The effect of medical honey on second intention wound healing in dogs

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ABSTRACT

The aim of our retrospective study was to observe the healing effect of medical honey on wounds in dogs. Honey debrides wounds, kills bacteria, lowers the pH value of wounds, reduces chronic inflammation, promotes the infiltration of fibroblasts and provides a moist environment, which is essential for wound healing. Twenty dogs with a total of 21 contaminated nonsurgical wounds were included. Wounds were treated with medical honey and left to heal by second intention. For the prevention of wound desiccation and bandage adherence, a low-adherent absorbent pad was used. The wounds smaller than 15 cm^2 healed in 28 to 49 days (mean 36.4±7.9 days), and wounds larger than 15 cm^2 healed in 35 to 77 days (mean 50.3±15.9 days). A low-adherent absorbent pad completely prevented adherence of the dressing to the wound bed, so that no pain or tissue damage occurred during dressing changing. The treatment of wounds with medical honey had a positive influence on wound healing, and all wounds in our study healed completely with minimal scarring and with regrowth of hair. Ten dogs received no antibiotic therapy and none of them developed wound infection. Medical honey therefore serves as a promising alternative antimicrobial chemotherapeutic. The use of honey is effective in tissue regeneration and wound healing in large wounds in dogs where surgery alone cannot guarantee satisfactory results.

Key words: dogs; medical honey; nonsurgical contaminated wounds; second intention wound healing

Introduction

The causes of wounds to the skin, subcutis and underlying muscles in dogs are diverse, including bites, traumatic injuries, lacerations and penetrations from sharp objects, incisions (O'DWYER, 2007; PAVLETIC, 2010a), and dehiscence of surgical wounds (PAVLETIC, 2010b). Bite wounds are among the most severe injuries in small animal practice and account for 10 - 15% of all veterinary trauma cases (PAVLETIC, 2010c). In bite wounds, compressive and tensile forces can be applied to regional tissue, which can significantly impair blood flow to the area, with an increased risk of necrosis,

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which, together with the contamination of the oral bacterial flora, can lead to infection (GRIFFIN and HOLT, 2001; PAVLETIC, 2010d). The majority of bite wounds are contaminated with aerobic bacteria at presentation (GRIFFIN and HOLT, 2001). In most cases the wound dehiscence occurs 3 – 5 days postoperatively. Wound dehiscence is the result of several factors, either alone or in combination, such as wound closure under excessive tension, closure of severely compromised skin, suture placement that compromises cutaneous circulation, infection, or lack of postoperative protection of the wound against motion and licking (PAVLETIC, 2010b).

Most wounds heal without complications (DAVIDSON, 2015), but careless wound management in more severe injuries can promote several wound complications, including tissue necrosis, infection and wound dehiscence (PAVLETIC, 2010d). In the early stages of wound care, the principles of open wound management, including lavage, debridement and gentle tissue handling, must be followed to keep infection under control (WILLIAMS, 2009; DAVIDSON, 2015). Open wounds often have to be treated for days or weeks until they can be closed or healed by second intention (DAVIDSON, 2015). There are many wound care products available that potentially minimize the stage of inflammation, debride the wound without damaging healthy tissue, reduce infection, promote the development of the reparative stage, and improve wound healing (DOYLE, 2012; DAVIDSON, 2015). As wounds heal, their needs vary, and all wounds benefit from a properly moist environment in which the cells and proteins involved in wound healing function best (BOHLING et al., 2007).

Honey has been used for centuries to treat wounds. It is a natural product prepared by bees from nectar, and contains about 180 different substances (DE ROOSTER et.al, 2008), such as amino acids, vitamins, sugars, and trace elements (DAVIDSON, 2015). The antimicrobial properties of honey are attributed to many factors, including acidity, release of small amounts of hydrogen peroxide and methylglyoxal, osmolarity, which dehydrates microorganisms, and phytochemical components (MOORE et al., 2001; DAVIDSON, 2015). Due to its anti-inflammatory effect, honey also reduces pain and decreases pressure on the tissues as a result of edema (TONKS et al., 2001; MOLAN, 2002; TONKS et al. 2003).

As a wound dressing, honey provides a moist healing environment, promotes wound debridement, clears infections quickly, deodorizes and reduces inflammation, edema and exudation. It increases the healing rate by stimulating angiogenesis, and promoting granulation tissue and epithelialization (MOLAN, 2001; PAVLETIC, 2010e). It accelerates collagen maturation and maintains optimal pH conditions for fibroblast activity (DAVIDSON, 2015). However, honey is reported to cause pain when applied to very inflamed wounds (MOLAN and BETTS, 2004).

The effect of medical honey for wound care in small animals has so far been documented by clinical observation and mainly single clinical cases (DE ROOSTER et al., 2008; ADEYEMI et al., 2017; SHRESTHA, 2017; LUKANC et al., 2020).

In the literature review, we could not find data on how long second intention healing using medical honey takes in dogs. Therefore, the aim of our study was to assess the time of healing in different types and sizes of wounds, pain after application, odor, exudate, necrosis, the time of appearance of granulation tissue on the wound surface, and cosmetic repair.

The expected progression of wound healing is important information for both the owner and the veterinarian when discussing prognosis and the costs of wound healing.

Materials and methods

The retrospective study was performed at the Small Animal Clinic of the Veterinary Faculty of the University of Ljubljana from 2014 to 2018. Twenty dogs: 1 Giant Schnauzer, 1 Maltese, 1 German Shepherd, 1 Galgo, 2 Boxers, 1 Cocker Spaniel, 1 West Highland Terrier, 1 Swiss Mountain Dog, 1 Bull Terrier, 1 Golden Retriever, 1 Chihuahua, 1 Malinois, 1 Greyhound and 6 mixed breed dogs, aged from 3 months to 13.5 years, 13 females and 7 males, weighing 0.6 to 41.7 kg and a total of 21 nonsurgical wounds, were included in the study. All the dogs were considered clinically healthy and were presented with contaminated or dirty wounds (Fig. 1-5). In cases of dehiscence after tumor excision, all margins were free of malignant cells and no metastases were found. Exclusion criteria were animals with systemic diseases, animals treated with immunosuppressant drugs, animals with surgical wounds that were closed with sutures or left to heal by second intention (i.e., relaxing incisions), and ulcerative wounds diagnosed with a malignant tumor (i.e., cutaneous carcinoma).

Fig. 1. Necrosis and dehiscence of the skin flap healed with medical honey in 42 days

Fig. 2. Dehiscence of sutured wound healed with medical honey in 63 days

Fig. 3. Traumatic wound with extensive necrosis healed completely in 42 days with medical honey without antibiotic therapy

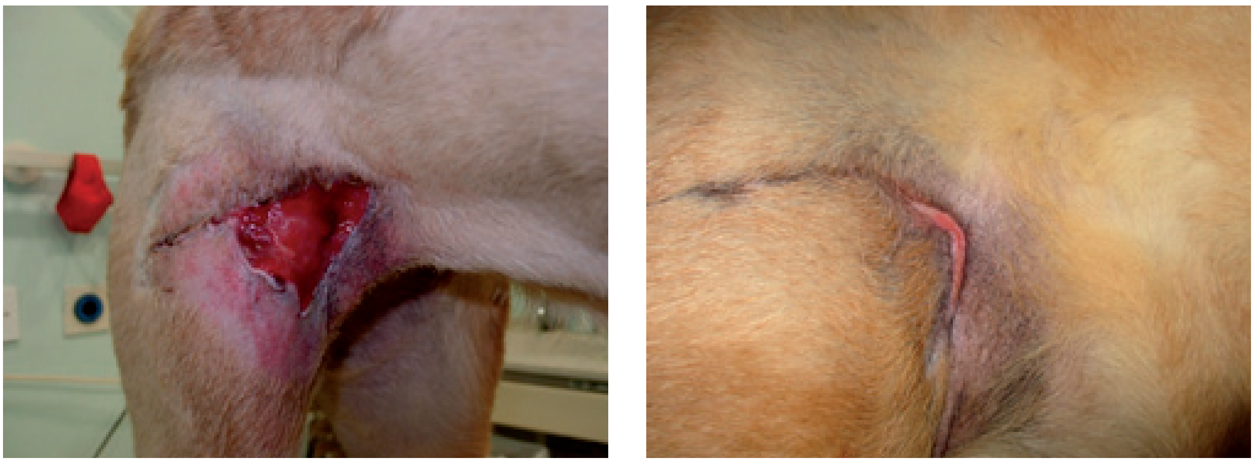

Fig. 4. Dehiscence after surgically treated traumatic wound in the region of intensive movement healed in 70 days

Fig. 5. Dehiscence after suturing a bite wound healed completely with medical honey in 28 days

Different types of wounds were included in the study: 11 cases of dehiscence after previous surgical procedures (Fig. 1, 2, 4, 5), 6 cases of dehiscence after previous complete tumor excisions with histopathologically confirmed clean margins (3 mast cell tumors, 1 hemangiopericytoma and 2 mammary gland tumors), and 5 cases of dehiscence after previous surgical closure of traumatic wounds, 5 traumatic wounds with deep skin necrosis (Fig. 3), 4 bite wounds, and one cut wound. Dogs with dehiscence (11) and bite wounds (3) had surgical treatment 5-7 days before inclusion in the study with medical honey. Four of these dogs were surgically treated by a referring veterinarian, namely, 3 dogs with traumatic wounds and 1 with a bite wound. Ten dogs were prescribed antibiotic therapy and another 10 received no antibiotics. Four dogs received metronidazole 20 mg/kg/12h (Efloran, Krka, Novo mesto, Slovenia) and amoxicillin with clavulanic acid 20 mg/kg/12h (Synulox, Zoetis Belgium SA, Louvain-la-Neuve, Belgium) for 5-7 days, 5 dogs received amoxicillin and clavulanic acid, and one dog received metronidazole only. All dogs were administered (Rimadyl, Zoetis Belgium SA, Louvain-la-Neuve, Belgium) 2mg/kg/12h for 7-10 days and 3 dogs were additionally given a fentanyl transdermal patch 3-5 μg/kg/h (Durogesic, Janssen Pharmaceutica NW, Beerse, Belgium).

In all the wounds, the skin and subcutaneous tissue were affected, but there was no bone or joint involvement. The wounds were divided into two groups according to the size of the wound. Ten wounds were smaller than 15 cm^2 and 11 wounds larger than 15 cm^2.

Participation in the research study was entirely voluntary, and the owner's consent to treatment was obtained for each animal.

Wound care. The date of inclusion of the animal in the study was the day of presentation of the animal at the clinic and was set as day 0. On day 0 wounds were not fresh, some previously surgically treated wounds had dehisced a day or two before the presentation, and some animals were presented with necrotic tissue in the wound. On day 0 the wounds were protected with a sterile swab and the hair was clipped. If necessary, surgical debridement of the devitalized tissue was performed, followed by irrigation with 500-1000 ml isotonic 0.9% sterile saline solution using a 50 ml syringe and an 18 G needle. The wound was dried with sterile swabs.

Wound dressing. From day 0 to day 6, the dressing was applied once a day, and from day 7 to wound healing the dressing was applied twice a week. Before each dressing, the wound was rinsed as described above. For treatment of the wounds, we used the medical honey L-Mesitran Soft wound gel (Theo Manufacturing BV, Maastricht, Netherlands). L-Mesitran Soft gel contains 40% medical grade honey, hypoallergenic medical grade lanolin (Medilan), propylene glycol, polyethylene glycol PEG 4000, vitamins C and E.

Medical honey L-Mesitran Soft was applied to the entire wound area and covered with a Melolin low-adherent absorbent dressing (Smith & Nephew Medical Limited, Hull, UK). Melolin consists of a low adherent perforated film, a highly absorbent cotton/acrylic pad and a hydrophobic backing layer. The Melolin was covered with sterile swabs, a Soffban Natural rolled cotton pad (BSN Medical, Inc., Charlotte, USA) and a Coban™ self-adherent elastic wrap (3M, St. Paul, USA).

All wounds were evaluated until they had healed.

Wound assessment (necrosis, granulation, odor, exudate and type of affected tissue) was performed on days 0, 3, 7 and then once a week until the wounds had healed. Wound size was measured with a ruler, and the wound was photographed on days 0 (after debridement), 3, 7 and then once a week until the wounds had healed. The area of the wound was determined using the program Image J.

Statistical analysis

In the results, all data are presented as mean ± standard deviation (SD). Before the statistical analysis, all data were evaluated with the Shapiro-Wilk test for distribution normality. Since most of the data were not normally distributed and the samples were relatively small, a non-parametric test was used for the statistical analysis. We used the non-parametric Mann-Whitney Test to compare healing in wounds smaller than 15 cm^2 and larger than 15 cm^2 on selected days, and to compare healing in dehiscence (Type I) and other wounds (Type II). All statistical analyses were performed using SPSS 17.0.

Results

Eleven out 21 wounds had necrotic tissue on the wound at the time of presentation. In seven wounds, up to 30% and in 4 wounds more than 80% of the surface was covered with necrotic tissue on day 0, necrotic tissue was detached from all wounds within 4 days. In all wounds any odor disappeared within 7 days after treatment with medical honey.

The first granulation tissue appeared in 11 wounds as early as 3 days after inclusion in the study. The time to cover the entire wound with granulation tissue was 7 days, except for 3 wounds, in which the entire wound was covered for up to 12 days. Exudate was most pronounced in the first week of healing. No discomfort was noticed during application of medical honey to the wound.

We considered wounds to be completely healed when the entire wound surface was closed by new skin or a scar formation (SORG et al., 2017). All wounds (10) smaller than 15 cm^2 (from 6.01 to 14.85 cm2) healed by day 49 (mean 36.4±7.9 days), 7 (70%) wounds healed by day 35. The mean percentage reduction in wound area was 19.9%±24.9 on day 7, 47.9% ±23.9 on day 14, 75.8%±14.8 on day 21, 88.1%±13.7 on day 28 and 95.3%±8.3 on day 35 (Fig. 6 and 7).

Wounds (11) larger than 15 cm^2 (from 16.41 to 100.08 cm^2) healed in 35 to 77 days (mean 50.3±15.9 days), 4 wounds (36.4%) healed by day 35, while 9 wounds healed by day 63, one wound by day 70 and one wound by day 77. The mean percentage reduction in wound area was 18.7%±25.3 on day 7, 45.3%±25.9 on day 14, 63.1%±22.1 on day 21, 77.3%±22.2 on day 28 and 83.7%±19.4 on day 35 (Fig. 6 and 7).

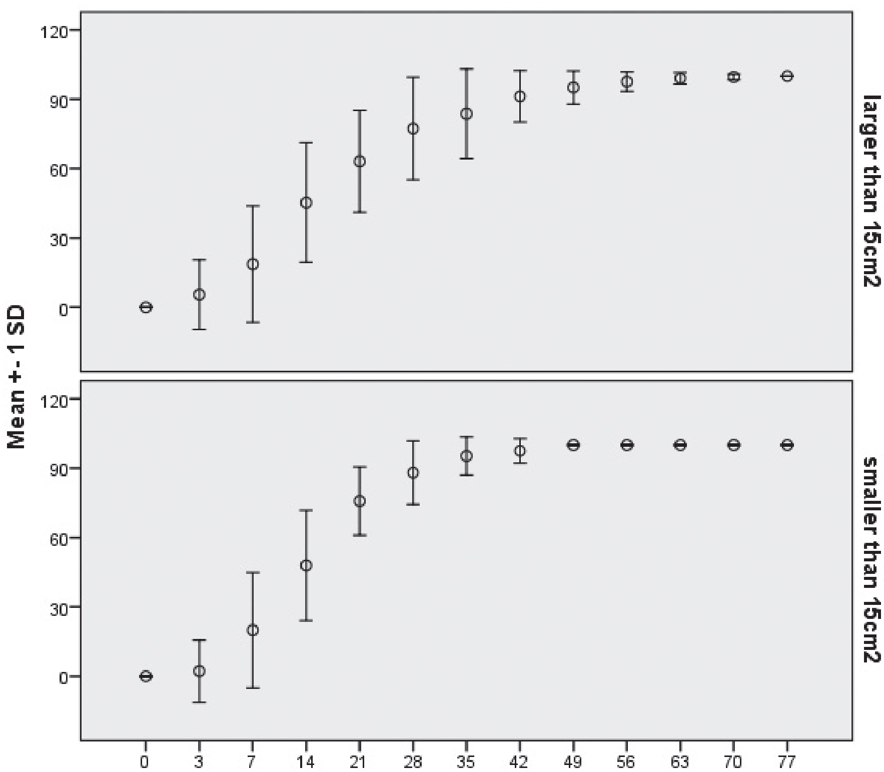

Fig. 6. Wound healing according to wound surface on selected days

Data represent mean ± SD. X- axis on the graph represents days of healing, y-axis represents mean percentage reduction of the wound. There were no statistically significant differences between groups on selected days.

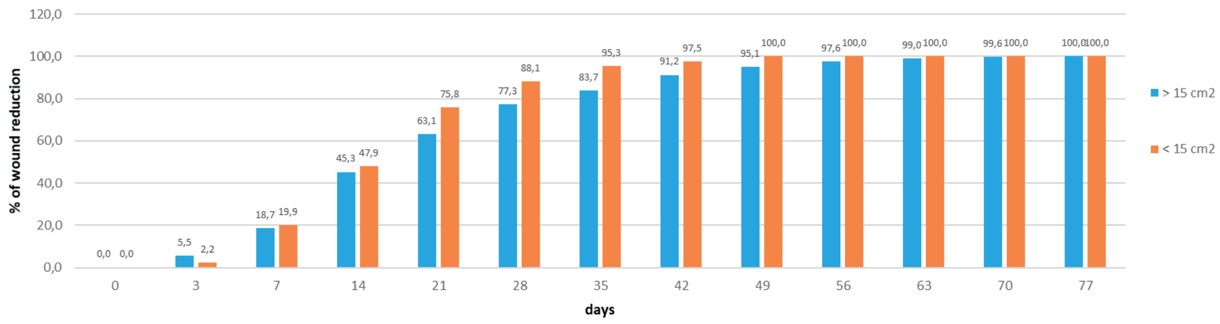

Fig. 7. Wound healing according to wound surface
Data represent mean ± SD. There were no statistically significant differences between groups on selected days.

Dehiscence (11 wounds) healed in 28 to 77 days (49.6±16.4 days). The mean percentage reduction in wound area was 14.6%±22.3 on day 7, 44.3%±23.1 on day 14 and 63.5%±16.2 on day 21, 77.9%±17.5 on day 28 and 85.9%±14.8 on day 35. (Fig. 8 and 9).

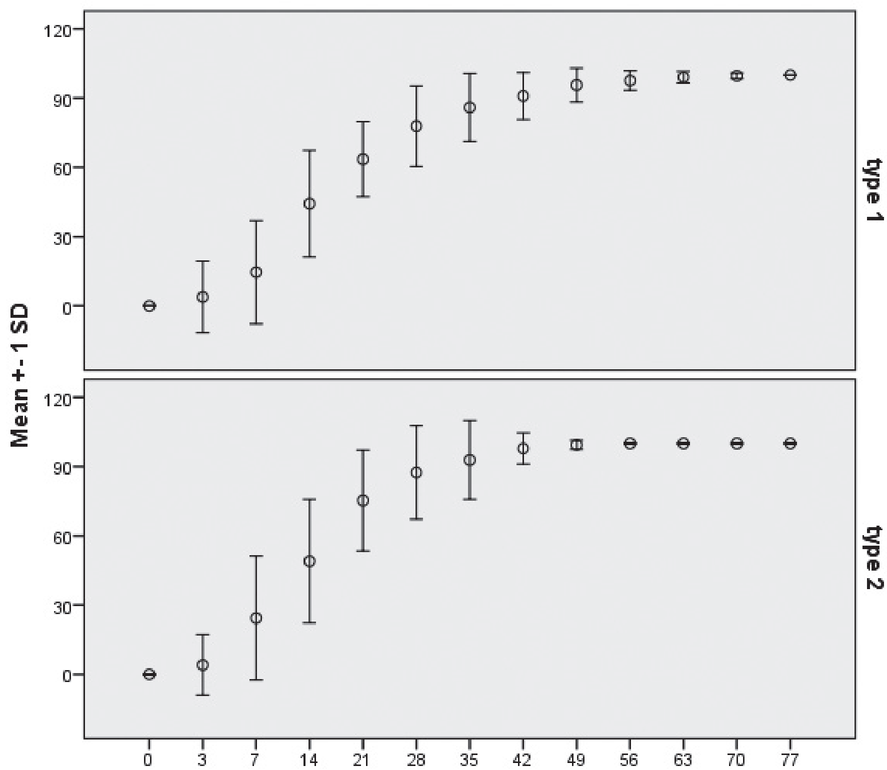

Fig. 8. Wound healing according to the type of wound on selected days
Type 1 – dehiscence, Type 2 – other wounds. The x- axis on the graph represents days of healing, the y-axis represents mean percentage reduction of the wound.

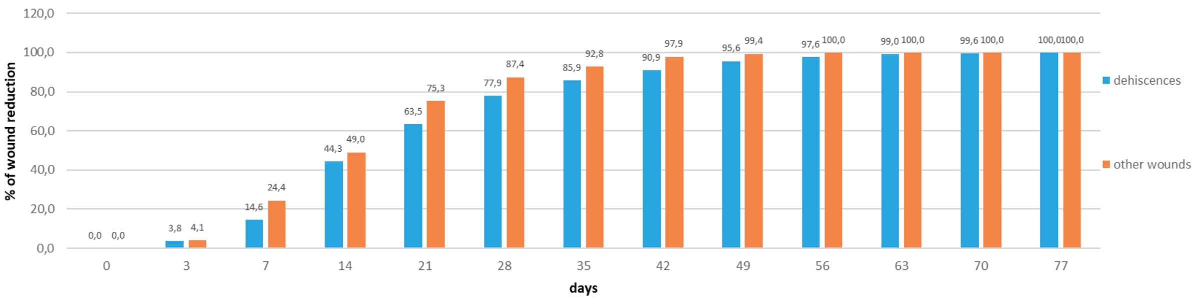

Fig. 9. Wound healing in dehiscence and other wounds

The Mann-Whitney test showed no statistically significant differences in wound healing between the groups in relation to wound size, or between dehiscence and other wound types on any of the selected days (P>0.05). However, there was a statistically significant difference in the time when the entire wound surface was closed by new skin or a scar formation between wounds smaller and larger than 15 cm^2. Smaller wounds healed on average 4 weeks earlier than larger wounds (Fig. 6 and 7).

Discussion

A number of challenging wounds affecting most parts of the body can be left to heal by a second intention (granulation, contraction and epithelialization). Such wounds are often infected and are covered with necrotic tissue (PAVLETIC, 2021).

An essential step in the treatment of open wound management is wound irrigation. In our study, we used a 0.9% sterile saline solution which rehydrates necrotic tissue, and reduces and removes bacterial contamination, foreign materials, toxins, cytokines and debris (ANDERSON, 1996; ANDERSON, 1997). Many ointments and creams are marketed for the purpose of applying something to a wound and promoting its healing (OVERGAAUW and KIRPENSTEIJN, 2005). Cleansing and debriding properties can also be attributed to medical honey, as it is believed that the high osmotic pressure in honey and the activation of proteases by the hydrogen peroxide contained in honey facilitate debridement (MANYI-LOH et al., 2011). It also contributes to painless lifting of slough and necrotic tissue (Fig. 3). DAVIDSON (2015) recommended the use of honey dressings for the inflammatory and early repair phase of healing, and to discontinue them when debridement is complete and healthy granulation tissue is present. As honey does not have any negative effects on the tissue and does not irritate it, it can be used in the long term until healing is complete (DE ROOSTER et al., 2008; ADEYEMI et al., 2017; SHRESTHA, 2017; LUKANC et al., 2018; LUKANC et al., 2020).

Honey has an antimicrobial and infection inhibiting effect, absorbs edema, facilitates deodorization of infected wounds (MOLAN, 1999), and stimulates granulation, epithelialization, tissue formation, and blood supply in the wound area (EFEM, 1988; MOLAN, 2001). The odor in all wounds in our study disappeared by day 7. The necrotic tissue detached gradually within 4 days from all wounds in which surgical necrectomy was not performed on day 0. Honey contributes to the painless detachment of slough and necrotic tissue (MANYI-LOH et al., 2011) (Fig. 3) which can be removed during wound irrigation without the animal being anesthetized.

In our study, granulation tissue appeared in small spots across the wounds as soon as in 3 days, and covered the surface in 7 days except for 3 wounds. The early appearance of granulation tissue was observed in dehiscence and in wounds initially covered by necrotic tissue. PAVLETIC (2010b) reported that in dehiscence of skin flaps, it took another 3 - 5 days to determine the extent of skin necrosis which would slough off. We hypothesize that the earlier occurrence of granulation tissue is due to the fact that the healing process in wounds started earlier, before dehiscence occurred (Fig. 4) or necrotic tissue was removed (Fig. 1), as the wound healing phases began immediately after the development of the wound (BALSA and CULP, 2015). The appearance of granulation tissue was earlier than in the study by BOHLING et al. (2004) in which the granulation tissue first appeared on day five, mainly from the wound center, and covered the wound surface on day 7. The time needed for granulation tissue to cover the bottom of the wound bed was 7 days, which is comparable to that of BOHLING et al. (2004), but the size of all wounds in our study was significantly larger and a longer healing period was expected.

In 3 wounds that were located in the area of increased skin movement, the granulation tissue covered the surface within 12 days. This aligns with the observation that in body parts with a large amount of movement, wound healing may be delayed (VAN HENGEL et al., 2013).

In our study, the small wounds healed in significantly less time (28 days) than larger wounds. All smaller wounds healed by 49 days, whereas 6/11 (54.5%) larger wounds also healed by day 49. In comparison with BOHLING et al. (2004), where the reduction in wound size on day 7 was 43.1%, the reduction in our study was 19.9% and 18.7% for smaller and larger wounds, respectively. We believe this is because many wounds in our study had to be cleaned due to the presence of necrotic tissue and contamination (Fig. 3). The wounds in our study were also much larger than those in BOHLING's study (2004). With the exception of two wounds sized 6 cm^2, all wounds were larger than 8 cm^2 and up to 100 cm^2 (two wounds), compared to BOHLING's study (2004) where the wounds were surgically created, with a size of 2x2 cm^2, they were clean and 97.6% of them healed in 21 days. We would expect that the surgical wounds with straight edges created in a sterile environment in BOHLING's study (2004) would heal earlier than the wounds in our study which had high exposure to bacteria, foreign bodies, necrotic material and uneven edges.

However, in the case report by ADEYEMI et al. (2017) 97% of a wound with a circumference of 92 cm in a dog healed in 168 days, and in the case report by the wound in a dog in the metacarpal region with an open fracture healed in 88 days. Both wounds were treated with honey dressings. In our study, the slowest wound healing was observed in one wound, which took 77 days. This wound was not the largest (25.3 cm^2) at presentation, but it was in the area of intensive movement (Fig. 4). Two of the largest wounds, located on the dorsal side of the back and on the atlanto-occipital region (100 cm^2 and 99.5 cm^2), healed in a shorter time, 49 and 42 days respectively, suggesting that wounds in regions with excess skin and minimal movement heal faster.

In the study by PRPICH et al. (2014) 29/31 wounds of a surface area from 18.84 to 113.1 cm^2 (median 43.98 cm^2), created by excision of soft tissue sarcoma on the distal aspect of the limbs, closed completely with second intention healing in 53 days (range, 25-179 days), which is also longer than in our study. Of particular note, in cases of extensive wounds, healing by second intention may exend over several months, as highlighted by HOSGOOD (2006). EFEM (1988) suggested that good regeneration of the skin can be attributed to the properties of honey, which mobilizes epithelial cells from the wound edges and activates still vital epithelial cells from the hair follicles. During the first 7 days, the dressing was changed daily to absorb excessive exudate, which decreased after the first week. Excessive exudate on a wound can cause wound maceration (PEREIRA and BÁRTOLO, 2016). Once the wounds stop producing fluid, it is sufficient to change the dressing twice a week to maintain the antibacterial activity of honey in the wound (DE ROOSTER et al., 2008).

According to our previous experience (LUKANC et al., 2018; LUKANC et al., 2020) with wound healing using a honey-soaked gauze, the gauze adhered to viable tissue, causing pain and irritation during removal. We also noticed that both L-Mesitran Tulle and L-Mesitran Net adhered to the wounds, although we applied medical honey underneath. The granulation tissue adhered and grew through the small opening in the mesh, which caused pain, bleeding, and damage to the granulation tissue during the removal of the dressing and delayed the healing of the wound. Due to difficulties encountered in previous studies, in the current study we covered all wounds with Melolin which never adhered to the wound. Despite the fact that the osmotic effect of honey drains fluid from the tissue, which can be painful (ADEYEMI et al., 2017), we observed no pain and no adherence of the dressing to the wound when using the low-adherent absorbent dressing Melolin. It has a plastic film to prevent the dressing from adhering to the wound surface, and is perforated to allow exudate to pass from the wound to the body of the pad.

Our current study, as well as previous studies on the treatment of old and contaminated wounds using medical honey for second intention healing showed that it had a positive impact on wound healing, none of the wounds became infected, all wounds were quickly cleared of odor and exudate, healthy granulation tissue was formed, and epithelialization was not altered. Additionally, no pain was observed after applying the honey to the wounds and the cosmetic outcome was minimally altered due to the minimal amount of scar tissue and regrowth of the hair. No dog in our study developed any functional disorder or wound break down.

Another advantage is that medical honey covered with Melolin can be used in all stages of wound healing, only the frequency of dressing changes should be reduced after the wounds are covered with granulation tissue.

Even extensive wounds in dogs can be treated with medical honey without advanced reconstructive surgery, and may be suggested to dog owners who are reluctant to subject their animal to multiple procedures under anesthesia due to possible surgical complications or the risk of anesthesia. Half of the dogs in our study received no antibiotic therapy and none of them developed wound infection. Medical honey therefore serves as a promising alternative antimicrobial chemotherapeutic.

Limitation of the study. The limitation of our study was that it was a retrospective study and that the animals included in the study had different wound types and sizes, and received different antibiotic therapy. Another limitation was the lack of a control group. Our previous experience with the intention to treat wounds in animals in a control group with wet to dry dressings during the first days of treatment was not successful. All the animals deteriorated and developed a severe inflammatory response with leukocytosis and a high temperature of 40°C, so we considered such treatment unethical. Another limitation of our study is the lack of histological examination to assess fibroblasts, epithelial cells, collagen, and new blood vessel formation.

Conclusions

Complete and successful wound healing without infections, high owner satisfaction, acceptable cosmetic appearance and no functional disturbances, and reasonable treatment costs all support the use of medical honey as an effective, safe, and economical form of treatment in second intention wound healing in dogs. We hypothesize that medical honey can be safely used for the treatment of contaminated wounds.

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SAŽETAK

Cilj je ovog retrospektivnog istraživanja bio praćenje ljekovitog učinka medicinskog meda na rane u pasa. Med uklanja devitalizirano tkivo rane, uništava bakterije, snizuje pH-vrijednost rane, smanjuje kroničnu upalu i potiče infiltraciju fibroblasta te omogućuje vlažnost koja je nužna za cijeljenje rane. U istraživanje je uključeno dvadeset pasa s ukupno 21 nekirurškom kontaminiranom ranom. Rane su tretirane medicinskim medom te su ostavljene da sekundarno zacijele. Da bi se spriječilo isušivanje rane i ljepljenje zavoja, upotrijebljen je zavoj s neprianjajućim slojem. Pritom deset pasa nije primilo antibiotsku terapiju. Rane površine manje od 15 cm^2 zacijelile su za 28 – 49 dana (prosječno 36,4±7,9 dana), a rane površine veće od 15 cm^2 zacijelile su za 35 – 77 dana (prosječno 50,3±15,9 dana). Zavoj s neprianjajućim slojem potpuno je spriječio ljepljenje na ranu tako da pri promjeni zavoja nije došlo do boli ili oštećenja tkiva. Tretiranje rana medicinskim medom pozitivno je utjecalo na njihovo cijeljenje, naime sve su rane u ovom istraživanju potpuno zacijelile, s minimalnim ožiljcima i ponovno uspostavljenim rastom dlačnog pokrova. Među deset pasa koji nisu primili antibiotsku terapiju ni jedan nije razvio infekciju rane. Može se stoga zaključiti da je medicinski med obećavajuća alternativa antimikrobnim kemoterapeuticima. Primjena meda učinkovita je u regeneraciji tkiva i cijeljenju rana velike površine u pasa kod kojih kirurški zahvat ne može jamčiti zadovoljavajuće rezultate.

Ključne riječi: psi; medicinski med; nekirurške kontaminirane rane; sekundarno cijeljenje rana

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