International Surgery Journal
Shivakumar S et al. Int Surg J. 2019 Jun;6(6):1901-1906
http://www.ijsurgery.com
pISSN 2349-3305 | eISSN 2349-2902

DOI: http://dx.doi.org/10.18203/2349-2902.isj20192223

Original Research Article

Honey–old wine in new bottle: a surgically viable antibacterial and antiinflammatory fixator

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Received: 24 April 2019
Revised: 17 May 2019
Accepted: 18 May 2019

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ABSTRACT

Background: Skin grafts are used to cover the healing wound, in which adherence of the graft to the wound bed is the important element. Honey has been shown to increase the adherence of skin grafts to wound beds and have antibacterial and anti-inflammatory effects and increase healing rate of wounds.
Methods: In a single centre based prospective comparative study from November 2016 to April 2018, 60 patients (in 30 patients graft was fixed with sterilised honey, in 30 patients it was fixed with conventional methods like skin staples/sutures). All patients in two groups were evaluated for area of graft uptake, graft contracture, incidence of hematoma/seroma, mean hospital stay post surgery, post-operative pain, Infection rate and Cost effectiveness. Statistical analysis used are chi-square test, independent t test/ Mann-Whitney test, paired t test/ Wilcoxon test. $P<0.05$ is considered statistically significant.
Results: Although graft uptake was same in both the groups, graft contracture, discharge from graft site and infection rate were less in the honey group. There was no seroma formation in the honey group. Honey significantly reduced postoperative pain ($p<0.0001\%$) and is also cost-effective as the hospital stay was shorter in the honey group ($p<0.0001\%$).
Conclusions: Honey has strong adhesive properties, anti-inflammatory action and helps in minimization of scarring, and stimulation of angiogenesis as well as tissue granulation and epithelium growth. It also reduces surgical time for skin graft fixation. Sterilized honey has proven advantage as a skin graft fixator.

Keywords: Sterilised honey, Split skin grafting, Conventional fixation, Graft uptake

INTRODUCTION

The skin also known as the integument or cutis forms a self-renewing interface between the body and environment. Loss of skin has a direct bearing on the various facets of health of the individual including susceptibility to infection, nutrient and electrolyte imbalance, derangements in mobility and cosmetic disfigurements and psychological impact. Hence, restoration of the skin lost becomes an objective of paramount importance, which can be accomplished by various means such as primary closure, secondary healing, use of split skin or full thickness grafts or by using flaps, either pedicle or free flaps. split skin grafting is the most commonly employed procedure because of its ease, better 'take' even in adverse conditions, ability to cover large areas and the possibility of re-harvesting from donor site. Honey has a long history of human consumption as health food and sweetener. Honey was mentioned in the writings of Egypt, India, and China since 5500 BC. The use of honey in therapy is described in 5000-old Egyptian writings: Papyrus Ebers is full of praises of the curative properties of honey.[1-4]

The antimicrobial activity of honey has been known since the 19th century and many in vitro and clinical studies have confirmed the broad-spectrum antimicrobial (antibacterial, antifungal, antimycobacterial, and antiviral) activity of honey because of its Acidity (low pH), osmotic effect, high sugar concentration, presence of bacteriostatic and bactericidal factors (hydrogen peroxide), antioxidants, phenolic acids and flavonoids, methylglyoxal (formed by conversion of dihydroxyacetone during honey maturation, bee peptides which are the natural antibacterial agents, anti-inflammatory properties of honey.[5-12]

Honey and its components acts synergistically when used with other antibiotics. honey has been found to have synergic action with gentamicin, amikacin, and ceftazidime against Pseudomonas.[13] Methylglyoxal was effective in inhibiting the formation of biofilms in P. aeruginosa and MRSA[14]. Compounds found in honey like vitamin C, phenol compounds, catalase, peroxides, glucose oxidase enzymes have antioxidant properties. Honey also contains flavonoids and carotinoids. High levels of these indicators ensure a high level of antioxidants in honey. Application of honey causes rapid clearance of infection, helps in debridement of wound and also suppression of inflammation while minimizing scarring and also stimulates angiogenesis, growth of epithelium and formation of granulation tissue.[15-17]

Honeys with an average level of antibacterial activity was expected to be effective in preventing the growth of pseudomonas on the surface of a wound even if the honey was diluted more than ten-fold by exudation of wound.[18]

The objective of this study is to use sterilized honey as skin graft fixator for wound beds instead of fixing it with conventional methods like sutures or skin staples.

METHODS

This study was conducted in JSS Hospital, Mysore during the period of November 2016 to April 2018 and sixty patients were included in this study (in 30 patients, graft was fixed with sterilised medical honey, and in 30 patients, it was fixed with conventional fixation using skin staples or suturing). The Ethical Committee of the JSS University of Medical Sciences approved the study. Eligible participants are (1) Patients undergoing split skin graft of more than 2×2 cm (2) who provided informed consent and (3) had no sensitivity to honey and honey products.

Under strict aseptic precautions and under anaesthesia, Split skin graft was taken from the donor area using Humby knife and meshing of graft was done. The recipient area was prepared. Honey sterilized by Autoclave was applied over the recipient area with a medicine dropper (syringe) evenly and later the meshed skin graft was placed in 30 patients, which was compared with placing the skin graft and conventional fixation with sutures/ skin staples in other 30 patients. Post-operatively pain was assessed by visual analog scale (VAS) on 6th hour, 12th hour, 24th hour, and third day and parameters were assessed for area of graft uptake, incidence of hematoma/seroma/discharge, infection rate and graft contraction. It was followed by alternate day dressings with wet gauze. Inferential statistics was done by chi-square test, independent t test/ Mann-Whitney test, paired t test/Wilcoxon test. All the measurements were done using SPSS 21.0 software. P<0.05 was considered statistically significant.

RESULTS

There were 53 (88.3%, 27 in honey group, 26 in conventional fixation group) men and 7 women (11.7%, 3 in honey group, 4 in conventional fixation group). The mean age of patients was 55.2 yrs in honey group and 50.5 yrs in conventional fixation group. No significant differences were observed according to age and sex.

In the group which used honey for fixation of split thickness skin graft, we observed the decrease of edema and wound exudates from the recipient area. No allergic reactions occurred during this study. Graft uptake was 97.53% in honey fixation group and 96.27% in conventional fixation group. Infection rate was more in conventional fixation group (23.3%) than in honey fixation group (13.3%). In conventional fixation group, 6.7% had Seroma formation. Graft contracture was more in conventional fixation group (16.7%) than honey fixation group (3.3%). Decrease in post-operative pain was faster and greater in honey group with significant statistical significance (p<0.0001) according to VAS. Mean hospital stay post surgery was less in honey group with significant statistical significance (p<0.0001).

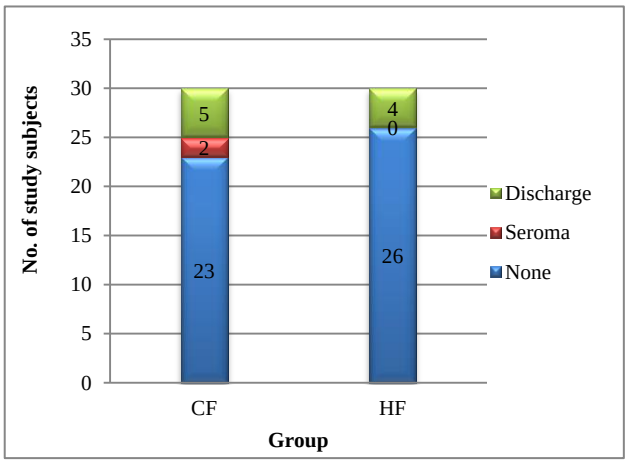

Figure 1: Graft site complications.

Table 1: Summary of all variables.

		Conventional fixation		Honey fixation		
		Number	**Percentage (%)**	**Number**	**Percentage (%)**	**P value**
Hematoma/seroma	No	23	76.7	26	86.7	0.3
	Seroma	2	6.7	0	0	
	Discharge	5	16.7	4	13.3	
Graft contraction	No	25	83.3	29	96.7	0.09
	Yes	5	16.7	1	3.3	
Postoperative pain	1.00	0	0	2	6.7	<0.0001
	2.00	0	0	14	46.7	
	3.00	1	3.3	11	36.7	
	4.00	7	23.3	3	10.0	
	5.00	14	46.7	0	0	
	6.00	4	13.3	0	0	
	7.00	3	10.0	0	0	
	8.00	1	3.3	0	0	
Infection rate	No	23	76.7	26	86.7	0.3
	Yes	7	23.3	4	13.3	

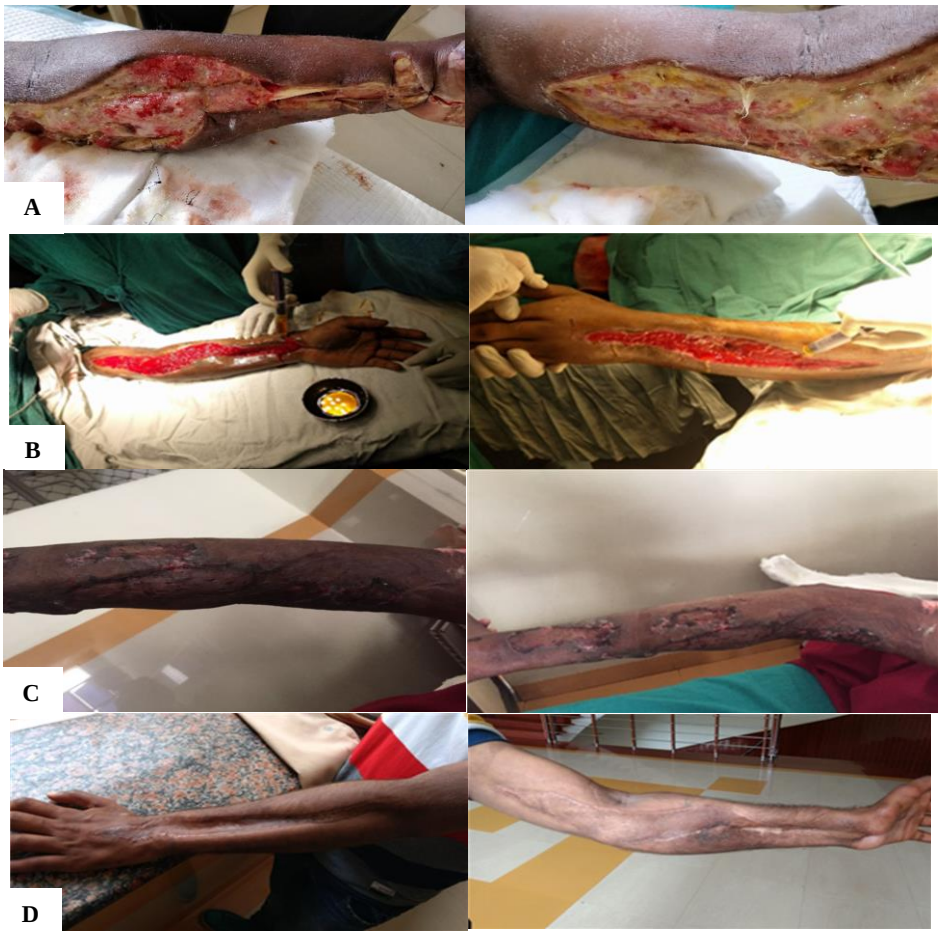

Figure 2: Applying honey and after wound inspection. (A) Non healing ulcer post debridement after injection of organophosphorous compound into the wrist and forearm; (B) honey was also used for wound healing in this particular case. Later wound was healing with red granulation as shown below. Honey was applied over the healing ulcer before application of split skin graft over the donor area; (C) post operatively graft was inspected and showed complete graft uptake with no graft site complications; (D) during follow up the graft site was healed well as shown.

Table 2: Postoperative pain and hospital stay from day of surgery.

	Group						
	CF			HF			
	Median	Q1	Q3	Median	Q1	Q3	P value
Postoperative pain	5.0	4.0	6.0	2.0	2.0	3.0	<0.0001
Hospital stay from surgery days	8.00	7.00	9.00	6.00	5.00	7.00	<0.0001

DISCUSSION

Antimicrobial agents are essential in combatting infections, however with the spread of resistant pathogens, the effectiveness of antibiotics have diminished. Such bacterial resistance poses a serious threat for overall health and is the basis for re-evaluation of alternative antimicrobial strategies derived from plants and plant based products including honey.[19]

Honey has extensive broad spectrum anti microbial activity when treated against pathogenic bacteria, including aerobes, anaerobes, gram positive and gram negatives. Honey is also hygroscopic and can draw moisture out of the environment and dehydrate bacteria, and its high sugar content along with low level pH prevents microbial growth, it's high viscosity provides a protective barrier. Honey is a rediscovered boon for the medical profession, particularly where conventional modern therapeutic agents fail. It is gaining acceptance as an agent for the treatment of ulcers, bed sores and other skin infections resulting from burns and wounds.[20,21]

Studies have proved that though oxygen is essential for life, it's metabolism results in by- products called as free radicals. Free radicals cause cellular damage by traveling through the cell, disrupting the structure and contributing to ageing. Antioxidants protect key cell components from damage by neutralizing the free radicals. Honey is a powerful antioxidant which can take up free radicals and prevent ranciditity[22,23]. The antioxidant potential of honey and it's property of quenching of free radicals help in resolving the state of inflammation typifing chronic wound[24]. These antioxidant properties of honey are due to the presence of antioxidant compounds such as vitamin C,monophenolics, flavonoids and polyphenolics to mention a few.

The antimicrobial agents in honey essentially are hydrogen peroxidase and non peroxides such as methyl syringate and methyl glyoxal. The characteristic acidic ph between 3.2 and 4.5 inhibits bacterial pathogens and is a significant antimicrobial factor. Microbial resistance to honey has never been reported.[25] Thereby making it a very promising antimicrobial agent against the infection of antibiotic resistant bacteria and in the treatment of chronic wound infections that do not respond to antibiotic therapy, a sort of last resort medication.

The uptake of skin graft depends on the ability of the graft to receive nutrients and vascular in-growth from the recipient bed. Split skin graft survives initially by plasma imbibition from the wound bed in the initial 24 hours, then by inoculation where fine anastomotic connections are made between the donor and recipient vessels between 24-72 hours and finally by angiogenesis where capillary ingrowth is seen after 72 hours then completes the healing process with fibroblast maturation. Factors affecting graft uptake are hematoma/seroma formation, discharge from graft site and infection rate. As the graft is held in place only by the natural fibrin, there is little resistance or displacement of graft due to shear forces. To avoid these skin graft is fixed in place by conventional methods like suturing, use of staples or application of fibrin glue. In this study we used sterilized honey for skin graft fixation.

In this study, honey significantly reduced postoperative pain as per VAS due to its anti- inflammatory action.[26,27] According to Maghsoudhi et al study, decrease of pain was faster and greater in honey group.[28]

Our study had no incidence of seroma or hematoma formation which raises and displaces the skin graft from the recipient bed preventing angiogenesis and revascularisation. This may be attributed to the adhesive properties of honey.[27,29,30]

Wounds with $>10^5$ organisms per gram of tissue will not support a skin graft. In our study, honey significantly decreased infection rate on the fifth day. This is due to antibacterial effects of honey.

Graft contracture was less in honey group which may be due to its adhesive properties, minimization of scarring, and stimulation of angiogenesis as well as tissue granulation and epithelium growth by honey.[26,27] Maghsoudhi et al concluded that contraction of graft was significant in honey group.[28]

Mean hospital stay post surgery was statistically significant in honey group because of good graft uptake and lesser graft site complications like seroma/hematoma, discharge from the graft site, infection rate, graft contracture and decreased post-operative pain. Hence use of sterilized honey as fixative proves to be cost-effective as it reduced hospital stay and sutures/staples are avoided.

Graft uptake depends mainly on angiogenesis and revscularisation which inturn depends on graft immobilisation which can be done by various techniques.

Commonly used technique is suturing the skin graft to the ulcer margins and the same will be removed after graft uptake. Suturing is time consuming, hence skin staples were introduced as a faster method of graft fixation but it is expensive and causes pain during removal of the same especially in children.[31] The other techniques useSteri-Strips W microporous tapes, cyanoacrylate or amniotic membrane for fixation.[32,33] Medical honey has been used in wound management since ancient times and it has been proven to be a very effective agent. The antibacterial adhesive and anti inflammatory properties of sterilized medical honey made it an excellent alternative to the conventional fixatives in this study.[34]

CONCLUSION

With the use of sterilized honey as skin fixative in comparison with conventional fixation using skin staples/sutures in Split Skin grafting, the following conclusions were derived.

Even though graft uptake was same in both the groups, there were other added advantages in patients where honey was used for graft fixation.

There was no seroma formation in the honey group due to its adhesive properties. Honey significantly reduced postoperative pain due to its anti-inflammatory action. Mean hospital stay was significantly low in honey group compared to conventional fixation using skin staples/sutures that require removal once the graft is healed. It is also cost-effective as it decreased hospital stay and sutures/staples are avoided. Graft contracture was less in honey group which is due its adhesive properties, minimization of scarring, and stimulation of angiogenesis as well as tissue granulation and epithelium growth. Lesser infection rate was seen in honey group which is due to the antibacterial effects. Skin staples/sutures are avoided in honey group, hence the added advantage is reduced surgical time using honey for skin graft fixation and ease of application. Our study concluded that sterilized honey has proven advantage as a skin graft fixator.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Shivabasappa S, Raghupathi DS, Kumar NU, Ravishankar N, Kotekar N. Honey–old wine in new bottle: a surgically viable antibacterial and antiinflammatory fixator. Int Surg J 2019;6:1901-6.