Combined use of honey, bee propolis and myrrh in healing a deep, infected wound in a patient with diabetes mellitus

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Diabetes mellitus is a group of diseases characterised by high levels of blood glucose resulting from defects in insulin production, insulin action, or both. Diabetes can be associated with serious complications including diabetic foot disease. Diabetic foot disease is estimated to affect 15% of people with diabetes.[1]

Wound healing is a process that involves inflammation, proliferation/regeneration and finally remodeling. The normal orderly pattern is disrupted in chronic non-healing wounds, which are characterised by decreased levels of growth factors and increased protease activity. Wound healing is affected by serum albumin, tissue oxygenation, infection, hyperglycaemia, cytokines and proteases.[2]

A marker of non-healing wounds may be the prolonged presence of extracellular matrix molecules in the dermis.[3] Other markers and potential mediators include increased levels of transforming growth factor (TGF)-β3,[4] proteolytic factors such as matrix metalloproteinases,[5] and the absence of IGF-I.[6]

Wound care includes a variety of approaches to enhance healing, with treatment of infection, vascular reconstruction, achieving adequate glycaemic control, removal of pressure, and ongoing wound debridement being important aspects of this care.[2]

A deep wound with tissue loss in the right foot of a 65-year-old male patient with diabetes mellitus was treated by a standard protocol that included strict control of blood sugar level. In addition, an antibiotic regimen was included to combat anaerobic and aerobic infection. Also, a paste consisting of myrrh, bee propolis and honey (MPH) was applied to the wound. Following treatment, the wound settled and healed well (Fig. 1).

The patient presented to the out-patient clinic of Minufiya University Hospital (MUH) with possible osteomyelitis. A foot wound showed severe oedema and the patient was unable to bear weight on the foot. On examination, the patient had a large abscess beneath the skin of the foot. An incision (3 cm) was made, pus was drained and the wound was cleaned. The patient returned home with antibiotic (gatifloxacin; 400 mg twice a day for five days) and an anti-inflammatory agent.

X-ray examination showed no bony abnormality and inflammation was prominent around the smallest toe.

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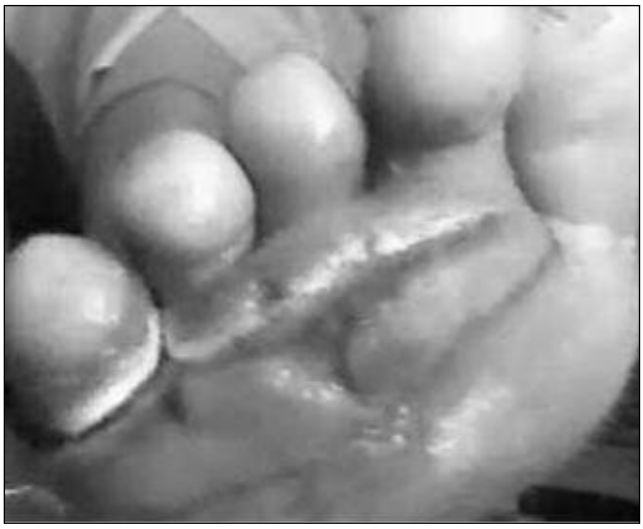

Fig. 1. The foot wound showing the healing process during treatment with the MPH paste.

Two days later, the patient's foot was re-examined and debridement of the wound was performed to remove dead skin and necrotic tissue inside the opened cavity.

At all times during treatment, blood sugar level was controlled (in the range 150–170 mg/dL) using insulin. The patient was kept on metronidazole (1500 mg/day) and combined amoxicillin with clavulanic acid (1500 mg/day) for 10 days. Thereafter, ciprofloxacin (1500 mg/day) was used instead of the combined amoxicillin with clavulanic acid. Pentoxifylline, vitacid calcium (vitamin C and calcium carbonate) and vitazinc (vitamins A and E plus zinc) were added to the treatment regimen to aid vascularity and healing. From the beginning of treatment until the deep wound healed, the patient was maintained on an oral dose of bee propolis (400 mg/day). Erythrocyte sedimentation rate (a good indicator of treatment efficacy) was 125 mm prior to treatment and dropped to 65 mm after two weeks and 25 mm after four weeks, where it stabilised.

The most significant results were obtained during the use of the MPH paste (800 mg bee propolis, 50 g myrrh, mixed together in honey). The paste was prepared every three days and stored in a refrigerator. Wound cleaning was performed daily using standard methods in addition to the MPH paste to fill the wound cavity. The effectiveness of the paste in keeping the wound clean was indicated by a complete absence of pus and cellular exudate. After four weeks the wound had healed well and the patient returned to work.

Poor wound healing in people with diabetes is well recognised.[7] However, there is little information about many aspects of foot care in people with diabetes, including wound healing.[8] The American Diabetes Association[9] suggests a range of predisposing factors to explain poor healing of wounds in people with diabetes, including abnormal cellular and/or inflammatory pathways, peripheral neuropathy and vascular disease and/or tissue hypoxia. Abnormal cellular function, particularly in fibroblasts and neutrophils, has been found in people with diabetes. *In vitro*, hyperglycaemia may be toxic to these cellular elements, while *in vivo* it may result in a greater susceptibility to infection.

Modest differences in the function of neutrophils, macrophages and fibroblasts associated with hyperglycaemia

have been postulated, but these have not been demonstrated conclusively *in vivo*. Advanced glycosylation end products accumulate in diabetes as a result of hyperglycaemia, leading to the non-enzymatic glycosylation of collagen.[10] This process results in the production of abnormal collagen, which is highly inflexible and prone to breakdown, particularly over pressure areas.[11]

In this report, a paste is described that keeps a wound clean, which is especially important in cases that involve tissue loss. The MPH paste contains safe and effective components that have prominent antimicrobial activity.

Myrrh is an oleogum resin obtained from the stem of the plant *Commiphora molmol*. It is a safe, natural flavouring substance approved by the US Food and Drug Administration.[12,13] In experimental studies on Swiss albino mice, myrrh from *C. molmol* exhibited no mutagenicity and proved to be a potent cytotoxic drug against Ehrlich solid tumour cells. The antitumour potential of *C. molmol* was comparable with that of the standard cytotoxic drug cyclophosphamide.[14] Studies with animal and human models demonstrate antischistosomal and other antiparasitic activity for myrrh and have found it to be safe and effective.[15,16]

Myrrh has considerable antimicrobial activity and is used in a variety of diseases.[17] It has antibacterial and antifungal activity against standard pathogenic strains of *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Candida albicans*.[18] In addition, it has an antidiabetic effect, especially in non-insulin-dependent diabetes mellitus (NIDDM).[19] Moreover, Myrrh has found pharmacological application in the reduction of cholesterol and triglycerides.[20]

Propolis is a resinous substance collected from trees by the bee *Apis mellifera*, which uses it as a building and insulating material in the hive. It is known that propolis has antimicrobial, antioxidative, anti-ulcer and antitumour, anti-inflammatory, hypotensive and immune stimulatory activities.[21]

Antimicrobial activity has been observed against *S. aureus*,[22,23] *Streptococcus pyogenes*,[24] Gram-positive and Gram-negative bacterial species and *Candida* species,[25,26] *S. mutans*,[27] anaerobic bacteria in the human oral cavity,[28] salmonellas,[29] and other microorganisms including mycobacteria.[30] Antibacterial activity of propolis against *Staphylococcus aureus* is higher when extracts are prepared in 60–80% ethanol.[22] *In vitro* synergy between propolis and antimicrobial drugs has been investigated,[31,32] and preparations combining propolis with antibiotic and antifungal agents are of potential medical interest.[26]

Honey is an ancient remedy that has regained popularity as an alternative treatment for antibiotic-resistant bacteria. Both honey and sugar pastes are considered useful as topical antimicrobial agents, mainly because of their high osmolarity and the ability to minimise water availability to bacteria.[33] Although the dilution of honey by wound fluid is likely to reduce the efficacy of its osmotic effect, the slow and sustained production of hydrogen peroxide by some types of honey (e.g., manuka honey) is capable of maintaining an antimicrobial effect at a concentration approximately 1000-fold higher than that used commonly in antiseptic solutions (i.e., 3%).[33] Also, certain components of manuka honey (e.g., flavonoids and aromatic acids) demonstrate antimicrobial properties.[33]

Honey is also an effective wound deodorant, an effect attributed to the presence of glucose, which is metabolised by bacteria in preference to proteinaceous necrotic tissue, resulting in the production of lactic acid and not the malodorous compounds generated by protein degradation.[33] In addition, the observed benefits of honey in infected wounds may be attributed to the high glucose content and low pH, both of which stimulate macrophages.[34]

In the present case study, application of MPH resulted in a clean and odour-free wound, which healed well. However, the results of this single case need to be confirmation in a study of a larger number of patients. In the meantime, use of the MPH paste would appear to reduce the cost of deep wound treatment and improve the outcome in the patients affected.

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Interleukin (IL)-1β, IL-6 and IL-8 in nasal secretions: a common role for innate immunity in viral bronchial infection in infants?

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There is growing evidence to support a role for the immune response in lower respiratory tract infection (LRTI) due to viruses in children.[1,2] Respiratory syncytial virus (RSV) is the most frequent aetiological agent of LRTI, but other respiratory viruses (human metapneumovirus [hMPV], parainfluenza virus types 1, 2 and 3, influenza virus B, adenovirus types 1, 2 and 5, and mycoplasmas) can produce symptoms indistinguishable from those elicited by RSV.

Currently, however, there is controversy over the ability of the different viral agents to induce pro-inflammatory cytokines. Differences in the locally secreted cytokine profile in nasal washes between RSV and metapneumovirus infections have been described, as have similarities between RSV and influenza.[3] Additionally, immune function in neonates differs from that in adults.[4]

At birth, the immune system is not fully mature. Neonatal antigen-presenting cells tend to be deficient in interleukin (IL)-12. Furthermore, T cells secreting interferon (IFN)-γ (Th1 cells) are more likely to undergo apoptosis after antigen exposure. This might explain in part the Th2-skewed immunity in newborns. Neonatal immune cells appear unable to provide strong responses because neonatal antigen-presenting cells fail to up-regulate major histocompatibility complex (MHC) class II and co-stimulatory molecules. Antibody levels and classes are also different in early life to those found in adulthood.

Neonatal antibody is characterised by increasing levels of maternal immunoglobulin during the last trimester of pregnancy, which is replaced during the first year of life progressively by neonatal IgM, then IgG and finally IgA production. These special features of the neonatal immune system mean that young children are much more susceptible to infectious disease; however, with ageing, mortality due to infection decreases rapidly such that by the age of 10 years it is reduced 10- to 100-fold.[4]

Greater understanding of the immune response in LRTI is important for better understanding of the physiopathology of the condition, which may contribute to the development

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