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The pro-healing effects of medical grade honey supported by a pediatric case series

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ABSTRACT

Introduction: The development of antibiotic resistance demands for novel complementary therapies for wound care. We here present a case series on the use of medical grade honey (MGH) in pediatric wounds. We aim to illustrate the specific antimicrobial and pro-healing activity of MGH and support its easy and safe use.
Methods: Four pediatric patients with wounds of different origin are discussed in this prospective observational case series. All wounds were treated via monotherapy with daily MGH application.
Results and discussion: Wound covering with MGH prevents pathogen infiltration and has antimicrobial activity. Moreover, MGH keeps the wound moist and possesses strong pro-healing effects, such as autolytic debridement of non-vital tissue and restoration of vascular structures. The anti-inflammatory and anti-oxidative action of MGH together with the supplemented vitamins C and E may inhibit scar formation.
Conclusion: MGH is safe and easily applicable and can be recommended in all kinds of wounds.

1. Introduction

Children are prone to injuries and wounds, as it is normal behavior to explore and play in adventurous environments while inadequately calculate the risks due to lack of experience.[1] However not all wounds are inflicted outside, and morbidities can also lead to wounds directly, or be caused by medical or surgical intervention. The skin forms the first line of defense against invading pathogens and infection.[2] The chance on infection depends on the wound size, type, and origin, and it is obvious that proper wound care using antiseptic measurements are of additive importance in the prevention and treatment of infections. The development of antibiotic resistance raises the demand for novel complementary therapies.[3,4]

Honey is used since ancient times and possesses antimicrobial and wound healing activities.[5–7] To assure the safety and efficacy of honey for clinical application, medical grade honey (MGH) has been introduced. MGH must be gamma-irradiated to kill dormant endospores, must be free of contaminants, such as herbicides, pesticides, heavy metals, and needs to follow strict quality, processing and storage standards and regulations. MGH has multiple physicochemical properties that act antimicrobial and therefore has less risk for the development of antimicrobial resistance.[4] The acidic pH, the osmotic effect caused by the high sugar content, and the release of hydrogen peroxide after the enzymatic breakdown of glucose, act antimicrobial.[8–10] Other antibacterial effects of honey may be attributed to the presence of antibacterial substances such as propolis, methylglyoxal and bee defensin-1.[4–6,9–11] The application of MGH to a wound shield a wound from invading pathogens and prevents infection. Besides these effects on the prevention and treatment of infections, honey also has strong pro-healing properties. MGH keeps the wound moisturized, has anti-inflammatory and anti-oxidative effects and induces angiogenesis and re-epithelialization.[9,12–14] The protective propolis and chrysin in the honey may further enhance wound healing.[15,16] MGH has demonstrated the successful application in a wide variety of wounds, such as traumatic injuries, burns, hematomas, pressure ulcers, diabetic foot ulcers, full and partial thickness wounds, lacerations and skin tears.[9,12–14,17,18]

Despite these characteristics, honey is seen as a last resort, especially in young children being afraid to get botulism, as unsterilized honey can cause botulism. However, this fear is unfounded as MGH is always sterilized using gamma irradiation which kills all spores of *Clostridium botulinum*.[19] We argue that MGH should be used more often as a go-to product, also in less complex wounds. Therefore, we here present multiple cases of different etiology to address the specific aspects of MGH on wound healing and to support its efficacy, safety and easy use on an outpatient basis.

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Table 1
Cases overview.

Case #	Age	Wound type	Wound location
1	9 months	Extravasation-induced injury	Arm
2	10 months	Hemangioma	Coccyx
3	13 years	Surgical removal of an abscess	Arm
4	10 years	Traumatic injury	Shin

2. Materials

Wounds were treated with L-MESITRAN OINTMENT (PROVIDED BY TRITICUM, MAASTRICHT, THE NETHERLANDS) CONTAINING 48% MEDICAL GRADE HONEY, HYPOALLERGENIC LANOLIN, VITAMIN C, VITAMIN E, ZINC OXIDE AND ESSENTIAL OILS.

2.1. Subjects

Four pediatric patients (excluding the case in the Supplemental figure) with age between 9 months and 13 years presented for consultancy to the hospital in Thessaloniki, Greece, with wounds of different origin (Table 1). The wounds of these patients are discussed in this prospective observational case series and were all treated on an outpatient basis. The wounds included are an extravasation-induced injury, a coccyx ulcer, an ulcer following the removal of an abscess, and a bad healing wound on a shin. The study was carried out in accordance with relevant institutional and national guidelines, and the protocol was approved by the Ethics committee of the St. Luke's hospital in Thessaloniki, Greece. The principles of the World Medical Association's Declaration of Helsinki were followed. The patients' representatives gave written informed consent to participate in the study and for publication of the data.

2.2. Treatment

All wounds were treated on an outpatient basis in the same manner, via monotherapy with daily medical grade honey (MGH) (provided by Triticum Exploitatie BV, Maastricht, the Netherlands) application to the wound area and close monitoring. The wound areas were cleaned using normal saline (0.9%) solution, and MGH was subsequently applied locally to the wound which was repeated daily. No antibiotics, sedatives, pain medication, or other topical therapies were given.

3. Results

3.1. Case 1: extravasation injury of the forearm

Patients that are hospitalized and need frequent infusions, e.g., patients that are malnourished or are critically ill, are at risk to develop extravasation-induced injuries.[20,21] Extravasation is the accidental leakage of fluid, such as medication or nutrients, into the surrounding tissue during infusion. This can lead to skin and soft tissue damage, and result in severe ischemia, infection, and necrosis.[21,22]

A 9-month female toddler was recovering from the surgical removal of a hepatoblastoma and subsequently developed a forearm ulcer 14 days later, caused by extravasation. Treatment of the wound was started upon presentation at day 0 (Fig. 1, day 0). At this time-point, the wound was necrotic, as visible by the black colored tissue. The red skin around the edges indicated the presence of inflammation (Fig. 1, day 6). At day 10 the partially autolytic debrided wound was soft and easily further debrided using gauze and saline (Fig. 1, day 10). The following days, the inflammation progressively decreased as shown by the transition of color (day 19). Over this period, granulation tissue was formed together with clear signs of angiogenesis in the deeper skin layers. At day 26, the shiny red color indicated restored blood vessels, and the wound size progressively decreased (day 30) until complete closure by epithelialization at day 41. After long-term follow-up, there is only a minimal scar visible and no functional defect. Application of MGH was considered as easy by the parents and did not cause any signs of pain or discomfort for the patient.

3.2. Case 2: coccyx ulcer

Hemangiomas are benign vascular tumors and have an incidence of 3–10% of all infants, with females and preterm infants having an increased risk.[23] The majority of infantile hemangiomas are uncomplicated and do not require treatment.[23,24] However, in approximately 10–15% an intervention may be necessary, for example because ulceration can lead to pain and risk of infection.[23,24]

A female toddler born with a congenital hemangioma presented at 10-month of age with an ulcerated hemangioma on the coccyx (Fig. 2, day 0). She was already successfully treated for an ulcerated hemangioma on the thigh with MGH previously, and therefore it was also decided to treat the coccyx ulcer similarly.

The coccyx ulcer presents a bulged area on the top right (green arrow in Fig. 2, day 0) and a red hemorrhagic area on the middle left side which was bleeding from time to time (blue arrow in Fig. 2, day 0). MGH therapy was started, and in 7 days there was complete healing of the small ulcer, and spontaneous hemorrhage was absent (Fig. 2, day 7). At 6-month follow-up, there is almost a complete regression of the lesion with an acceptable esthetic result. No signs of pain or discomfort by the MGH were noticed, and the application of MGH was easy according to the parents which applied the MGH.

3.3. Case 3: infected ulcer

Patients can develop pathologies that need surgical intervention, such as abscesses that need to be removed. Although surgeries are performed in an aseptic environment, this can still lead to infected wounds.

A 13-year-old female girl had a large circular abscess (4 cm in diameter) in the right axillary region. This abscess was surgically removed and resulted in a large skin deficit. Upon presentation, the wound had signs of infection, and it was decided to treat the ulcer with monotherapy of MGH (Fig 3, day 0). After two weeks the wound has shifted from a pink sloughy wound into a vitalized red wound and halved in size. At this time point, any sign of inflammation or infection had disappeared (Fig 3, day 14). The color and shine indicated that the wound was well-vascularized and moist, which both are signs for fast wound healing. The wound progressively healed and was fully closed after one month of MGH therapy. One month later only a small scar remained (Fig 3, day 30). The patient did not experience any pain during the treatment and she easily applied the MGH herself.

3.4. Case 4: wound dehiscence

Children are often playing and can behave free and non-precautious, which can result in accidents and injuries.

A 10-year-old boy had a traumatic injury on his shin. He received sutures by his general practitioner to minimize the open space and decrease the chance of getting an infection (Fig. 4, day -5). However, the wound dehisced as shown by the edges of the wounds that were ascending and together with signs of excessive scarring; this urged to remove the sutures (Fig. 4, day -1). Since the wound was dry and presented with a hard crust, we decided to start MGH treatment for keeping the wound moist and enhance the wound healing (Fig. 5, day 0). After 5 days of MGH treatment, the wound impressively healed progressively with reduced signs of scar formation (Fig. 5, day 5). At day 9, the wound was almost completely closed (Fig. 4, day 9). In time, the wound remodeled resulting in reduced wound size and less scar formation. The boy easily applied the MGH himself without pain or discomfort.

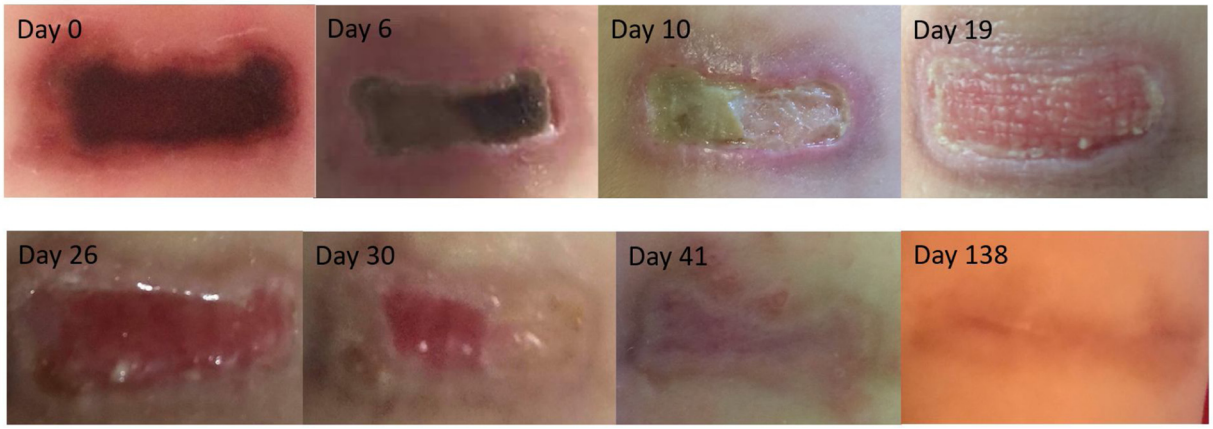

Fig. 1. The healing of an extravasation-induced injury in time is facilitated with MGH therapy, resulting in a minimal scar.

Fig. 2. The healing of a coccyx ulcer in time. The green arrow indicates a bulging area and the blue arrow indicates the small ulcer. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article)

4. Discussion

We presented four diverse cases in which MGH was used to treat wounds. In all cases, the patients were treated on an outpatient basis. MGH was easy and safe to apply with the absence of adverse events and was very effective. The beneficial effects of MGH for wound care are based on the antimicrobial activity and pro-healing effects.[5–14] We will next discuss some properties of the MGH that are supported by the presented case series in more detail.

We demonstrated that MGH controls inflammation, and MGH leads to autolytic debridement of the necrotic tissue (case 1). These effects of MGH were also supported by other studies.[25,26] To further demonstrate the effects on autolytic debridement, we added a clear example in Supplemental Fig. 1 of an extravasation-induced wound on the forearm of a preterm neonate (36 weeks of gestation) at the third week of her life. This eschar was autolytic debrided and almost released completely by itself, which next could very easily be removed. MGH therapy can easily be performed in an outpatient setting or by nurses and should be considered for such kinds of wounds. In case there is soft necrotic tissue or slough present, the scrubbing with gauze and saline may further assist the debridement.

It has been described that MGH is safe and can be effective in the wound care of ulcers.[12,17,27] In the presented small ulcer in case 2 it was also effective, further recommending the use of MGH at a home setting in young pediatric patients.

The surgical-induced trauma described in case 3 clearly illustrates that MGH reduces the signs of infection. The antimicrobial effects of MGH may be orchestrated by the low pH in which pathogens hardly persist, the osmotic effect leading to dehydration of bacterial cells, and the formation of low amounts of hydrogen peroxide that can be lethal for bacteria. Moreover, MGH demonstrated pro-healing properties by the fast closure of this relatively large wound in the armpit.

The wound in case 4 tended to develop excessive scar formation as shown by the ascending acellular wound edges with a typical appearance of collagen and scar formation. The wound was not healing well with the sutures and dried out, and therefore MGH treatment had a high chance to be beneficial. After only 5 days, the ascending wound edges disappeared, and there were reduced signs of scarring, which can be

Fig. 3. The healing of a lesion following an abscess removal receiving MGH therapy.

Fig. 4. The healing of a bad sutured wound on the shin using MGH therapy resulting in a properly closed wound.

explained by the reduction of oxidative stress and inflammation. This way, the antioxidants supplemented in the used MGH formulation (vitamins C and E) may enhance the anti-scarring effects.[28–31] The observed pro-healing effects support to use MGH in simple wounds. The viscosity of honey aids in preserving a physical barrier that prevents the infiltration of pathogens, keeps the wound well hydrated, while simultaneously providing nutrients for the proliferation of new skin cells. Together, this and the osmotic effects of MGH lead to enhanced wound healing as the migration of epithelial cells and reepithelialization are stimulated.[32] MGH can also enhance angiogenesis and stimulate blood flow.[33,34]

The reason of the reserved use of honey for wound care in pediatrics may lie within the fear to cause botulism as honey may contain spores of Clostridium.[35] However, MGH is safe because it must be sterilized using gamma irradiation. Other sterilization methods such as heat being used in supermarket honey will inactivate the enzymes responsible for the pro-healing effects, making the honey unsuitable for wound care. The MGH used to treat wounds should therefore carefully be selected.

Multiple MGH formulations exist containing different amounts and origins of honey. Please note that higher concentrations of honey are not necessarily better, and in some cases is reported to cause a temporary stinging pain by possibly the low pH or strong osmotic effects.[26] We did not experience this pain sensation with the MGH used in the cases we treated. The MGH used in this study contains 48% of honey, which is substantially lower than the 80–100% used in many other MGH products. In addition, the MGH used in this study is supplemented with certain oils and the antioxidants and vitamins C and E, which further can enhance wound repair and decrease scar formation.[28,29,31] A reduced wound healing time reflects decreasing wound care costs because hospital stays can be shortened using MGH[36] and less medical attention may be needed, especially as MGH is easy to apply also on an outpatient basis. We presented only a few cases, but our experience teaches us that MGH can be used in almost all kinds of wound types.

5. Conclusion

MGH has two major pillars that are beneficial for wound healing. First, MGH has multiple characteristics inducing its antimicrobial action, and so can prevent and treat infections. Secondly, MGH has several mechanisms that lead to enhanced wound repair. Although MGH is often used as a last resort for chronic and complex wounds and is reserved to use in children, with this manuscript we demonstrated that it could also be used in small and more simple wounds. The multiple pro-healing mechanisms which lead to effective wound healing, together with its safety and easy applicability, recommend MGH as a solid base for the first line of therapy in all kinds of wounds.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.ctim.2019.05.014.

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