International Journal of Life Sciences, Biotechnology and Pharma Research Vol. 13, No. 11, November 2024 Online ISSN: 2250-3137
Print ISSN: 2977-0122

DOI: 10.69605/ijlbpr_13.11.2024.11

ORIGINAL RESEARCH

Comparative study of efficacy of local application of colloidal silver solution versus honey in eradication of biofilm in chronic wounds

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Received Date: 15 October, 2024 Accepted Date: 31 October, 2024

ABSTRACT

Background: Biofilm structures are complex entities that develop at wound surfaces. Microbes make an extracellular polymeric substance, or EPS, matrix. Biofilms are most commonly associated with chronic wounds, which are predisposed to delayed healing. Various topical agents, including honey and colloidal silver, have been used to eradicate biofilm, although the effectiveness of these treatments has been questioned. This was aimed at evaluating the relative effectiveness of honey and silver dressings regarding the eradication of biofilm, the process of wound healing, and general clinical outcomes.**Methods:** This is a prospective comparative study whereby, 168 patients were assessed for the biofilm and 72 patients that were positive were alternately assigned either to honey groups (n = 36) or silver dressing groups (n = 36) with the assessment of the wound done biweekly intervals of five days for biofilm reduction, wound discharge, foul smell, and granulation and length of hospital stay and time required for definitive treatment.

Results: These results showed that the reduction in biofilm, wound discharge, and foul smell were alike for both honey and silver dressings. The purulent discharge in both groups had become serous by day 3. Formation of granulation tissue was documented in both groups, although this was a little quicker in the silver group. The average hospital stay was shorter in the honey group, 25.8±14.8 days versus 28.3±19.2 days in the silver group (p=0.54). Not surprisingly, time to definitive therapy was also a bit shorter in the honey group: 20.2±12.5 days versus 26.5±17.4 days (p=0.18).

Conclusion: At the end, honey and silver dressings were found to be equal in their effectiveness toward healing varied chronic wounds. Both types show comparability in aspects such as reduction of biofilm, control exudate, and healing of the wound. Probably, the choice is going to be between honey and silver will depend on wound-specific characteristics, cost considerations, and patient preference. Further research with a larger sample size is much needed to provide more definitive guidelines for selection of local applicants.

Keywords: nanoparticles; wound healing; chronic wounds; granulation

INTRODUCTION

Chronic wounds are prevalent in millions of people globally and impose a heavy burden on the health care system. However, the biofilm in chronic wounds is very common. Biofilms are defined as a complex microbial structure adhering to wound surfaces that are embedded in an extracellular polymeric substance (EPS) produced by the microorganisms themselves.[1,2] Biofilms act as a shield for microbes from an external immune response of the host and make them resistant to conventional antimicrobial therapies, thereby delaying the healing process of wounds.[3]

Traditional treatment approaches to biofilm-associated chronic wounds include debridement, antibiotics, and topical agents. In fact, newer emerging contemporary therapeutic options are more in vogue. Honey and colloidal silver may be two of

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the most promising alternate therapies used for treatment of biofilm-infected chronic wounds.

Colloidal silver is an aqueous solution carrying silver nanoparticles, and has been a focus of much attention due to its broad-spectrum antimicrobial activities.[4] Experiments show that silver nanoparticles will compromise bacterial cell membranes, suppress DNA replication, and induce oxidative stress, all together providing a symbiotic killing of harmful microorganisms. Being very small in size, nanoparticles can penetrate the EPS matrix of biofilms to enhance their action against infections caused by biofilms.[4,5]

Honey is a natural compound that has been used for the treatment of wounds for hundreds of years because of its potent antibacterial and antibiofilm properties. This makes the wound environment unfavourable for microbial colonization: honey has properties consisting of acidic pH, high osmolarity, and an activity similar to hydrogen peroxide.[6,7] Some other varieties of honey are composed of certain chemical compounds called methylglyoxal, which augment its antibacterial effectivity.[9] It has been proven that honey prevents biofilm maturation and even dissociates pre-formed biofilms in wounds.

Although there is some evidence suggesting that these materials are useful in wound care, there is limited scientific study on the effectiveness of honey and colloidal silver solution as biofilm removers from chronic wounds. This study aims to fill this gap by comparing the effectiveness of local applications of honey and colloidal silver solution in removing biofilm from chronic wounds.

This study aims to compare the efficacy of the local application of colloidal silver solution versus honey in the eradication of biofilm in chronic wounds.

MATERIALS& METHODOLOGY

This prospective comparative study was conducted among patients admitted with chronic ulcer to general surgical ward in Shri BM Patil Medical college, Hospital and Research centre from July 2022 to June 2024.With anticipated proportion of time for healing of wound in honey dressing method vs silver colloidal solution 9 %and 37%, the study would require a sample size of 35 per group. (i.e., a total sample size of 70 assuming equal group sizes), to achieve a power of 80% for detecting a difference in proportions between two groups at a two-sided p-value of 0.05 using G*Power 3.1.9.7 software.The sample size of this study is 72.[8]

After the approval form institutional ethics committee, patients with chronic ulcers were recruited in the study with informed consent.

Patientswho were immunologically compromised, allergic to silver containing compounds and critical ischemic limb with ABPI <0.3 were excluded from the study. They underwent detailed evaluation. Wound cultures were sent and when the cultures were positive for organisms, they were subjected to detection of biofilms with the tube adherence technique. Patients with biofilm in their ulcers were recruited in the study.Patients were assigned to both study groups alternately. Both groups received standard care according to their needs, which included mechanical debridement, when necessary, antibiotic therapy, dietary correction andmanagement of comorbidities.

Topical application of gauze soaked in honey (Dabur honey) was applied to the honey group. Using a sterile piece of gauze, 10–30 ml of raw, unprocessed honey was diluted with a few drops of regular saline and applied to the ulcer bed. In the silver group silver colloidal solution was sprayed to their wounds. Every fifth day, culture swabs were taken to look for the presence of organisms and biofilms.

Every five days, the wounds in both groups were assessed for the presence/reduction of discharge, foul smell, granulation tissue, size of the ulcer and presence or absence of biofilms. In both groups, ulcers with good granulation tissue and negative biofilm were selected for definitive management. The length of hospital stay, the time taken for wound to become biofilm negative and time taken for definitive treatment were recorded.

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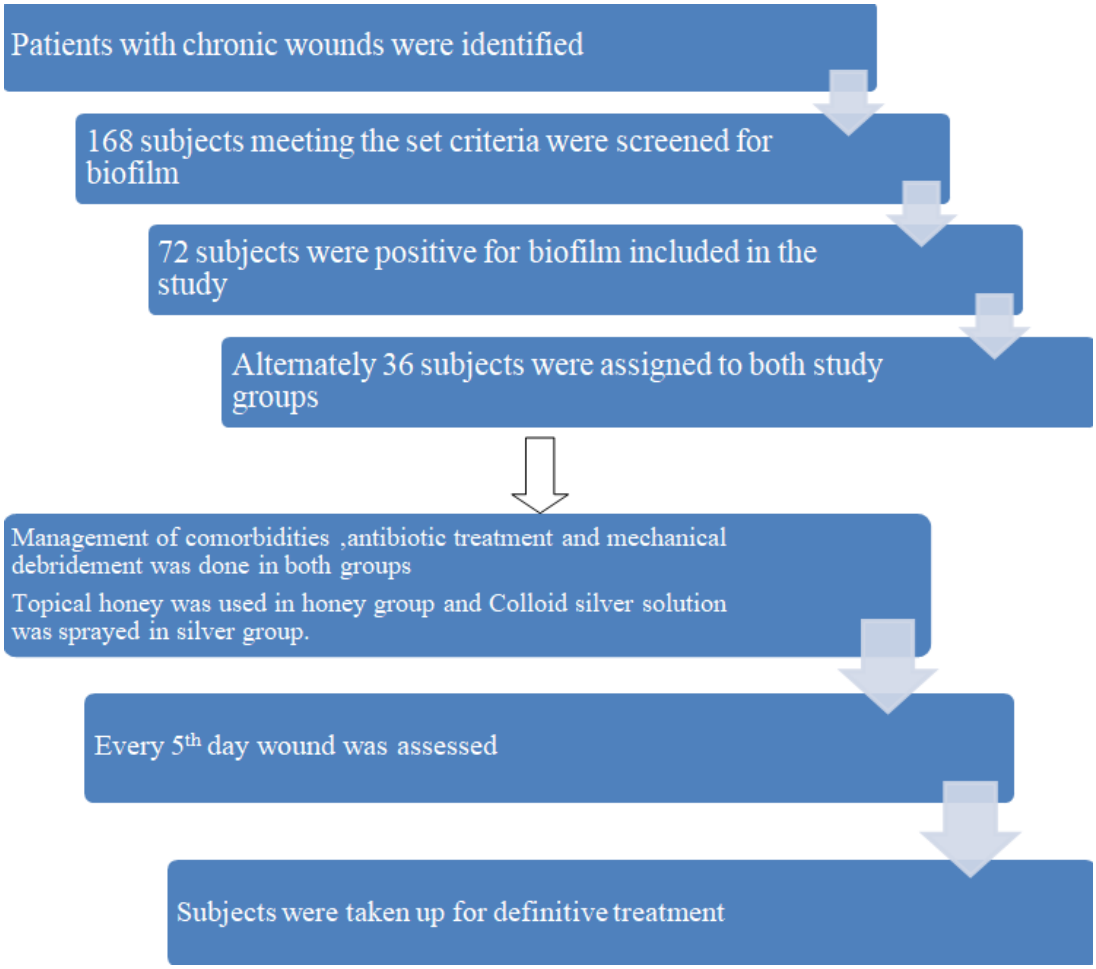

Statistical analysis

Data was entered in MS excel sheet and analysed using the Statistical Package for the Social Sciences 20(SPSS Inc. Chicago). Results were presented in tabular and graphical forms Mean, median, standard deviation and ranges were calculated for quantitative data. Qualitative data were expressed in terms of frequency and percentages. Appropriate test of significance like Chi-square test, T-test and Man Whitney U tests was applied to compare categorical data with P value <0.05 was considered significant.

RESULTS

Age distribution was similar between groups with median age group between 41-60 years. Among 72 patients, 53 were males and 19 were females.Most of the ulcers were secondary to debridement of necrotising fasciitis, diabetic foot, cellulitis and traumatic ulcers. Other causes were abscesses, bedsores, Fournier's gangrene etc.

Table 1: Showing size of ulcer between the groups

Size of ulcer (Mean±SD)	Honey	Silver	p-value
Day 5	106.3±147.8	130.6±202.7	0.56
Day 10	103.2±148.1	128.2±201.8	0.55
Day 15	102.6±142.4	124.9±196.05	0.601
Day 20	81.5±122.3	155.5±170.9	0.144
Day 25	192.7±242.9	224.4±198.7	0.81
Day 30	-	227±212.1	-
Day 35	-	209±196.5	-

Table 2: Showing the discharge from ulcer between the groups

	Honey	Silver	p-value
Day 5			
Serous	14 (38.9%)	10 (27.8%)	0.48
Purulent	7 (19.4%)	6 (16.7%)	

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Seropurulent	15 (41.7%)	20 (55.6%)	
Day 10			
Serous	30 (83.3%)	27 (75%)	
Seropurulent	6 (16.7%)	9 (25%)	0.38
Day 15			
Serous	31 (86.1%)	32 (88.9%)	
Seropurulent	1 (2.8%)	2 (5.6%)	0.602
Day 20			
Serous	18 (50%)	18 (50%)	1.0
Day 25			
Serous	4 (11.1%)	7 (19.4%)	0.32
Day 30			
Serous	0	2 (5.6%)	0.15
Day 35			
Serous	0	2 (5.6%)	0.15

Both groups transitioned from purulent/seropurulent to predominantly serous discharge by day 10, with no significant difference between groups in discharge characteristics (p>0.05).

Table 3: Comparison of the ulcer parameters between the groups

	Days	**Honey**	**Silver**	**p-value**
Foul smell from ulcer	Day 5	11 (30.6%)	17 (47.2%)	0.14
	Day 10	1 (2.8%)	3 (8.3%)	0.303
	Day 15	0	0	-
	Day 20	0	0	-
	Day 25	0	0	-
	Day 30	0	0	-
	Day 35	-	0	-
Presence of biofilm	Day 5	36 (100%)	36 (100%)	1.0
	Day 10	32 (88.9%)	34 (94.4%)	0.39
	Day 15	16 (44.4%)	19 (52.8%)	0.62
	Day 20	4 (11.1%)	8 (22.2%)	0.41
	Day 25	0	2 (5.6%)	0.32
	Day 30	0	1 (2.8%)	0.35
	Day 35	-	2 (5.6%)	0.15
Granulation tissue	Day 5	13 (36.1%)	17 (47.2%)	0.33
	Day 10	34 (94.4%)	36 (100%)	0.15
	Day 15	31 (86.1%)	34 (94.4%)	0.406
	Day 20	17 (47.2%)	18 (50%)	0.59
	Day 25	3 (8.3%)	7 (19.4%)	0.25
	Day 30	0	2 (5.6%)	0.15
	Day 35	-	-	-

Both groups showed reduction in foul smell over time with no significant difference between groups in odour control (p>0.05). Both the groups were effective in biofilm elimination in most subjects by 15 days. Also, both groups promoted granulation tissue formation with slightly higher rate in silver group, but not statistically significant (p>0.05)

Table 4: Comparison of the outcomes between the groups

	Honey	**Silver**	**p-value**
Biofilm negative	14.2±8.2	17.7±12.6	0.17
Hospital stay	25.8±14.8	28.3±19.2	0.54
Definitive treatment	20.2±12.5	26.5±17.4	0.18

Both groups showed progressive reduction in biofilm presence over 7 days and no significant difference between groups in biofilm reduction (p>0.05). Mean hospital stay was 25.8±14.8 days in Honey group compared to 28.3±19.2 days in silver group (p=0.54) and time takenfor definitive treatment was 20.2±12.5 days in Honey group compared to 26.5±17.4 days in Silver group (p=0.18).

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DISCUSSION

Many therapeutic techniques are being studied to improve healing of chronic wounds, which continues to be a major concern in surgical practice. The intention of this study was to assess the efficacy of silver and honey dressings in removing biofilm from chronic wounds. Silver and honey have both been shown to have anti-biofilm qualities and the ability to promote the healing of wounds. Thisstudy attempted to compare and analyze the clinical results of these twoanti-biofilmagents.

Biofilm Production and Healing of Wounds: Due to the emphasis on free-floating bacteria, little is known about biofilm as a cause of infection that resistantto regular treatment. This is due to the behavior of biofilm being distinct from that of bacteria present on the surface of wounds. Biofilms are considered to be involved in about 80% of diseases.[10,11] About 80% of thebiofilms are made up of extracellular polymeric substances (EPS), sometimes known as slime, while the other 20% are made up of bacteria residing in communities inside the EPS matrix. These bacteria are resistant to both the host's immune system and antimicrobial treatment because of their limited penetration, metabolic inhibition and protection from quiescent bacteria. They also exhibit diversity in their geno/phenotype composition.[12,13] Comparable biofilm eradication between honey and silver dressings was one of our study's main observations. Throughout the course of the observation period, both treatments gradually reduced the amount of biofilm present; and showed similar efficacy in both groups.

Percival et al noted that biofilm was one of the major hurdles in healing of chronic wounds.[14]According to Vallabha T et al, 43 (67.2%) out of 64 patients with ulcers developed biofilms. The overall healing period for ulcers without biofilms was 42.56 days, while it was 52.31 days for patients with biofilms. There is a statistically significant difference ($p < 0.002$). Ulcers develop healthy granulation in 10–30 days on average, with a mean of 18.1±5.5 days. 43% of the patientsdeveloped granulation tissue in 10-15 days. Biofilms were eliminated in a maximum of 25 days, with an average of 17.5 days.[8]

Odor Control and Wound Discharge: Honey and silver dressings both showed promise in reducing foul smell and wound discharge. By day 3, both groups' purulent or seropurulent discharge changed to mostly serous discharge, indicating similar effectiveness in controlling wound exudate. This is consistent with research by Jull et al. (2003), who found that honey was useful in controlling wound exudate in their Cochrane review.[15] Both groups saw a noticeable decrease in the foul smell arising from their wounds, with a marginal benefit shown with honey dressings, however it was not statistically significant. This confirms earlier research by Gethin et al., who noted that honey was useful in lowering the foul smell of chronic wounds.[16,17]

Granulation Tissue Formation: Granulation tissue formation was promoted by both honey and silver dressings, with the silver group showing a somewhat better rate of granulation tissue formation—a rate that was not statistically significant. This discovery contributes to the body of data that both agentshave properties that help in improving rate of wound healing, as stated in Vandamme et al.'s systematic review.[18]

Duration of hospital stay and definitive treatment: The honey group had a shorter mean hospital stay and time to definitive treatment, but these differences were not statistically significant. Given that shorter hospital stays might result in lower healthcare expenditures, this trend raises the possibility of honey dressings having financial advantages. Imran et al., made comparable findings.[18]

In their analysis of the effectiveness of honeyin treating wounds by Suryaprakash A et al., a significant p-value of 0.004 was found, and the averageduration of hospital stay for the honey group was 34.1±15.7 days, whereas the debridement group's was 36.0±15.8 days. Honey was also proven to reduce hospital stays overall in other experiments. The study conducted by Vallabha T et al. found that mean length of hospital stay was 26.4±3.1 days and varied from 20 - 30 days.[8]

Limitations and Future Directions: The variability of wound types and the relatively small sample size of this study were its main drawbacks. More extensive and uniform patient cohorts should be the focus of future studies in order to further clarify the unique benefits of each kind of dressing for different types of wounds. More studies are required to establish clear criteria for the best dressing material selection in various clinical circumstances.

CONCLUSION

The study contributes to the existing evidence favouring the use of honey as well as silver dressings in modern wound healing. Although not significant, honey dressing has shown better results in terms of time period for wound to become biofilm negative, time taken for definitive treatment and length of hospital stay; while silver colloid dressing has shown faster rate of granulation and reduction in size of the ulcer.Larger, multicenter studies with longer follow-up periods should be part of future research efforts to establish significant differences between the two therapeutic agents.

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