The Impact of Different Dressing Methodologies on the Outcomes of Wound Healing In Diabetic Foot Ulcer Patients: A Systematic Review

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ABSTRACT

Aim: The objective of this review was to assess the impact of different dressing methodologies on the outcomes of wound healing in diabetic foot ulcer (DFU) patients.

Methods: Systematic review analysis was performed by using search engines, like PubMed, Science Direct, Google, and Google Scholar. We retrieved selected published articles based on our study criteria and included the suitable articles published till January 2019. The keywords used for the retrieval of studies are “Diabetes mellitus”, “Dressing methodology”, “Diabetic foot ulcer”, and “Wound healing.” After screening the abstracts of the retrieved articles, eligible full-text articles were chosen for systematic review analysis.

Results: We found 17 eligible studies that contained 9 research articles, 7 randomized controlled trials (RCTs), and 1 random study.

Conclusion: Honey dressing methodology seemed to be effective in the treatment and outcomes of wound healing of different grades of DFUs. However, the efficacy of the other dressing methodologies, involving biological material and herbal extracts, needs to be validated with a greater number of trials in different types of DFUs.

Keywords- diabetic foot ulcers, wound healing outcome, dressing methods

INTRODUCTION

Diabetic foot ulcer (DFU) is one of the most significant complications of diabetes mellitus (DM). It includes a group of syndromes classified into ischemic, neuropathic diabetic foot ulcer and infection of ulcer result in tissue decay. \[1\] It is the major complication observed with diabetic patients that often leads to impairment of limb or amputation. About 15% of DM patients develop foot ulcers during their lifetime, and 85% of the cases proceed to amputation. The overall prevalence of diabetic foot ulcer was 6.3% worldwide. \[2,3\] Diabetic foot ulcers present medical, social, and economic burden that greatly affects the quality of life in diabetes patients worldwide. \[4\] Diabetic neuropathy and peripheral vascular disease are the main etiologic causes of diabetic foot ulceration. Several factors are responsible for the development of diabetic foot ulcer, and the risk factors can escalate the complications of foot ulcer and lead to impairment of wound healing. The diabetic foot ulcer is one of the common manifestations that result in frequent hospitalization of diabetic patients. \[5\] About 20% of the hospital admissions of diabetic patients are due to DFU. \[6\] In diabetic patients, the risk of chronic complications, such as renal damage, cardiovascular disease, eye damage, and diabetic foot ulcer can impose a heavy economic burden on the health system. \[7\] It is noteworthy that treatment and management of diabetic foot ulcer is expensive and demands special intensive care. Therefore, effective treatment of diabetic foot ulceration is vital to avoid limb amputation and preserve the quality of life in diabetic patients. Thus, patients with diabetic foot ulcers require significant care and monitoring from both care...
providers and the community around them. Lack of essential care for DFU patients might result in infection, gangrene, amputation, and even death. An appropriate dressing method represents the effective management of diabetic foot ulceration. An ideal dressing method should protect the wound from infection, alleviate the symptoms, and fasten the wound healing. There exist different types of dressing methods, from basic wound intact dressings to more advanced specialist dressing methods, available with flooded ingredients and showing specific beneficial properties like antimicrobial activity. Research and knowledge about dressings in diabetic foot ulcer are poor. Despite the existence of numerous studies on the management of wound healing in DFU, there is no ideal dressing for effective wound healing. A clear and up-to-date overview of the different dressing methodologies is essential to aid the clinicians and practitioners to choose specific and effective dressing for different DFUs. Therefore, knowledge about the updated data on specific dressing methodologies is important for the management of diabetic foot ulcer and to improve the quality of life in diabetic patients.

MATERIALS AND METHODS

A systematic literature search was conducted in February 2019 to review the impact of different dressing methodologies on the outcomes of wound healing in DFU patients. The exclusion criteria include: (1) The studies reporting complications other than diabetic foot ulcer, (2) The studies not reporting the outcomes of the wound healing, (3) The studies using animal models, (4) The studies evaluating the supplements on the outcomes of wound healing, (5) The studies not published in any journal, and (6) The studies published in a language other than English. In order to perform systematic review analysis, the search engine tools like PubMed, ScienceDirect, Google, and Google Scholar were searched using the terms “Dressing methodologies”, “Diabetic foot ulcer”, “Wound healing”, and “Diabetes mellitus”. Studies published up to January 2019 were included in this study.

Selection of studies

Initially, after screening the titles and review articles from the collection, suitable studies were selected for abstract evaluation. Eligible full-text articles were retrieved after excluding duplicates and the studies providing incomplete data for systematic review analysis.

RESULTS

The initial search resulted in the collection of 65 documents. After excluding non-relevant studies, and review articles (10), 25 studies were selected for abstract and full-text screening. Seven studies were excluded due to duplication (3) and incomplete data (5). Finally, we identified 17 studies and included them for the review (Figure 1). Among the 17 eligible studies, 9 studies were original research articles, 7 were randomized controlled trials (RCTs), and 1 was random study. Data extracted from the selected studies were tabulated under the following sections: author, year of publication, study objectives, study design, sample size, age range, dressing methodology, wound healing outcomes, and conclusions for the analysis (Table 1).
**Table 1: Characteristics of the studies included in the systematic review.** [18-27]

<table>
<thead>
<tr>
<th>Author of study</th>
<th>Year</th>
<th>Study objectives</th>
<th>Study design</th>
<th>Sample size</th>
<th>Age range</th>
<th>Dressing methodology</th>
<th>Wound healing Outcomes</th>
<th>Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iniran</td>
<td>2015</td>
<td>Comparison of honey impregnated and normal saline dressing for DFU</td>
<td>RCT</td>
<td>348</td>
<td>&gt;18 years</td>
<td>Honey impregnated dressing</td>
<td>1 and 2 &amp; 18 days</td>
<td>75.9% of honey impregnated patients were recovered vs. saline dressing, 57.4%</td>
</tr>
<tr>
<td>Mohajeri-Tebrani</td>
<td>2016</td>
<td>Comparison of honey impregnated and normal saline dressing for DFU</td>
<td>RCT</td>
<td>57</td>
<td>NA</td>
<td>Bioprint implant dressing</td>
<td>2.4 &amp; 6 weeks</td>
<td>58% wound in surface area. 48.3% treated with Bio implant compared wet dressing.</td>
</tr>
<tr>
<td>Nasiri</td>
<td>2015</td>
<td>To evaluate the topical olive oil on the wound healing in patients with diabetic foot ulcer</td>
<td>Randomized study</td>
<td>34</td>
<td>30-65 years</td>
<td>Olive oil</td>
<td>1.2 &amp; 4 weeks</td>
<td>Olive oil significantly reduced surface area and depth of wound in 73.3% patients vs. Control 13.3%. (P = 0.003)</td>
</tr>
<tr>
<td>Ragab</td>
<td>2015</td>
<td>To evaluate the effect of propolis dressing technique on healing of septic diabetic foot ulcer patients</td>
<td>Random Case control study</td>
<td>60 (30+30)</td>
<td>18 to &gt;65 years</td>
<td>Propolis dressing</td>
<td>1 and 2 &amp; 3 weeks</td>
<td>16.6 % of the study group had complete ulcer healing compared to control where none had complete healing</td>
</tr>
<tr>
<td>Viswanathan</td>
<td>2011</td>
<td>To assess the effects of a polyherbal formulation cream with that silver sulfadiazine cream on DFU</td>
<td>Prospective study</td>
<td>40</td>
<td>&gt;18-60 years</td>
<td>Group 1 polyherbal formulation, Group B silver sulfadiazine cream</td>
<td>1 and 2 &amp; 43 weeks</td>
<td>Significant decrease in size of wound in both the groups</td>
</tr>
<tr>
<td>Dandekar</td>
<td>2015</td>
<td>To evaluate ampicare dressing for different diabetic wounds</td>
<td>Retrospective study</td>
<td>100</td>
<td>&gt;18-60 years</td>
<td>Ampicare dressing</td>
<td>NA &amp; 45 days</td>
<td>96.2% showed wound healing</td>
</tr>
<tr>
<td>Moghazy</td>
<td>2010</td>
<td>To check freshness of bee honey</td>
<td>Prospective study</td>
<td>30</td>
<td>NA</td>
<td>Bee honey dressing</td>
<td>1-3 &amp; 3 months</td>
<td>43.3% of the patients reduction size of the ulcer</td>
</tr>
<tr>
<td>Edmond</td>
<td>2017</td>
<td>To compare the sucrose octasulfate with control dressing</td>
<td>RCT</td>
<td>240 (126- sucrose 114- control)</td>
<td>&gt;18 years</td>
<td>Sucrose octasulfate</td>
<td>1 and 2 &amp; 20 weeks</td>
<td>40% of the patients underwent sucrose octasulfate showed wound closure</td>
</tr>
<tr>
<td>Alam</td>
<td>2012</td>
<td>To compare the pyodine dressing with honey dressing in wound healing</td>
<td>Prospective study</td>
<td>100 (50+50)</td>
<td>36-70 years</td>
<td>Pyodine dressing and honey dressing</td>
<td>1-4 &amp; 10 weeks</td>
<td>72% of the honey dressed patients showed complete wound healing, 66 % in pyodine dressed</td>
</tr>
<tr>
<td>Kamaratos</td>
<td>2014</td>
<td>To assess Manuka honey-impregnated dressings in neuropathic DFUs</td>
<td>Prospective randomized study</td>
<td>63 (32+31)</td>
<td>&gt;60 years</td>
<td>Manuka Honey impregnated dressing, 31 conventional dressing</td>
<td>1 and 2 &amp; 6 weeks</td>
<td>No significant difference between the two groups but wound healing time was 314±4 days in group I versus 43±3 ys for group II</td>
</tr>
<tr>
<td>Nagoba BS</td>
<td>2010</td>
<td>To evaluate the potential citric acid in DFUs of different grades</td>
<td>Retrospective study</td>
<td>115</td>
<td>&lt;20 years</td>
<td>Citric acid dressing</td>
<td>1-3 &amp; NA</td>
<td>In 94 % of the patients the wound healing was effective with control of bacterial infection</td>
</tr>
<tr>
<td>Buzzi</td>
<td>2016</td>
<td>To evaluate Calendula officinalis Hydrogelic is extract in treatment DFU</td>
<td>Prospective study</td>
<td>109</td>
<td>18-90 years</td>
<td>Calendula officinalis Hydrogelic is extract</td>
<td>1 and 2 &amp; 30 weeks</td>
<td>78% of the DFU were healed with 30 week follow-up</td>
</tr>
<tr>
<td>Suravash</td>
<td>2013</td>
<td>To assess the efficacy of topical royal jelly on healing of different DFUs</td>
<td>RCT, case control</td>
<td>64 ulcers (32x32) in 25 patients</td>
<td>&gt;60 years</td>
<td>Royal jelly</td>
<td>1-3 &amp; 38 weeks</td>
<td>93.8% of patients with royal jelly showed complete wound healing compared to control 90%</td>
</tr>
<tr>
<td>Veves</td>
<td>2002</td>
<td>To compare the effectiveness of Promogran with standard dressing</td>
<td>RCT</td>
<td>276</td>
<td>23-85 years</td>
<td>collagen/oxidized regenerated cellulose and conventional dressing</td>
<td>1and 2 &amp; 12 weeks</td>
<td>37% of patients with promogran showed complete wound closure</td>
</tr>
<tr>
<td>Shukrini</td>
<td>2008</td>
<td>Compare the Honey and Povidone iodine. Dressing for DFU</td>
<td>Prospective case control study</td>
<td>30</td>
<td>31 to 65 years</td>
<td>Honey and Povidone dressing</td>
<td>2 &amp; 26 weeks</td>
<td>Mean days for wound healing was less than 15.4 days compared to povidine 15.4 days</td>
</tr>
<tr>
<td>Abdelatif</td>
<td>2008</td>
<td>To assess safety and efficacy of a new honey ointment on diabetic foot ulcers</td>
<td>Prospective study</td>
<td>60 patients</td>
<td>&gt;18-70 years</td>
<td>Honey ointment dressing</td>
<td>1.5 &amp; 9 weeks</td>
<td>96% of patients with grade 1 and 2 ulcers showed complete healing of wound in 9 weeks</td>
</tr>
<tr>
<td>Jude</td>
<td>2007</td>
<td>To study of Hydro fiber containing ionic silver and calcium alginate dressing in non-ischaemic DFUs</td>
<td>RCT</td>
<td>67 + 67</td>
<td>&gt;18-70 years</td>
<td>Hydro fiber and calcium alginate</td>
<td>1 and 2 &amp; 8 weeks</td>
<td>Hydro fiber-treated ulcers reduced in depth nearly twice as much as CA-treated ulcers 0.25 cm vs. 0.13 cm</td>
</tr>
</tbody>
</table>

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DISCUSSION
Diabetic foot ulcers (DFUs) are characterized by varied thicknesses of foot ulcers in diabetic patients. The DFUs are the major source of morbidity in DM patients and significantly result in amputation. [28] Currently, there are various interventions available to treat the adverse effects of DFUs, which include traditional and biological dressing methods. [29] It is crucial to select the appropriate medical dressing method for the effective treatment and management of DFUs from amongst the limited number of specific and effective dressing methods available. Most of the medical dressing methodologies include general strategies, such as saline, povidone, ionic silver, and honey, for the treatment of DFU. However, there are few studies on the herbal extracts in the treatment of DFUs. The healing properties of honey were well recognized since ancient times, and there is a revival of interest in its DFU wound healing potential, with many reports showing its benefits in the treatment of DFUs. The aim of our analysis was to investigate the different dressing methodologies on wound healing in the treatment of different DFUs in diabetic patients. A total of 6 studies, including 2 RCTs and 4 prospective studies, have reported about the effectiveness of honey and royal jelly dressing on DFU healing. [11,17,19,23,25,26] Honey provides a moist atmosphere with antimicrobial and anti-inflammatory activities, reduces exudates and edema, and induces wound shrinkage, collagen synthesis, and accelerates epithelialization of the wound. [30] The study analysis suggests that honey dressing may be more effective than control interventions for the complete treatment time. Therefore, selection of honey dressing proves to be promising for the clinical treatment of the different grades of the DFUs. However, the RCT of royal jelly dressing outcomes in wound healing is not significant with the control group and requires more RCTs to validate the potential of royal jelly. [23] Mohajeri-Tehrani et al. conducted a RCT for evaluating the bioimplant dressing in the treatment of DFU (grades 1-4) and found the advantages of wound healing by bioimplant dressing over wet dressing. [12] Olive oil dressing was found to be effective in the treatment of grade 1 and 2 DFUs. However, more RCT studies are warranted to validate the potential of wound healing for different grades of DFU. Dressing methodologies involving biological extracts were shown to be active in the wound healing process. In our study, we analyzed 1 retrospective and 2 prospective studies reporting the polyherbal formulations, *Calendula officinalis*, and ampcare dressings in the treatment of DFUs that showed effective wound healing and time reduction with *C. officinalis* herbal extract dressing. [16,22] This evidence shows that herbal properties have the potential to reduce the burden of recovery time in the wound healing process. Several studies have reported different biological substances and gelling materials in the dressing methodology for the treatment of the different DFUs in diabetic patients. In our review, we analysed 3 RCTs evaluating the efficacy of
sucrose octasulfate, promogran, and hydrofiber with ionic silver in diabetic wound healing. The outcome of wound healing was appreciable in the case of sucrose octasulfate and hydrofiber dressing method that showed a significant reduction of non-ischemic wound depth. [27] A retrospective study revealed the effectiveness of citric acid dressing in controlling the infections of DFUs and the speedy recovery of the patients. [21]

Nevertheless, our systematic review shows some limitations in terms of lack of more RCTs on the efficacy of herbal extracts in the treatment of DFUs, studies included for analysis are without information about specific grading and the type of DFUs, and publications in only English language were considered. Therefore, more studies validating the efficacies of specific herbal extracts is warranted for the treatment and management of different diabetic foot ulcers to improve the quality of life in diabetic patients.

**CONCLUSION**

Several interesting regimes are available for the treatment of diabetic foot ulcers. The honey dressing was found to be an effective and safe method in the management of different diabetic ulcers. The studies reporting the other dressing methods are effective for specific wound conditions, like septic ulcer (propolis), neuroischemic DFUs (sucrose octasulfate), depth of wound (hydrofiber), and infectious wound (citric acid). However, more studies are warranted to validate the potential of these findings for exploring the ideal dressing methodology for the different types of DFUs in diabetic patients.

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**Declaration of Conflicting Interests**

The author declares to have no conflict of interest.

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