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ORIGINAL ARTICLE

Efficacy of Honey Dressing Versus Mechanical Debridement in Healing of Ulcers with Biofilms A Comparative Study

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Abstract:

Background: Chronic and delayed healing wounds are the significant health problems globally. Microbial bio burden in the form of biofilms contribute significantly for chronicity and delayed healing. Management of biofilm is complex task. Effective management of biofilms significantly reduces healing time. Raw unprocessed honey has several antibacterial properties and factors stimulating wound healing. *Aim and Objectives:* A comparative study was taken to compare the efficacy of local application of raw unprocessed honey versus mechanical debridement and antiseptic application in terms of biofilm eradication and enhanced wound healing. *Method and Materials:* Ninety patients with non healing wounds having biofilms were included and divided equally (forty five each) for local application of honey and mechanical debridement respectively. They were managed similarly and assessed for presence or eradication of biofilms, healing process and final outcome regularly. *Results:* Data analysed showed presence of biofilms in chronic wounds was 60% and 68% in study and control groups respectively. Time for appearance of healthy granulation tissue was significantly less (P=0.022) Mean duration for eradication of biofilms was less with (P=0.025) Mean hospital stay was also reduced (P=0.004). *Conclusion:* Raw unprocessed honey is a good, simple and effective solution for eradication of biofilms and enhances healing in non healing ulcers.

Keywords: Honey, Biofilm, Wound Healing, Eradication of Biofilm, Chronic Wound

Introduction:

Chronic wounds are significant health problems globally. Management of chronic wounds is a challenge to health care providers and have added to the costs and morbidity [1]. The prevalence of chronic wounds and their associated complications continue to escalate in spite of tremendous progress in science of wound healing [2]. Microbial bio burden in wound is an important factor responsible for the chronicity of wounds. Effective management of bacterial bio burden is an essential element of wound care. Wound infection results from the complex interaction between an individuals' immune system, the condition of the wound and the number and virulence of bacteria present [3]. Bacterial biofilms play a pivotal role in the development and maintenance of chronic wounds [4].

Chronic wounds are known to host complex microbial communities containing bacteria as biofilms. These can be of single or multiple bacterial species [5]. They are found to be present in 60% chronic wounds [6] and contribute significantly to delay in healing chronic wounds are in a state of continuous inflammation of will heal if predisposing factors are addressed [7]. Biofilms in wounds act as one of the major reasons for of delayed healing as they metabolically dormant with poor penetration of antibiotics [8, 9]

and are recalcitrant to antibiotic therapy and due to various mechanisms [10,11].

Though clinical signs [3] suggestive of biofilms are there, confirmation has to be done and effective eradication is essential. There are variety of treatment strategies for managing biofilms which include repeated debridement, antibiofilm agents and antibiotics [12, 13] with limited success. In the view of challenges, an effective agent which can eradicate biofilms effectively and easily was searched. Raw unprocessed honey which was used for treating acute and chronic wounds since 2500 BC [14] and mentioned in Ayurveda, was proposed as alternative. Honey has properties like osmosis [15] low pH [16], hydrogen peroxide like activity [17] and antibacterial activity [16, 18]. Phytochemicals [19] obtained from honey bee and plants it visits aid in wound healing. Honey acts by disruption of quorum sensing (mechanism of chemical signalling between cells within biofilm), facilitates removal of dead tissue, forms protective barrier over wounds and encourages neovascularisation and enhances healing. Keeping the challenges of managing biofilms in chronic wounds, raw unprocessed honey was considered as an alternative and a comparative study was taken with the objective of testing efficacy of honey in comparison with traditional methods for eradication of biofilms in wounds.

Material and Methods:

This study was carried out in the Department of General Surgery, of a teaching hospital from October 2015 to June 2017 after approval of the Institutional Ethics Committee. Written informed

consent was obtained from all the participants. Patients with ulcers were assessed thoroughly and subjected for detection of biofilm in the ulcers by tube adherence method. Patients with ulcers having biofilms were included in the study. Patients who were Immune compromised, history of recent chemotherapy or radiotherapy were excluded. The study subjects were divided into two groups, Honey (H) or study group and Debridement (D) or control group. The honey group was treated with topical application of dressing soaked with unprocessed raw honey. Regular treatment as per needs which included management of co morbidities, antibiotic therapy etc was followed in both the groups. Raw unprocessed honey of 10-30 ml was taken on a sterile gauze piece and diluted with few drops normal saline and spread over ulcer bed. Later the ulcer was dressed using sterile pads. Regular dressings were done daily. Control group was treated with mechanical debridement and dressed with 10% Povidone Iodine soaked dressings daily. Culture swabs were taken every 5th day for detecting presence of biofilms. Wound assessment was done in both groups every 5th day regarding a) discharge b) foul smell c) granulation tissue, d) size of the ulcer and e) presence or absence of biofilm. Ulcers which were free from biofilm and had healthy granulation tissue were taken up for definitive management in both groups. Total time taken for healing and duration of hospital stay was documented. Statistical analysis was done by using Fisher exact test and Chi square test. P value <0.05 was considered significant.

Results:

Table 1: Comparison between Two Groups

Age (Yrs)	Honey Group		Debridement Group	
	Number	Percent	Number	Percent
<15	3	6.7	2	4.4
16-30	7	15.6	2	4.4
31-45	8	17.8	12	26.7
46-60	10	22.2	14	31.1
61-75	16	35.6	13	28.9
>75	1	2.2	2	4.4
Mean age	49.8±19.0		53.4±17.5	
Male	37	82.2	37	82.2
Female	8	17.8	8	17.8
Acute	18	40	14	31.1
Chronic	27	60	31	68.9
HTN	1	2.2	3	6.7
DM	6	13.3	17	37.8
Smoker	1	2.2	4	8.9

Table 2: Comparison of Healing Process in both Honey and Debridement Groups

Days	Granulation tissue		Time for healing of wounds		Length of hospital stay	
	Study group	Control group	Study group	Control group	Study group	Control group
<10	12(26.7%)	12(26.7%)	4(8.9%)	5(11.1%)	0(0%)	1(2.2%)
11-15	19(42.2%)	8(17.8%)	13(28.9%)	8(17.8%)	1(2.2%)	6(13.3%)
16-20	9(20%)	12(26.7%)	10(22.2%)	4(8.9%)	4(8.9%)	3(6.7%)
21-25	4(8.9%)	7(15.6%)	11(24.4%)	6(13.3%)	14(31.1%)	1(2.2%)
26-30	1(2.2%)	5(11.1%)	4(8.9%)	13(28.9%)	8(17.8%)	8(17.8%)
>30	0(0%)	1(2.2%)	3(6.7%)	9(20%)	18(40%)	26(57.8%)
Mean	14.7±5.4	17.9±7.5	21±10.5	24.9±10.8	34.1±15.7	36±15.8
p Value	0.025*		0.022*		0.004*	

*means significant at 5% level of significance ($p<0.05$)

Table 3: Comparison of Organisms Isolated in Both Groups

Organisms isolated	Study group	Control group
<i>Staph. aureus</i>	53.3%	46.7%
<i>Klebsiella pneumonia</i>	48.9%	37.8%
<i>Pseudomonas aeruginosa</i>	35.6%	48.9%
<i>Citrobacter species</i>	15.6%	8.9%
<i>E. coli</i>	8.9%	11.1%

The mean age was 49.8±19.0 yrs in study group and 53.4±17.5yrs in controls. Maximum patients were in the age group of 61-75yrs in the study group and 45-60yrs in controls with male predominance in both the groups (82.2%). Most of the ulcers were chronic ulcers in groups, 60% and 68.9% in study and control groups respectively.

The mean duration of appearance of healthy granulation tissue was 14.7±5.4 days in honey group and 17.9±7.5 days in debridement group with significant p value=0.025. Most of the patients underwent split skin grafting once the

wound was healthy and the mean time for healing of wounds with biofilm was 21.0±10.5 days in honey group and 24.9±10.8 days in debridement group. Most of the patients in the honey group were discharged in less than 25 days whereas the debridement group, discharge time was more than 30 days with significant p value of 0.004. Mean duration of hospital stay was 34.1±15.7 days and 36.0±15.8 days in honey and debridement groups respectively. Mild burning type of pain was felt by patients in the honey group but did not produce any adverse effects.

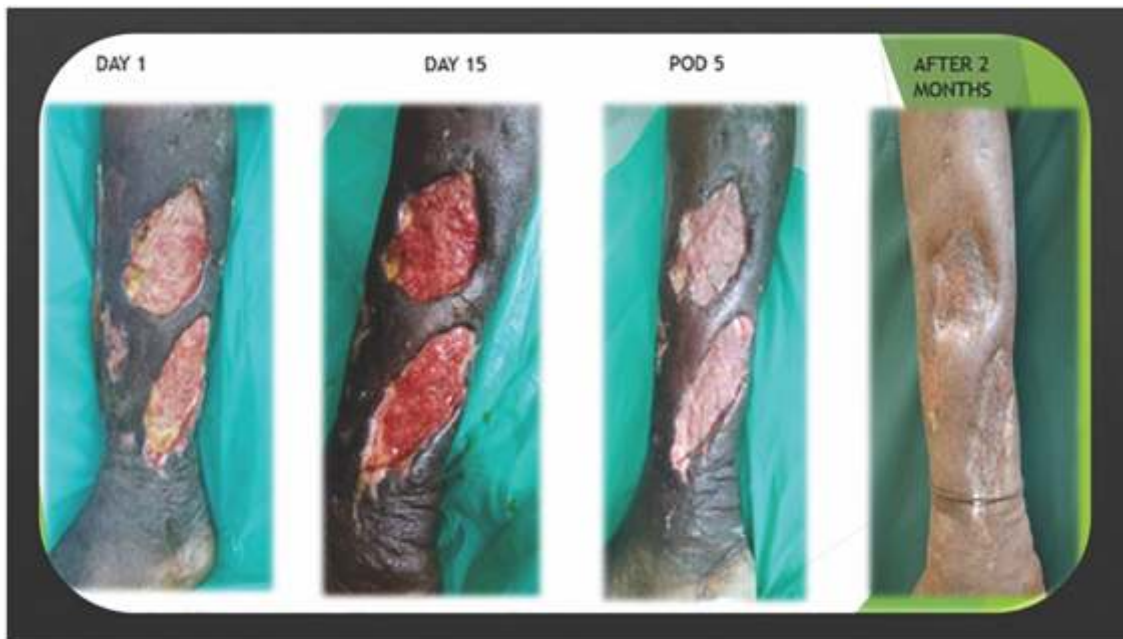


Fig. 1: Shows Progression of Healing After Application of Honey



Fig. 2: Shows Healthy Granulation by Day 25 in a Large Post Cellulitis Wound

Discussion:

Chronic non healing wounds add to significant morbidity, reduced productivity for the patients leading to financial and service burden in the health care sector. USA alone spends around one billion dollars for managing chronic wounds annually. In spite of advances in the knowledge and wound healing and improved method for managing chronic wounds, they remain elusive. Though presence of biofilms was known since the time of Luwen Hooke, its role in chronicity and poor healing was reconsidered in 2008 [20] biofilms are known to form over catheters, IV cannulae etc, causing persistence of infection due to leering of microorganisms in the matrix. Keast proposed clinical signs to suspect presence of biofilms (i) antibiotic failure (ii) infection persisting for more than 30 days duration (iii) friable granulation tissue (iv) presence of gelatinous material which is easily removable but reappears quickly [3]. Once the

presence of biofilms is confirmed with tube test [21], appropriate strategy needs to be planned for its eradication in addition to systemic therapy.

At present regular wound debridement and application of newer agents like Poly-hexamethylene-biguanide (PHHB) or silver based hydrogels is suggested. Repeated mechanical debridement is cumbersome, painful and bleeds often. Most of the hydrogel preparations are tested in vitro for their biofilm eradication capacity and good clinical evidence needs to be built [22-23]. With the emergence of bacteria which are resistant to antimicrobial therapy, older methods like use of honey were roped in. With the experience of its utility [24] local application of honey was studied. With variety of properties [15-19] honey is a good alternative in clearing the biofilm and hastening the healing time. Incidence of presence of biofilm in wounds ranged from 6% in acute ulcers to 70%

[21-22]. However, we noticed the increased incidence in acute ulcers too (40% & 31.1%). *S. aureus* remains the commonest organism isolated forming biofilm [25]. Other organisms are *K. pneumoniae*, *E. coli*, *Pseudomonas aeruginosa* and *Citrobacter* species. These micro-organisms are often resistant to common antimicrobials and are known to form biofilms which are difficult to eradicate and recalcitrant to common wound management methods. Honey stimulates healthy granulation tissue (42.2% within 15 days with mean 14.7 ± 5.4) in comparison with debridement, where only 26.7% of ulcers showed healthy granulation in 16-20 days with a mean of 17.9 ± 7.5 days and the difference was significant $p=0.025$, as observed by Subramanyam [26] in burn wounds. Honey application enhanced complete healing (100%) in comparison with Mafenide acetate application (84%) by 21 days with $p<0.001$ [27].

In this study, 60% of the ulcers in the honey group healed completely within 3 weeks in comparison with debridement where 30.1% ulcers healed and $p=0.022$ was significant (Table 2), with mean duration of healing was 21.0 ± 10.5 days in honey group and 24.9 ± 10.8 days in debridement group. Medhi *et al.* [28] conducted a meta-analysis to evaluate the efficacy of honey in treating wounds observed complete healing within 4-12 weeks in clinical trials and within 2-9 weeks in observational studies.

In this study most of the patients underwent definitive procedure split thickness skin grafting within 3 weeks in honey group and in 30 days in the debridement group. The mean duration of hospital stay was 34.1 ± 15.7 days in honey group and 36.0 ± 15.8 days in debridement group with significant p value 0.004. Honey reduced total duration of hospital stay in other studies as well [26]. Diabetic patients also had enhanced recovery in the form of reduction in the time taken for appearance of healthy granulation tissue, 16.5 ± 4.2 days and 19.5 ± 7.3 days respectively. The mean time for healing of ulcers was 21.0 ± 5.2 days and 26.6 ± 11.9 days, the mean hospital stay was 38.8 ± 16.6 days and 40.5 ± 15.5 days in honey and control group respectively suggesting efficacy in diabetic individuals as well.

Conclusion:

Honey as a local application is effective in eradicating biofilms in chronic wounds and enhances healing. It is cheap, easily available simple alternative with no recorded side effects for management of biofilms. It has an added advantage of supporting healing process and works equally well in diabetics too. It has a potential to be safe alternative for managing multi resistant organism infections which are a global challenge if this concept is bolstered by validating with more studies.

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