeted at gram-positive cocci in many acutely infected patients. High risk patients for example those in the intensive care unit, those with history of hospital admission and infection with resistant organisms should be given broader spectrum antibiotics in fear of infection by antibiotic-resistant organisms. (Lipsky et al. 2012).

Most diabetic foot infections require some surgical intervention, ranging from minor (debridement) to major (resection, amputation). Debridement of necrotic tissue is the removal of all non-viable tissues and slough from ulcer until healthy bleeding soft tissue or bones are encountered. Debridement must be done first before carrying out any application of topical wound healing agents, dressings or wound closure procedures. For abscess, immediate incision and drainage is needed. Osteomyelitic bones, joint infection or digital gangrene usually require resection or partial amputation.

Wounds must also be properly dressed and off-loaded of pressure, and patients need regular follow-up. Proper dressing after debridement is crucial for protection from trauma and bacterial contamination. Type of dressing and topical agents to be applied is determined by wound size, depth, location, surface and discharge. Transparent films, hydrogels, foam, hydrocolloids, calcium alginates, gauze pads, collagen dressing and antimicrobial dressing are the examples of dressing that often used in modern medicine.

HONEY AND ITS COMPOSITION

Honey is an ancient treatment that has been used widely for modern medicinal purposes. It continues to be a popular medicine all over the world except in United States and it is easily available throughout the world. Honey is originated from nectar that is collected from flowers by bees. In the beehive, the workers bees remove the liquid from the nectar and add some enzymes to convert it into syrup honey. (Udwadia, 2011).

The actual composition of honey varies according to the species of plant that the bee forages but generally, the main composition of honey is moisture (17.2%), fructose (38.19%), glucose (31.28%), sucrose (1.31%), disaccharides/maltose (7.3%), higher sugars (1.5%), free acid as gluconic (0.43%), lactone as gluconolactone(0.14%), total acid as gluconic (0.57%), ash (0.169%) and nitrogen (0.041%). About more 95% of solids in honey are carbohydrate and there are other constituents that have been identified such as isomaltose, nigerose, turanose, maltulose, kojibiose, alpha beta-trehalose, gentiobiose and so on that are formed during process of storage of the honey. The pH of honey is acidic which is between the ranges of 3.2 to 4.5 (Udwadia, 2011).

Honey is classified according to the predominant flower source. Manuka honey is derived from flowers of Leptospermum species from New Zealand (Bell, 2007) while most of the commercial honey is produced by the species, Mimosa and Eucalyptus through Africanized honeybees, *Apis mellifera*. Study of 6 honey samples from Malaysian namely tualang (Koompassia excels), gelam (Melaleuca cajuputi), acacia and forest honeys showed that potassium and sodium were the most abundant minerals covering from 69.3–78.6% and 14.1–28.7%, respectively (Chua et al. 2012).

Allah said in the Holy Quran (Surah An-Nahl 16: 68-69), "And your Lord inspired the bee, saying: "Take your habitations in the mountains and in the trees and in what they erect. Then, eat of all fruits and follow the ways of your Lord made easy (for you). There comes forth from their bellies, a drink of varying colour wherein is healing for men. Verily, in this is indeed a sign for people who think.". Physicians in the past millennia like Aristotle (384-322 BC) and Dioscorides (50 AC) agreed that pale honey is good for healing of eyes and wound. Large variation of honey gives different therapeutic effect on the disease (Molan, 2001).

HONEY ON DIABETIC FOOT ULCER

Honey has good effect on all type of skin lesion like malignant lesions, chronic venous ulcer, diabetic foot ulcers, infected ventral hernia mesh hernioplasty and post-caesarean wound dehiscence. It is also used to cure

many other ailments including stomachache. Narrated Abu Said Al-Khudri: A man came to the Prophet and said, "My brother has some abdominal trouble." The Prophet said to him " Let him drink honey." The man came for the second time and the Prophet said to him, "Let him drink honey." He came for the third time and the Prophet said, "Let him drink honey." He returned again and said, "I have done that", the Prophet then said, "Allah has said the truth, but your brother's abdomen has told a lie. Let him drink honey. So, he made him drink honey and he was cured." (Sahih Bukhari, 7:71:588) (Muhsin, 2009).

Earlier study showed that diabetic ulcer was healed when the myrrh, honey and propolis paste were maintained from the beginning of the treatment (Lotfy et al., 2006). However, the effect of in-vivo hyperglycaemia (honey) is different with in-vitro hyperglycaemia. The hyperglycaemia properties of honey are toxic to the abnormal cellular elements in diabetic wound while hyper glycaemia in-vivo may increase risk of getting infection. Therefore, most of studies of honey for diabetic wound healing used honey externally (as dressing).

A study was done using manuka honey-impregnated dressings (MHID) on the healing of neuropathic diabetic foot ulcers showed that MHID provided faster healing process and rapid disinfection of ulcer when compared to conventional dressing (Alexandros et al, 2014). Moghazy et al. (2010) also demonstrated the ability of honey to treat diabetic foot ulcer. In his study, complete healing was achieved in 43.3% of subjects with foot ulcer. For another 43.3% patients, the sizes of ulcers were significantly reduced with presence of healthy granulation. This is supported by earlier study by Eddy & Gierdenson (2005) where they found that applying honey in addition to conventional management reduced the duration of wound healing by 60 days. As a result, healthcare cost for wound management and hospitalization could be reduced significantly.

The best-characterized role of honey in wound healing is in the prevention and limitation of bacterial infection, thereby reducing the bio-burden of the wound. The ability of honey to combat bacteria is mainly attributed to the presence of hydrogen peroxide. (Temaru et al., 2007), As hydrogen peroxide decomposes, it generates highly reactive free radicals that react and kill the bacteria. Nevertheless, some honeys for example Manuka honey and jelly bush have different unidentified antimicrobial activity (non-peroxide) which resulting in a much more persistent and stable antibacterial action (Alvarez-Saurez et al., 2009). For example, exceptionally high levels of an antimicrobial compound methylglyoxal (MGO) have been found in Manuka honey (Adam et al 2008). Based on a strong correlation between the MGO

levels and the potential of honey to inhibit the growth of *S. aureus*, it has been suggested that MGO is fully responsible for the non-peroxide antibacterial activity of Manuka honey (Paulus et al 2012).

Different honey has different antimicrobial activity against different bacteria. Manuka honey as mentioned earlier, is highly active against *S. aureus*. Henriques et. al (2010), discovered that Manuka honey-treated *Staphylococcus aureus* colonies showed arrest at cell division, suggesting an ability of honey to impair bacterial cell cycle progression. Gelam honey from Malaysia has also been shown to have lowest minimum inhibitory concentration (MIC) value against *Staphylococcus aureus* with 5% (w/v) MIC and minimum bactericidal concentration (MBC) of 6.25% (w/v) as compared to other honeys from Malaysia. Another study showed both Tualang and Gelam honey were also able to inhibit the growth of vancomycin-resistant enterococci (VRE) (Ng et al 2014). Honey seems to have lesser activity against gram-negative bacteria. Pineapple honey and acacia honey from Malaysia showed high MIC 25% (w/v) and MBC 50% (w/v) against *E. coli* and *P. aeruginosa* (Zainol et al 2013).

Furthermore, honey is a supersaturated sugar solution; these sugars have high affinity for water molecules leaving little or no water to support the growth of microorganisms (bacteria and yeast). Consequently, the microorganisms become dehydrated and eventually die. In addition, the natural acidity of honey inhibits many pathogens. The usual pH range of most of the pathogens is around 4.0- 4.5.

The immunomodulatory activity of honey is highly complex because of the involvement of multiple quantitatively variable compounds among honeys of different origins. Honey and its components are able to either stimulate or inhibit the release of certain cytokines (tumor necrosis factor-α, interleukin-1β, interleukin-6) depending on wound condition. Activation of macrophages and neutrophils by honey promotes debridement of a wound and expedite wound healing. Similarly, human keratinocytes, fibroblasts, and endothelial cell responses (e.g., cell migration and proliferation, collagen matrix production, chemotaxis) are positively affected in the presence of honey; thus, honey may accelerate re-epithelization and wound closure (Majtan 2014).

Anti-inflammatory property of honey was established from clinical observation of wounds after honey application. In addition to pain soothing property, application of honey on wounds resulted in reduction of oedema, (Molan, 2001). Excessive inflammatory process causes delayed

wound healing, thus honey dressing on wounds may accelerate healing by minimizing inflammatory response.

Honey has been found to have a significant antioxidant content measured as its capacity to scavenge free radicals (Gheldof et al., 2002). This anti-oxidant activity may be at least part of what is responsible for its anti-inflammatory action where it stimulates cell growth by evidence of rapid healing process in the wound dressing. This process occurs due to ability of honey to promote healthy granulation tissues formation, hastens epithelization of wound and stimulates the synthesis of connective tissues components for improvement of the strength of collagen.

CONCLUSION

Honey has been used as an alternative in treatment of diabetic foot due its anti-bacterial, anti-inflammatory, anti-oxidant and various other properties. It is proven by scientific research that honey is beneficial for wound healing. Expensive standard and routine dressing of diabetic foot wound can be replaced by honey particularly in low-income countries. The antibacterial properties of honey are useful in the management of diabetic foot, as it will accelerate the closure of the wound, the main intention in the management of diabetic foot. All type of honey has good effects on wound healing but at different speed and intensity. Thus the duration of treatment varies. More studies should be done to ascertain the standard regime of each different honey to be used in diabetic foot management.

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