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A Comparative Study of Honey Dressing Vs Silver Sulfadiazine Dressing on Wound Healing in Burn Patients

Amritjot Singh
SBLS civil hospital, Jalandhar, Punjab, India

Satinderjit Singh Bajaj
SBLS civil hospital, Jalandhar, Punjab, India

Jagminder Kaur Bajaj
SBLS civil hospital, Jalandhar, Punjab, India

ABSTRACT

Aim and Objectives: To compare the effects of honey vs silver sulfadiazine for wound healing in burn patients. Material and Methods: Study was conducted in 60 patients. 30 in each group i.e. honey group and SSD group with age between 18-70 years. clinical assessment of wound encompassing the sight, affected BSA, degree, depth, absence/presence of slough and additional treatment was documented chronologically. Results: By the end of 6 weeks number of patients showing complete healing was significantly increased with honey dressing than SSD. Swab cultures to both the groups showed the prevalence of S. aureus, Pseudomonas and Klebsiella and treated with drugs like Fluroquinolones, Amoxicillin-clavulinic acid and Linezolid. Conclusion: Honey causes complete healing of wound faster than SSD and the mean percentage decrease in wound size is significant with Honey Dressing in 2nd and 4th week.

INTRODUCTION

Burn injuries, characterized by damage to the skin or other tissues resulting from exposure to heat, radiation, electricity, or chemicals, pose a significant health concern. In our country, burn incidents represent the second-largest category of injuries, following road accidents, according to data extrapolated from leading hospitals [1]. With annual incidence reported to be 7 million cases [2].

Morbidity is a considerable concern due to the presence of necrosed tissue, and high susceptibility to infections. The primary goal of burn management is prompt wound healing and epithelization to prevent infections and minimizing functional and aesthetic repercussions. Consequently, extended periods of dressings are required, often resulting in contractures and deformities [3].

Topical application of antimicrobial/antiseptic agents plays a crucial role in reducing the incidence of burn wound sepsis and in improving the survival rates of patients with major burns. A variety of agents possessing antiseptic / antimicrobial properties have been used in burn dressings. Honey, derived from the nectar collected and modified by Apis mellifera (honey bee), has a rich history of medicinal use in wound care [4]. It possesses diverse medicinal

properties such as anti-inflammatory, anti-bacterial, anti-mutagenic, expedited wound healing, anti-diabetic, anti-viral, anti-fungal, anti-tumoral effects and has shown promising results in various clinical trials [5-12]. The anti-bacterial effects of honey can be attributed to its acidic pH, peroxidase-mediated H_2O_2 production, osmotic effects of sugars & presence of non-peroxidase substances (flavonoids, lysozyme, and phenolic acids) [13-15]. Methylglyoxal (MGO), and defensin-1, production also contribute to antimicrobial properties of honey [15-17].

Silver sulfadiazine (topical sulphonamide) is a bacteriostatic antibiotic, active against gram-positive, gram-negative bacteria as well as yeast. It inhibits bacterial folic acid synthesis pathway & disrupt DNA synthesis [18]. It is extensively used for burn dressings. Present study aims to compare the efficacy of Honey and Silver Sulfadiazine as topical antibacterial/antimicrobial agents in healing of burn wounds.

Objectives

1. To compare the effects of honey vs silver sulfadiazine for wound healing in burn patients.
2. To compare complications of honey dressing vs. silver sulfadiazine dressing.

METHODS

Place of Study

The present study was conducted in the Department of General Surgery, SBLS Civil Hospital, Jalandhar, Punjab.

Type of Study

It was a prospective, randomized, parallel group, open label, interventional study.

Study Duration

The study was conducted for a period of 12 months after obtaining the Institutional Ethics Committee approval to conduct the study.

Study Population

Patients visiting the Department of General Surgery, SBLS Civil Hospital, Jalandhar, Punjab, with second degree burn, during the study period, fulfilling the inclusion and none of the exclusion criteria and those willing to provide their voluntary informed consent to participate in the study formed the study population.

Patient Selection

Inclusion Criteria:

1. Patients of age between 18 to 75 years of all genders.
2. Patient with second degree burn.

Exclusion Criteria:

1. Patient on chemotherapy or steroid therapy
2. Patient with renal and/or liver failure
3. Patient in immuno-compromised state (e.g. AIDS)
4. Patient allergic to the study drugs (silver sulfadiazine or honey)

Randomization

Randomization of the patients was done using computer generated numbers. A total of 60 patients were enrolled, who were randomly divided into two equal groups of 30 patients each.

- **Group 1 (Honey Group):** The patients in this group received honey dressings.
- **Group 2 (Silver Sulfadiazine Group):** The patients in this group received silver sulfadiazine dressings.

METHODOLOGY

All the eligible patients were explained about the study in detail in their own language. After obtaining a voluntary written informed consent from the patient and/or his/her legally acceptable representative for participation in the study, all the study related procedures were initiated.

Upon admission to the burn ward, the patient's general condition was evaluated. Shock was managed through the rapid intravenous infusion of Ringer lactate and other supportive measures, including tetanus toxoid and antibiotics. Swabs culture were taken at the time of admission and weekly thereafter.

After enrolling the patients into the study, these patients were treated according to the treatment group they were randomized to.

In the **Honey group (Group 1)**, wounds were carefully examined and washed with normal saline. Sterile gauze soaked in undiluted, pure honey was applied to the wounds. Subsequent dressing changes involved surgical debridement as necessary to remove necrotic tissue and slough. Dressings were changed every 48 hours during the patient's hospital stay. Weekly evaluations assessed signs of healing, such as a decrease in size, inflammation, formation of granulation tissue, and the degree of epithelialization. After discharge same treatment was continued and patients were followed up weekly till complete wound healing. The number of dressings required for complete healing was recorded.

In the **Silver Sulfadiazine Group (Group 2)** also, dressings were done at 48-hour intervals with silver sulfadiazine, and ulcer evaluations were conducted as in the Honey group. Standard antibiotic treatment and wound debridement, according to the patient's needs, were continued. Patients were treated until complete wound healing was achieved.

RESULTS

Age

Mean age of patients in Group I (honey) was 37.2 ± 13.7 years and in Group II (SSD) 36.5 ±14 years. The differences in age between the two groups were not significant statistically ($p > 0.05$). Age range was 18-72 years in group 1 and 18-68 years in group 2.

Gender Distribution

Both groups had more males than females. In group I there were 60% males and rest females, whereas Group II had 54% males and rest (46%) females. However, these differences in gender distribution in two groups were not statistically significant.

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Height and Weight
The differences in mean height & weight were not statistically significant (p>0.05)

Socioeconomic Status of Patients in Both the Groups
Both groups had patients belonging to upper, middle and lower socio-economic class. However, the differences in frequency distribution of socioeconomic class between two groups were not statistically significant.

Total Body Surface Area:
Out of 30 patients in group I, four patients with more extensive burns (100%) expired in first follow up week. Remaining 26 patients of group I and 30 of group II were followed up for eight weeks' time. Table 1 shows comparison of mean total body surface area (TBSA) involved in burn injury in both groups. The differences in mean TBSA in both groups are not statistically significant.

Table 1: Total body surface area (TBSA) involved

	Group I	Group II	p value
Mean ± S.D. of TBSA involved	49.0± 8.6	44.7± 10.5	0.097
Median TBSA involved	47.5	45.0	

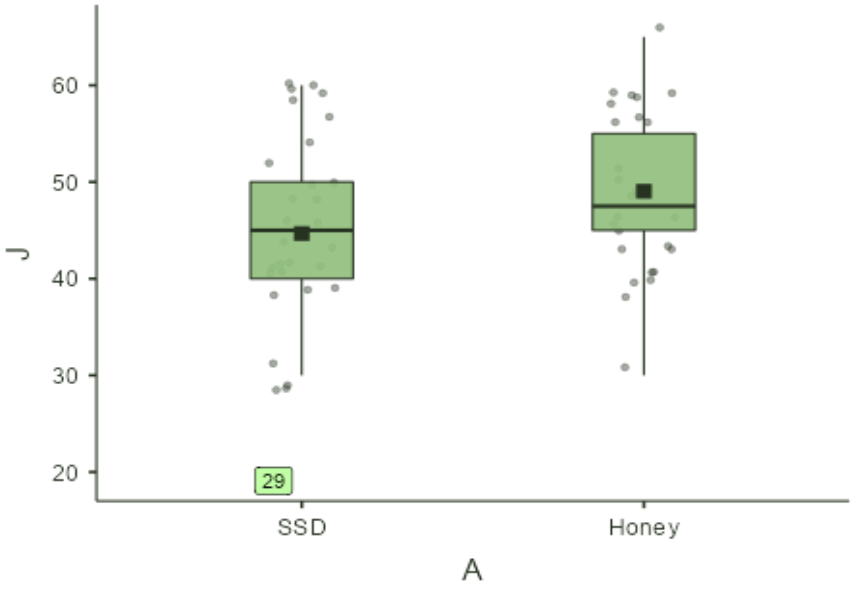

Figure 1: Box plot with mean of Total body surface area affected

Time Gap Between Burn Injury and Hospitalization
Time gap between burn injury and hospitalization in both the groups ranged from 1 -48 hours. Figure 2 shows comparison of mean time gap between burn injury and hospitalization in two groups to be not significantly different.

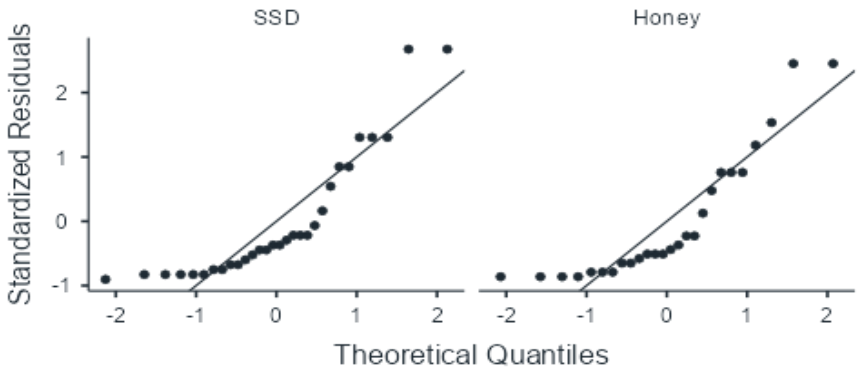

Fig 2: Q-Q plot showing time gap between burn injury and hospitalization in two groups

Presence of Necrotic Tissue

Necrotic tissue was present in 19 patients at beginning of treatment in honey group I, the numbers having necrotic tissue then decreased progressively and none had necrotic tissue by end of 7 th week. (Table 2). In group II receiving SSD also, necrotic tissue was present in 10 patients at beginning, increased in 2nd week and then decreased such that none had necrotic tissue at end of 7th week. Thus, necrotic tissue was absent in all patients in both groups at end of 7th week

Table 2: Number of Patients with necrotic tissue

Time after starting therapy	Honey group	SSD group
week 1	19	10
week 2	12	23
week 3	9	20
week 4	6	14
week 5	2	7
week 6	2	1
week 7	NIL	Nil

Appearance of Granulation Tissue:

Table 3 shows that Granualtion tissue started appearing in first week of treatment in more than 85% patients in both the groups.

Table 3: Appearance of Granulation tissue

Time after starting therapy	Honey group	SSD group
week 1	23 (88.5%)	26 (86.7%)
week 2	24 (92%)	30 (100%)
week 3	26 (100%)	-

All patients in Groups I & II had granulation tissue by end of week 3 and week 2 respectively**.**

Percent Decrease in Wound Size Per Week

Table 4 shows frequency (ν) distribution of percent decrease in wound size at weekly intervals. Cumulative frequency ((Cν) at weekly interval is also mentioned. In both the groups maximum patients showed 10-15% decrease in wound size in all 4 weeks.

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Table 4: Frequency (ν) distribution of percent decrease in wound size per week

Week after starting treatment	Percent decrease in wound size per week								p value
	0-5%		5-10%		10-15%		15-20%		χ^2 test
	Group I ν (Cν)	Group II ν (Cν)	Group I ν (Cν)	Group II ν (Cν)	Group I ν (Cν)	Group II ν (Cν)	Group I ν (Cν)	Group II ν (Cν)	
1st week	2	6	9	13	14	11	0	1	0.281
2nd week	0 (2)	3 (9)	1 (10)	10 (23)	23 (37)	17 (28)	2 (2)	0 (1)	**0.005**
3rd week	0 (2)	1 (10)	1 (11)	5 (28)	19 (56)	16 (44)	6 (8)	8 (9)	0.315
4th week	8 (10)	9 (19)	0 (11)	6 (34)	12 (68)	15 (59)	6 (14)	0 (9)	**0.007**
cumulative frequency (Cν) at 4 weeks	10	19	11	34	68	59	14	9	

This was followed by 5-10% decrease in size every week. χ^2 test applied to compare frequency distributions at end of each week shows differences between honey and Silver sulfadiazine groups to be significant in week 2 and week 4 only.

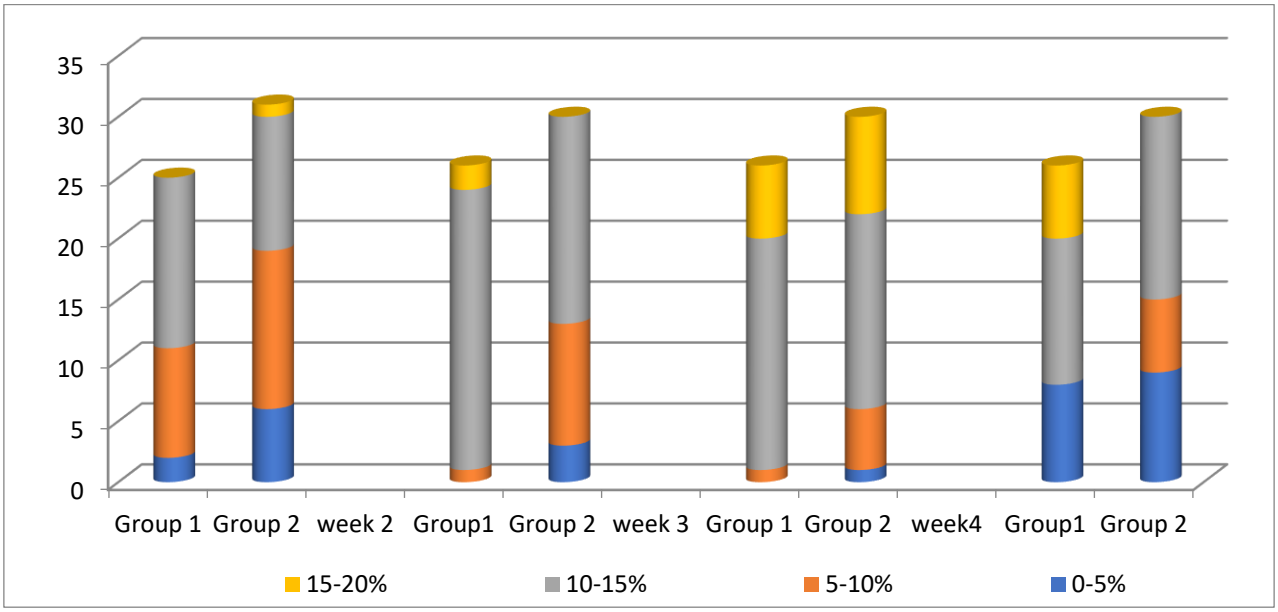

Fig 3: Frequency distribution of patients & percent decrease in wound size in two groups from week 1 to week 4.

Number of Patients Showing 'Complete Healing' in Two Groups

Table 5 shows number of patients showing complete healing with treatment in two groups at end of 4th, 5th, 6th, 7th & 8th weeks.

Table 5: Number of patients showing complete healing versus duration of treatment in two groups

Duration of treatment	Group I Number (Percent)	Group II Number (Percent)	p value χ^2 test
4 weeks	6 (23%)	2 (6.7%)	0.08
5 weeks	13 (50%)	9 (30%)	0.12
6 weeks	21 (80%)	14 (46.7%)	**0.009**

7 weeks	22 (85.3%)	21 (70%)	0.196
8 weeks	23 (88.5%)	25 (83.4%)	0.58

In all week's number and percentage of completely healed patients is more in group 1 than group 2. However, the differences between honey and SSD treated groups are statistically significant only at end of 6th week. Thus, at end of 8 weeks' time 88.5% patients treated with honey and 83.4% treated with silver sulfadiazine showed complete healing of wounds, however these differences between two groups are not statistically significant.

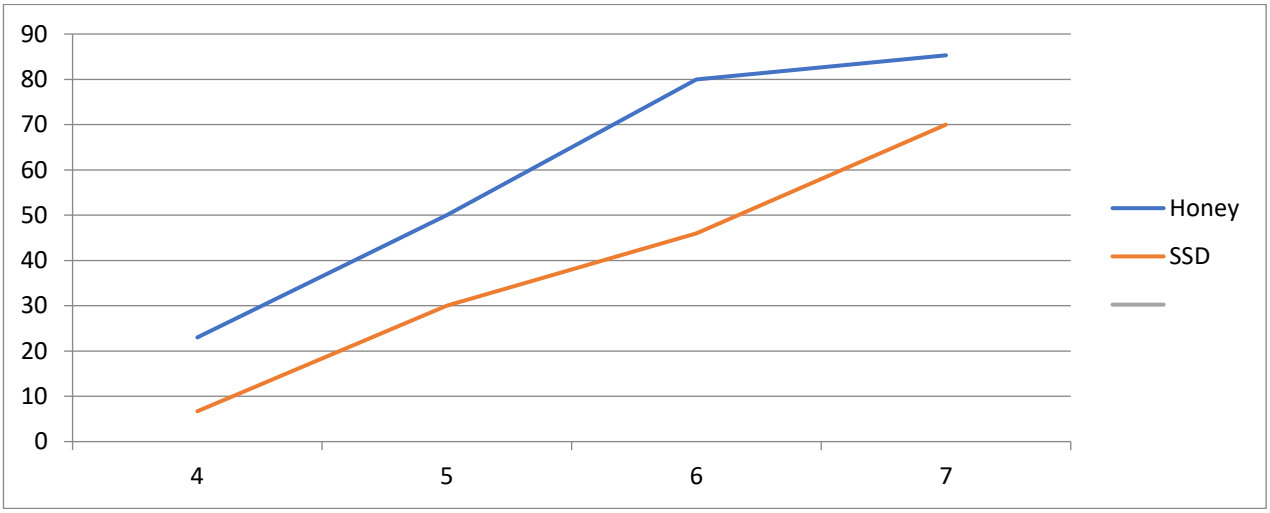

Fig 4: Line Graph showing cumulative frequency of patients showing complete healing with honey versus SSD with time (weekly intervals from 4 -8 weeks)

Incomplete Healing

Total 6 patients out of 56 (14.3%) had incompletely healed wounds at end of 8 weeks period. Out of these 8, 3 pts were in group I and 5in group II. Some factors that might be involved in delayed healing are shown in Table 9. Most (62.5%) patients with incomplete healing were from low socioeconomic strata. Half of the patients were male and rest females. 25% were aged above 60 years, were smokers, were suffering from diabetes, hypothyroidism. 12.5% had alcoholism, hypertension.

Table 6: Features of Patients with incomplete healing at 8 weeks

	Male	**Female**	**Age >60**	**Low SE**	**Diabetes**	**H↑T**	**Smoker**	**Alcoholic**	**H↓thyroid**
Group I N=3	1	2		1	1	1	1		1
Group II N= 5	3	2	2	4	1		1	1	1
Total N=8	4 (50%)	4 (50%)	2 (25%)	5 (62.5%)	2 (25%)	1 (12.5%)	2 (25%)	1 (12.5%)	2 (25%)

Culture Sensitivity of Swabs:

Throughout the duration of treatment, swabs were taken for culture sensitivity from sites showing signs of infection. Table 7 shows swab reports and organisms detected in two groups.

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Negative swabs were observed in more patients in group I than Group II and the differences between two groups are statistically significant (p=0.004)

Table 7: Swab culture reports

Swab	**Group I**	**Group II**	**p value χ^2 test**
Positive	10	23	
Staphylococcus aureus	7	13	
Pseudomonas	2	10	
Klebsiella	1	nil	
Negative	16	7	**p= 0.004 i.e. p<0.05**
χ^2 test			
Swab reports	Value	df	p
χ^2	8.40	1	0.004
N	56		

Antimicrobial drugs given to patients with positive swab cultures based on sensitivity reports are shown in Table 8. Fluoroquinolones were prescribed most frequently followed by amoxicillin+ Clavulanic acid and linezolid.

Table 8: AMAs prescribed to culture positive cases

Antimicrobial agent		**Number of patients**
Fluoro-quinolones		**14**
	Ciprofloxacin	9
	Ofloxacin	3
	Norfloxacin	2
Amoxycillin+ Clavulanic acid		11
Linezolid		10

Time Taken to Sterilize Wounds

Table 9 shows that Median time for wound sterilization was lesser (14 days) with honey than silver sulfadiazine (21 days). Mean time for sterilization of wound was also less for honey treated patients, however the differences are not statistically significant

Table 9: Time for wound sterilisation

Time (days)	**Group I**	**Group II**	**p value**
Mean	17.5±10.9	23.9±9.66	p= 0.068 i.e. p>0.05
Median	14	21	
Independent sample t test			
Time	statistic	df	p
student's t	-1.88	36.0	0.068

Time to Healing in Days

Table 10 The range of time taken for healing was 21-56 days in both the groups. However mean time and median were both lesser in honey treated group than silver sulfadiazine treated group. However, the differences in time for complete healing in two groups were not statistically significant**.**

Table 10: Time for complete healing

Time (days)	**Group I**	**Group II**	**p value**
Mean	38±9.66	43.2±10.5	p= 0.060 i.e. p>0.05
Median	35	42	
Independent sample t test			
Time	statistic	df	p
student's t	1.92	54.0	0.060

Mean and median times for healing in both groups are shown in fig 5

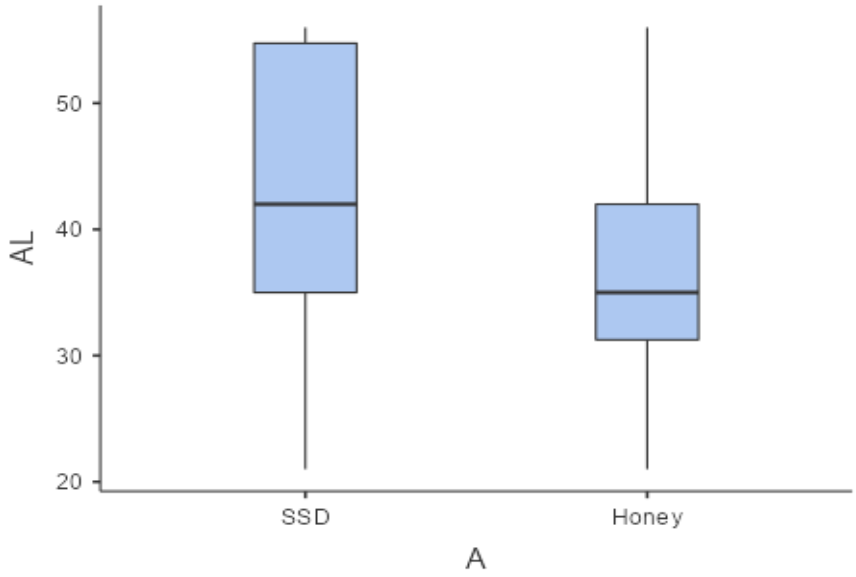

Fig 5: Box plot showing time to complete healing with SSD and honey

DISCUSSION

Topical antimicrobial agents improve wound healing in burns patients and are important strategy in management of burn cases.

Variety of agents are used for this indication. Present study compared efficacy of Honey with SSD in healing of burn wounds.

Honey possesses antiseptic, anti-bacterial properties due to presence of inhibin, hydrogen peroxide, flavonoids, phenolic acids etc. [1-3].

Its high acidity and low water activity causing osmosis, also contributes to its anti-bacterial properties [4]. The production of hydrogen peroxide while using honey leads to cell proliferation, fibroblastic activity and angiogenesis [5]. Honey can be a non-toxic, non-allergenic and economical alternative to SSD for treating burns. Patient were randomly allocated for topical treatment with Honey or SSD.

Thus, there were no significant differences in age, sex, height, weight, socio-economic status, TBSA affected, time gap between injury and hospital treatment in the two groups. Necrotic

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tissue disappeared in all patients in study population by end of 7th week & granulation tissue started appearing in 1st week and was present in all patients by the end of 3rd week of treatment in both groups. Our results are not agreement with a study by **Subrahmanyam et al [19]** with reported early appearance of granulation tissue in patients treated with Honey as compared to SSD.

Mean time taken for wound sterlisation was lesser with Honey (17.5 days) than SSD (23.9 days) although the difference is not statistically significant, it agrees with findings of **Gupta et al** [21], **Sami et al** [22] and **Aziz et al [28]**. Patients taken in Honey group had statistically significant negative swabs as compared to those in SSD group. Hence more patients in SSD group needed anti-microbial treatment.

Fluoroquinolones were prescribed more frequently followed by Amoxicillin-clavulanic acid and Linezolid. Decrease in wound size in two groups showed significant difference in week 2nd and 4th only. Maximum number of patients showed 10-15% decrease in wound size per week. Similar results were reported by **Choudary et al [27]** who reported significantly better decrease in wound surface area and pain score with honey as compared to SSD. 80% patients treated with Honey and 46.7% treated with SSD showed completed healing at end of 6weeks of treatment.

This difference in complete healing in 2 groups was statistically significant (p = 0.009) at 6 weeks. However, at 8 weeks differences were not significant. Similar results of more complete healing with Honey than SSD have been reported by many investigators. **Mashhood et al [20]** also reported earlier complete healing with Honey at 4th weeks than with SSD at 6th week. Mean time taking for complete healing in our study was 38 days with Honey and 43.2 days with SSD (p = 0.060). So, Honey caused faster healing than SSD. **Sopandi et al** [23] also reported Honey as a good alternative for shortening the duration of healing in burn wounds. **Lindberg et al [26]** also found Honey to take lesser time for complete healing. **Mujalde et al [24]** also concluded that honey takes lesser time for epithelization and healing as compared to SSD. However, a systematic review by **Jull et al** [25] on 26 trials on 3011 participants identified very low-quality evidence for faster healing of burns with Honey than with SSD treatment. In our study 3 cases treated with Honey and 5 cases with SSD showed incomplete healing at 8 weeks. Most cases of incomplete healing were from lower socio-economic strata. Factors like smoking, diabetes and hypothyroidism were present in these cases.

CONCLUSION

Honey causes complete healing of wound faster than SSD and the mean percentage decrease in wound size is significant with Honey dressing in 2nd and 4th week.

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