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Optimizing wound healing in diabetic foot ulcers: impact of ulcer location and treatment approaches

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ABSTRACT

Background: Diabetic foot ulcers (DFUs) are a common and severe complication of diabetes mellitus, often leading to prolonged healing times and increased risk of amputation. *Aim*: This study evaluates the healing period among diabetic cases with ulcers affecting different anatomical areas and assesses the impact of honey and hydrogel treatments on wound closure time. *Methodology*: A prospective, single-blinded, randomized controlled trial was conducted at the Diabetic Foot Center, King Fahad Specialist Hospital, Saudi Arabia, from February 2019 to February 2023. The study included 120 participants with type 2 diabetes and second-degree foot ulcers. Participants were divided into four treatment groups: honey alone, hydrogel alone, honey and hydrogel combination, and a control group receiving Fucidin ointment. Healing times were analyzed based on ulcer location and treatment type. *Results*: The mean healing time across all groups was 12.76±4.08 days. Healing times varied significantly based on the ulcer location (p=0.002), with hindfoot wounds taking the longest to heal. Among treatment groups, the combination of honey and hydrogel demonstrated the shortest healing time (10.83 ± 3.5 days), which was significantly faster than the control group (p=0.004). This combination was particularly effective in ulcers on the forefoot. Additionally, greater wound size correlated with longer healing times (p<0.001). *Conclusion*: Wound location significantly affects healing duration in diabetic ulcers. The combination of honey and hydrogel enhances wound closure rates, especially in ulcers affecting the forefoot. These findings support the incorporation of honey-hydrogel therapy in clinical management of DFUs.

KEYWORDS

diabetic foot ulcer, wound healing, randomized controlled trial, advanced wound care

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1. INTRODUCTION

Diabetic foot ulcers (DFUs) are among the most severe complications of diabetes mellitus, leading to prolonged healing, increased infection risk, and amputation in severe cases [1]. The estimated 15%. diabetes people are susceptible to a foot ulcer with amazing 70% getting diabetic foot [2]. Ulcer location plays a significant role in healing time, with anatomical differences influencing wound vascularization and pressure distribution [3,4]. Understanding healing variations based on ulcer location and treatment modalities can enhance DFU management. Honey has antibacterial properties, which can help to control infection and prevent further tissue damage [5,6]. Anatomical categorization involves three categories: Forefoot, Midfoot & Hindfoot [7].
This study investigates healing times among diabetic patients with ulcers affecting different anatomical areas and evaluates the efficacy of honey and hydrogel treatments.

2. METHODOLOGY

2.1 Study design and setting

This study was conducted as a prospective, single-blinded, randomized controlled trial. Recruitment and data collection took place at the Diabetic Foot Center, King Fahad Specialist Hospital, Buraidah, Saudi Arabia, over a four-year period, from February 2019 to February 2023.

2.2 Study population and randomization

A total of 120 participants with type 2 diabetes mellitus and second-degree diabetic foot ulcers were enrolled. Participants were randomly assigned using a concealed allocation method to one of four treatment groups (n = 30 per group):

- Honey alone group: treated with medical-grade honey.
- Hydrogel alone group: treated with a standard hydrogel dressing.
- Combination group: treated with alternating applications of honey and hydrogel.
- Control group: treated with standard fucidin ointment.

2.3 Inclusion Criteria

- Adults (≥18 years) with type 2 diabetes.
- Presence of second-degree foot ulcers.
- No severe infection or gangrene.

2.4 Exclusion criteria

- Peripheral vascular disease.
- Uncontrolled diabetes (HbA1c >10%).
- Active osteomyelitis.

2.5 Outcome measures

The primary outcome measure was the healing time, defined as the number of days from randomization until complete epithelialization of the ulcer was observed and confirmed. Secondary outcome measures included changes in wound size (area and depth) over time and the incidence of wound infection during the treatment period.

2.6 Statistical analysis

All data were compiled and analyzed using the Statistical Package for the Social Sciences (SPSS), version 26.0. Descriptive statistics were used to summarize baseline characteristics. Analysis of Variance (ANOVA) was employed to compare the mean healing times across the different treatment groups and anatomical ulcer locations. Where significant differences were found, post-hoc tests (e.g., Tukey's HSD or Bonferroni) were conducted for pairwise comparisons. A *p*-value of less than 0.05 was considered statistically significant for all tests performed.

2.7. Ethical approval

All the aspects and protocols of this study have been reviewed by the Regional Research Ethics Committee and registered at the National Committee of Bio and Medical Ethics (NCBE). Registration Number: H-04-Q-001. With the permission and approval from committee the study was initiated**.** All the aspects and protocols were reviewed and the registration on the clinical trials.gov is ID: NCT 038816618

Patients' consent: Informed Consent and Consent of Authorization of voluntary Participant was collected for each patient.

3. RESULTS

Participant characteristics**:** A total of 120 participants completed the study, consisting of 63 males (52.5%) and 57 females (47.5%). The mean age of the participants was 59.64 ± 10.21 years. A

thorough comparison of baseline characteristics, including age, gender distribution, duration of diabetes, baseline HbA1c levels, and initial wound dimensions, confirmed that there were no statistically significant differences among the four treatment groups at the outset of the study (p>0.05 for all comparisons), indicating successful randomization.

Overall healing time and impact of ulcer location: Across all participants, the mean healing time for diabetic foot ulcers was 12.76 ± 4.08 days. Analysis revealed a statistically significant difference in healing duration based on the anatomical location of the ulcer (p=0.002). Ulcers situated on the hindfoot required the longest mean time to heal (15.75 ± 4.30 days), followed by those on the midfoot (14.24 ± 4.10 days). Ulcers located on the forefoot demonstrated the fastest mean healing time (12.24±3.92 days). This can be presented in Table 1.

Table 1. Healing time by ulcer location.

Ulcer Location	Healing Time (Mean ± SD, days)
Midfoot	14.24 ± 4.10
Forefoot	12.24 ± 3.92
Hindfoot	15.75 ± 4.30

p=0.002

Impact of treatment modalities on healing time: the healing times across the four distinct treatment groups are presented. The mean (± SD) healing times recorded were:

- Honey alone group: 12.20 ± 3.8 days
- Hydrogel alone group: 13.97 ± 4.1 days
- Honey & Hydrogel alternately group: 10.83 ± 3.5 days
- Control group (fucidin ointment): 14.03 ± 4.2 days

4. DISCUSSION

This study highlights that the anatomical location of a diabetic foot ulcer (DFU) and the chosen treatment significantly impact healing time. Ulcers on the hindfoot exhibit the longest healing duration, a finding consistent with existing literature suggesting that increased mechanical stress and potentially reduced vascularization in this area impede wound repair [8]. Conversely, forefoot ulcers healed fastest, indicating a potentially better response to offloading and treatment.

The most effective treatment modality identified was the alternating combination of honey and hydrogel, which significantly accelerated healing compared to a standard control (p=0.004). This synergy likely arises from honey's established antimicrobial and tissue-regenerative properties [5, 6, 9] working in concert with hydrogel's ability to maintain an optimal moist wound environment [10]. This dual-action approach appears more effective than either honey alone or hydrogel alone, with the latter showing efficacy comparable only to the control.

The finding that larger wounds heal more slowly (p<0.001) reinforces the critical need for early DFU detection and intervention, a key strategy in reducing diabetic limb complications [1,3]. These results advocate for a tailored approach to DFU management, considering both the prognostic significance of ulcer location and the enhanced efficacy of multi-action topical therapies like the honey-hydrogel combination. Implementing such strategies holds promise for improving patient outcomes and reducing the substantial healthcare burden associated with DFUs, particularly in high-prevalence regions like Saudi Arabia. While acknowledging the limitations of a single-center study, the robust, randomized design provides strong support for these conclusions.

5. CONCLUSION

This study demonstrates that healing time for diabetic foot ulcers is significantly influenced by both their location and the treatment applied. We found that hindfoot ulcers heal slowest (p=0.002), highlighting their high-risk nature.

Crucially, an alternating combination of honey and hydrogel proved most effective, significantly accelerating wound healing (p=0.004) compared to standard care or individual treatments. This synergistic approach, combined with the finding that larger wounds heal slower (p<0.001), underscores the need for early intervention and advanced wound care.

These findings support implementing location-aware treatment protocols using effective, multi-action therapies like honey-hydrogel to improve outcomes and reduce amputations. Further multi-center research is encouraged to validate these results.

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CONFLICT OF INTEREST STATEMENT
The author declares no conflicts of interest.

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