TOPICAL RAW HONEY APPLICATION IN POST TRAUMATIC NON- INFECTED OPEN WOUNDS: A COMPARATIVE STUDY WITH POVIDINE-IODINE.

By
Edmund Ndalama Eliezer (M.D)

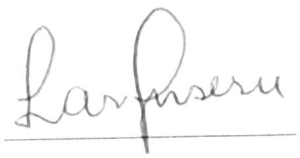
A dissertation submitted in partial fulfillment for the award of the degree of Master of Medicine in Orthopaedics and Traumatology of Muhimbili University of Allied Health Sciences

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CERTIFICATION

The undersigned certify that he has read and hereby recommend for acceptance by the Muhimbili University of Allied Health Sciences a dissertation entitled: Topical raw honey application in post traumatic non-infected open wounds. A comparative study with povidine-iodine in partial fulfillment of the requirements for the degree of Master of Medicine (Orthopaedic and Trauma) of the Muhimbili University of Allied Health Sciences



Prof. L. M. Museru (MD, MMed, Msc, FCS (ECSA))

(Supervisor)

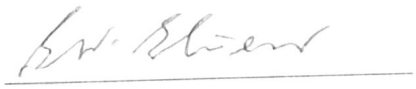
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DEDICATION

This dissertation is dedicated to my lovely wife Upendo and our beloved daughter Gladys for their love and support.

ABSTRACT

Introduction

Wound management is a common surgical problem in most hospitals. Open wounds following trauma are prone to high infection rate, resulting in prolonged hospitalization and morbidity.

Proper management of wounds to overcome the infection is challenging. There have been many reported studies of the effectiveness in management of infected wounds using honey due to its chemical and physical properties in killing bacteria and supply of nutrient necessary for wound healing.

Main objective

Main objective of this study was to determine the effectiveness of honey in comparison to povidine-iodine in promoting/enhancing healing in posttraumatic non-infected wounds. Specifically the study was aiming at comparing the rate of granulation tissue formation after dressing with honey or povidine- iodine, the antibacterial action to wound pathogen strains using honey or povidine-iodine and the duration of hospitalization/dressing for those treated with honey as compared to those treated with Povidine –iodine

Methodology

A randomised clinical trial was conducted at Muhimbili Orthopaedic institute (MOI) to compare the effectiveness of honey and povidine-iodine in promoting/enhancing healing

in post -traumatic non-infected wounds. Patients who presented with open wound and met the criteria for inclusion in study were recruited. All patients underwent surgical debridement and were given prophylactic antibiotics. Wounds were assessed and dressed on day 1,3,5,7,9,11,13,15,17,19,21,23,27th and 33rd. Wounds were assessed for the presence or absence of healthy granulation tissue and swabs were taken on every dressing day for pathogen strains isolation. The duration of wound healing was observed. In each group were 34 patients.

Results

A total of 68 patients were recruited for the study, 19% were female and 81% male. The mean age in honey group was 30.9 years while in the povidine-iodine group the mean age was 33.8 years. A relatively higher proportion of patients 20 (29.4%) were in the age group of 35-44 years old.

Healthy granulation tissue was observed in 1 (2.9%) patient dressed with honey from day 7. By day 15th, 34 (100%) out of 34 patients dressed with honey had healthy granulation tissue while those with povidine- iodine were only 8 (23.5%) out of 34 patients ($p<0.05$).

S aureus and E. Coli were the pathogen isolated from wounds dressed by either povidine Iodine or honey. But in povidine Iodine dressed wounds besides the E.Coli and S.aureus, Klebsiela and S.pyogenes were also isolated. The proportion of wounds with higher

bacteria growth was higher in Povidine iodine group than in honey group on day 7,($p<0.05$) and day 9,($p<0.05$)

The mean duration of dressing in honey group was 19 days with a standard deviation of ±4.15 while for povidine iodine group was 25 days with standard deviation of ±4.67. Of wounds treated/dressed with honey twenty one percent (21%) were treated/healed within 15days of dressing as against zero percent (0%) in povidine iodine group.

Conclusion

Topical application of honey in post traumatic non infected wounds is very effective, as it quickly enhances the formation of healthy granulation tissue, heals wounds and control infection better compared to povidine-iodine.

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LIST OF ABBREVIATIONS

EF	External Fixator
IL – I	Interleukin I
IL – 6	Interleukin 6
NIMR	National Institute for Medical Research
MOI	Muhimbili Orthopaedic Institute
MRSA	Methicillin – resistant Staphylococcus aureas
MUCHS	Muhimbili University College of Health Sciences
MUHAS	Muhimbili University of Allied Health Sciences
MNH	Muhimbili National Hospital
POP	Plaster of Paris
RTA	Road Traffic Accident
SD	Surgical Debridement
TGF	Transforming Growth Factor
TNF	Tumour Necrosis Factor
WHO	World Health Organization

1.0 INTRODUCTION

The use of honey as a wound dressing material is becoming of interest as more reports of its effectiveness are published. Clinical records show that infection is rapidly cleared, while inflammation, swelling and pain are quickly reduced. Similarly odour is reduced, sloughing of necrotic tissues is induced while granulation and epithelialization are hastened and leads to rapid healing with minimal scarring. Unlike other topical antiseptics, honey causes no tissue damage and is particularly good in secondary wound healing [1]

Honey has been reported to have an inhibitory effect to around 60 species of bacteria including aerobes and anaerobes, gram-positives and gram-negatives [1]. An antifungal action has also been observed for some yeasts and species of *Aspergillus* and *Penicillium* as well as all the common dermatophytes [1,2]. The current prevalence of antibiotic-resistant microbial species has led to a re-evaluation of the therapeutic use of ancient remedies, including honey [3].

Honey has also been found to promote and accelerate healing. Scientific analysis attribute the healing promotion or facilitation due to its many factors including nutritional contents such as fructose and laevulose which may promote epithelialization [4, 5]. It has hygroscopic effect which help to reduce tissue edema, it helps in facilitation

of separation of slough, deodorization of offensive wounds and promotion of granulation tissue [6].

In 1991 it was suggested that honey was effective for treatment of burn wounds because of the following factors; it prevents infection due to its bactericidal or bacteriostatic properties (i.e., inhibits the growth of both Gram- negative and Gram-positive bacteria), it provides a viscous barrier to fluid loss and wound invasion by bacteria thus preventing infection, it contains enzymes which aid the healing process by promoting tissue formation, it absorbs edema fluid (pus) thereby cleaning the wound finally it reduces pain , irritation and eliminates offensive smell [7].

Biochemically, honey is made of a simple sugar (40% glucose, 40% fructose and 20% water). In addition it contains amino acids, vitamins including bioten , nicotinic acid ,folic acid, pantothenic acid ,pyridoxine and thiamine; The vitamin C content of honey, which is typically more than three times higher than that in serum, could be of particular importance because of the essential role of this vitamin in collagen synthesis [8, 9]. It contains enzymes glucose oxidase and catalase as well as minerals including iron, magnesium, phosphorus, copper and calcium[5].

Honey is also an ideal first-aid dressing material, especially for patients in remote locations where infection could set in before medical treatment is obtained. It is readily available and simple to use. Honey acts as highly viscous barrier preventing bacterial penetration and colonization of wound surface [10].

2.0 LITERATURE REVIEW

2.1 Antimicrobial Properties of Honey.

2.1.1 Osmotic Effect

This was first recognised in 1892 by van Ketel [11].Like other saturated sugar syrups and sugar pastes , honey has an osmolarity sufficient to inhibit microbial growth [12, 13, 14, 15, 16, 17, 18, 19, 20].

Although wound exudates may reduces the osmolarity to a level that ceases to control infection, honey can prevent growth of *Staphylococcus aureus* if diluted 7-14 fold beyond the inhibitory point [6, 21, 22, 23, 24].

2.1.2 Acidity

Honey is characteristically acidic; its pH ranges between 3.2 and 4.5, which is low enough to be inhibitory to many pathogens [1, 25, 26, 27]. The optimum pH for growth in most of pathogens normally falls between 7.2 and 7.4. The minimum pH values for growth of some common wound-infecting species are: *Escherichia coli*, 4.3; *Salmonella sp.*, 4.0; *Pseudomonas aeruginosa*, 4.4; *Streptococcus pyogenes*, 4.5. But if honey is diluted, the pH will not be so low and the acidity of honey may not be an effective inhibitor of many species of bacteria.[1,25,26,27]

2.1.3 Hydrogen Peroxide

The major antibacterial activity in honey has been found to be due to hydrogen peroxide produced enzymatically in the honey. The enzyme glucose oxidase is secreted from the hypopharyngeal gland of the bee into the nectar to assist the formation of honey from the nectar.

The hydrogen peroxide and gluconic acid are produced through the following reaction:

$$\text{Glucose} + H_2O + O_2 \longrightarrow \text{gluconic acid} + H_2O_2$$

The hydrogen peroxide produced has concentration about 1000 less than in 3% hydrogen peroxide solution which is commonly used as antiseptic, hence is not tissue-damaging .[1,25,26,27,28]

2.1.4 Phytochemical Effect

There have also been some reports of isolation of antibacterial substances from honey that are not from peroxide generating system. Several chemicals with antibacterial activity have been identified in honey by various researchers, they include; pinocembrin, terpenes, benzyl alcohol, 3, 5-dimethoxy-4-hydroxybenzoic acid (syringic acid), methyl 3, 5-dimethoxy-4-hydroxybenzoate (methyl syringate), 3, 4, 5-trimethoxybenzoic acid, 2-hydroxy-3-phenylpropionic acid, 2-hydroxybenzoic acid and 1, 4-dihydroxybenzene. However, the quantities of these were far too low to account for any significant amount of activity.[1,28]

2.1.5 Increased Lymphocytic and Phagocytic Activity.

The killing of bacteria when honey is applied to a wound does not depend only on its antibacterial properties. Recent research shows that honey also activates the immune system. The proliferation of peripheral blood B-lymphocytes and T-lymphocytes in cell culture is stimulated by honey at concentrations as low as 0.1%; and similarly phagocytes are activated by honey at concentration as low as 0.1%. Honey at concentration 1% stimulates monocytes in cell culture to release cytokines, tumour necrosis factor (TNF)-alpha, IL-1 and IL-6, which activate immune response to infection [29, 30, 31, 32].

2. 2 Wound Healing

2.2.1 Types of Wound Healing

i. Healing by first intention

This occurs in clean, uninfected surgical incision approximated by surgical sutures. The incision causes death of a limited number of epithelial cells and connective tissue cells as well as disruption of epithelial basement membrane continuity. Healing takes place without complication, with a small fibrous scar.

ii. Healing by second intention

When there is more extensive loss of cells and tissue, and surface wound that create large defects, the reparative process is more complicated. These wounds heal by granulation and contraction.

iii. Healing by third intension

In this type of healing approximation of tissue by sutures, staples or tapes is delayed for several days following surgery or trauma. Delay in wound closure is to prevent infection due to significant contamination, extensive tissue trauma or poor blood supply to the area.

2.2.2 Pathophysiology of the Healing Wound

The first phase of wound repair is characterized by inflammation after the formation of clot. The initial fibrin –platelet clot is accompanied by platelet degranulation with release of growth factors including transforming growth factor –alpha (TGF-α), TGF-β ,epidermal growth factor, fibroblast-derived growth factor, and platelet-derived growth factor [33].

The early clot is rapidly invaded by neutrophils followed by macrophages over the next 48 hours, resulting to the release of cytokines, and increase in vascular permeability of the wound margins which allows the accumulation of edema.

The inflammatory phase gives way to the formation of granulation tissue, in the proliferation phase. Fibroblasts are the key cells involved in the production of the extracellular matrix. The production of extracellular matrix is seen clinically as formation of granulation tissue. The existing matrix in and around the wound margin is degraded by several proteolytic enzymes such as matrix metalloproteinases and plasminogen activator. The combination of the new tissue formation and contraction of surrounding tissue is essential to wound healing.

Re-epithelialization progresses as marginal keratinocytes flatten and then migrate to the periphery of the wound. A moist wound environment encourages re-epithelialization, whereas a dry one impedes the process and this association forms the basis of modern open wound care. As the wound enters the remodeling phase, granulation tissue matures and it acquires more type II collagen to replace the type I collagen associated with the immature wound [34]. Collagen deposition in normal wound healing reaches a peak by the third week after injury. Remodeling of the resulting scar takes place over months or years with a reduction of both cell content and blood floor to the scar tissue. Maximum tensile strength is achieved by the 12th week and the ultimate resulting scar has only 80% of tensile strength of the original skin that has been replaced.

2.2.3 Factors that Affect Wound Healing

There are several factors that impair wound healing. These include both systemic and local factors.

Systemic factors are:

The circulatory status regulates wound healing. Inadequate blood supply usually caused by arteriosclerosis or venous abnormalities that retard venous drainage impairs wound healing.

Nutrition has profound effects on wound healing. Protein deficiency, for example, and particularly vitamin C deficiency inhibit collagen synthesis and retard healing.

Metabolic status can change wound healing. Diabetes mellitus, for example is associated with delayed healing.

Hormones, such as glucocorticoids, have been well documented to have anti-inflammatory effects that influence various components of inflammation and fibroplasias; In addition these agents inhibit collagen synthesis.

Local factors that influence healing include:

Infection is the single most important cause of delay in healing.

Mechanical factors, such as early motion of wounds, can delay healing.

Foreign bodies, such as unnecessary sutures or fragments of steel, glass, constitute impediments of healing.

2.2.4 Useful Teminology in Wound Infection

It is important to have a clear understanding of the terms used in wound infection. Since 1985 the most commonly used terms have included wound contamination, wound colonisation, wound infection and, more recently, critical colonisation. These terms can be defined as:

Wound contamination - the presence of bacteria within a wound without any host reaction.

Wound colonisation - the presence of bacteria within the wound which do multiply or initiate a host reaction.

Critical colonisation - multiplication of bacteria causing a delay in wound healing, usually associated with an exacerbation of pain not previously reported but still with no overt host reaction.

Wound infection - the deposition and multiplication of bacteria in tissue with an associated host reaction.

Table 1. Classification of Wounds and Basic Treatment Option

Clean	Non traumatic, aseptic surgical wound	Primary closure
Clean-contaminated	Surgical wound entering a viscus	Primary closure
Contaminate	Open traumatic wound or incision in area of non purulent inflammation	Delayed primary closure
Dirty	Open traumatic wound with infection	Secondary intention healing

2.3. Honey in Wound Management

Cavanagh et al used honey in open wounds after radical vulvectomy and noted less bacterial colonization and faster wound healing [22]. In another study in an animal model honey was applied topically to open wound of 12 mice and another 12 mice in the control group had their wounds dressed with normal saline solution. Those wounds which were treated with honey healed much faster than the wounds of the control group [9].

In a study of 59 patients in Nigeria with wounds and ulcers of which 80% had failed to heal with conventional treatment, the use of unprocessed honey was successful [6]. In a study of local application of honey for treatment of neonatal post operative wound infection in which conventional treatment had failed, it was observed that all infants showed marked clinical improvement after 5 days of treatment with topical application

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of unprocessed honey twice daily. All wounds were closed, clean and sterile after 21 days of honey application [29].

Subrahmanyam M in a randomized controlled trial between honey versus Silver Sulfadiazine in patients with burns noted that honey dressed wounds, showed early subsidence of acute inflammatory changes, better control of infection and quicker wound healing occurred much earlier [30].

In another randomized study using honey treatment, 26 patient with post- operative wound infections, had infection eradication, achieving complete healing in less half of the time compared to 24 who had povidine- Iodine applied [35].

Dungford C et al noted that in wounds infected with pseudomonas, which were not responding to other treatments, infection was cleared rapidly using honey, thus allowing successful skin grafting [36,37].

Similarly, in wound infection due to resistant strains of bacteria, good results have been achieved after application of honey in five weeks [38]. Wounds infected with Methicillin – resistant Staphylococcus aureus (MRSA) have also been cleared of infection and healed by application of honey [39].

It has been shown that, honey shortens the inflammatory stage of wound healing through its antibacterial action, while its acidic pH may promote Oxygen delivery to the healing tissues [8]. The high Carbohydrate Components of honey provide a rich source of nutrient and energy for the healing tissue, and the amino acids play a major role in Collagen formation and maturation, improving contraction and epitheliazation [8, 9].
In KCMC, Tanzania, good results have been reported in patients with infected chronic ulcers healed with locally produced honey [23].

In another randomized study comparing medihoney versus mupirocin, it was observed that the use of honey was safe, cheap and effective than that of mupirocin [40].

3. STATEMENT OF THE PROBLEM AND RATIONALE OF THE STUDY

There is no doubt that injuries are increasing in many developing countries, Tanzania being one of them [41, 42, 43, and 44]. Open wound management following a trauma is a challenging problem due to high infection rate, prolonged hospitalization and existence of multi-drugs resistant bacteria creates challenges in wound management.

At Muhimbili Orthopaedic Institute, between 5 and 6 patients a week are admitted with open wounds accounting to about 24 patients a month and 288 patients a year.[45] The majority of these patients have grade III open fractures of the tibia [46, 47]. Due to lack of ambulances services and poor referral system in the city of Dar-es-salaam, the majority of the patients are received at Muhimbili Orthopaedic Institute's casualty, 6 hours after injury. This long duration stipulated to high infection rates in open wounds [48].

In another study at Muhimbili Orthopaedic Institute wound infection was recorded in 20.8 % of all patients presenting with open wounds, among these 13.3% had wound infection progression and led to bone infection [47]

On the other hand there is a controversy in the use of antiseptics in wound dressing. This is compounded by the absence of a standard protocol for wound dressing at Muhimbili Orthopaedic Institute, some surgeons prefer to use povidine-iodine, others still use hydrogen peroxide, while others believe in expensive agent such as mupirosin or sofratulle, agents which are not always available.

Therefore given the above infection rate of open wounds and the outcome, wound management is a challenge at Muhimbili Orthopaedic Institute. If honey is found to be equally good or better than povidine-iodine in this comparative study it will avail to us an alternative effective dressing agent that is easily available and affordable in our hospitals, health centres and dispensaries where wounds management is a major problem.

4.0 STUDY OBJECTIVES

Main Objective

To determine the effectiveness of honey as compared to povidine-iodine in promoting/enhancing healing in post traumatic non-infected open wounds.

Specific Objective

1. To determine the rate of granulation tissue formation following honey or povidine- iodine dressing.
2. To compare the antibacterial action of honey to wound pathogen strains to that of povidine-iodine.
3. To determine the duration of hospitalization/dressing for those undergoing honey dressing as compared to Povidine –iodine dressing .

5.0 MATERIALS AND METHODS

Study Design

A simple randomized method was used to recruit eligible patients at MOI. The history of all eligible patients admitted with post traumatic open wound was taken regarding mode of onset (mechanism), duration of illness, pain, and other associated illness. A structured questionnaire was used.

Inclusion criteria

- Extremity wound with no fracture i.e. degloving injury, laceration and crushed injury.
- Patients with grade I and II, open fractures (Gustillo and Anderson classification), that were not closed primarily.
- Patients with grade III open fracture (Gustillo and Anderson classification)
- Patient with open fracture dislocation that were not closed primarily
- Wounds left open after amputation following trauma.

Exclusion criteria

- Patients with grade I and II open fractures (Gustillo and Anderson classsfication), where wounds were closed primarily.
- Patients with other pre-existing diseases such as Diabetic melllitus, vascular diseases, malignancy conditions or other debilitating disease.
- Patients with infected wounds following a trauma.

Randomization

After establishing eligibility, 68 patients were entered in the study and randomly assigned in sequence using a service of sealed envelopes to either the honey-dressing group or povidine-iodine dressing group.

Sample size

It was estimated that when topical honey dressing was applied, good healing response is 84.4 %, the good healing response with povidine- iodine is 50% [35]

The sample size calculated from a general Epi Info 6 (2000)

$$N = \frac{(U + V)^2 [P1 (100 - P1) + P2 (100 - P2)]}{(P1 - P2)^2}$$

N – Is the desire Sample Size.

P1 – The proportion of patient treated with honey, with good response.

P2 – The proportion of patient treated with povidine-iodine with good response.

U – Power of the study, that is the probability of finding a significant result estimated at 80% hence U = 1.28.

V – The percentage point of the normal distribution corresponding to the two sided significant level that is the error 5% and hence V = 1.96

$$N = \frac{(1.28+1.96)^2 [84.4(100-84.4)+50(100-50)]}{(84.4-50)^2}$$

N = 33.9 ↔ 34 in each group

The Sample Size N should be 68.

Study area

The study was conducted at the Muhimbili Orthopaedic Institute, Dar-es-Salaam. This is a major orthopaedic and trauma centre, which covers for Dar-es-Salaam's population of about 4 million, as well as acting as a referral centre for orthopaedic, and trauma patients for the whole of Tanzania.

Application and Treatment

After surgical debridement, subsequently dressing was done using honey or povidone-iodine. Change of dressings was done after every 48hrs. All patients were given intravenous ceftriaxone one gram daily which is a third generation cephalosporins to for a period of 5 days.

In the study group honey was applied in the gauze and dressed up. In the Control group the povidine- iodine was also applied on the gauze and dressed up.

Observational Parameters

Swabs were taken from the wounds and put into the Stuart transport media and delivered to the microbiology laboratory for culture and sensitivity. The first swab was taken just after surgical debridement. Then, the second swab was taken on the third day. Subsequently swabs were taken every after two days until the wounds became sterile.

The wound and its surroundings environment were inspected every 2 days. Every 2 days the situation of the wound especially the formation of granulation tissue. Granulation tissue formation were measured by observing the colour of the wound floor. Wound reported to have un-healthy granulation tissue formation when there was a pale, blue or patchy granulation, where by healthy granulation when there was a completely red granulation tissue.

The discharge and smell were also judged /noted.

The subject was followed up until either the wound was healed by epithelialization or it become ready for skin grafting or secondary closure.

Time Frame:

The study was conducted from March 2006 to December 2006.

Ethical issues:

Ethical clearance was obtained from MUHAS ethical committee. Detailed explanation was given on why honey was used in the management of the open wounds, all its advantages and disadvantages, what type of investigations and specimens would be taken. Thereafter a written informed consent was obtained from the patient before the recruitment started.

Data analysis:

Data was entered using Epi Info, version 6 and analysed by Intercool STATA version 9. Data was summarized using frequency distribution and two way tables. Comparison of proportions between two-treatment groups was done using the Fishers exact Test. A P-value of less than 0.05 was considered significant

6.0 RESULTS

A total of 68 people were recruited. Patients with non-infected post traumatic wounds who met inclusion criteria, were enrolled in the study .The study group consisted 34 patients dressed with raw honey while the other 34 patients were dressed with povidine-iodine formed the control group.

There were 55 (80.9%) male and 13 (19.1%) female patients. There was no significant difference in sex distribution between the two treatment groups *(See table: 2)*

Table 2. Sex distribution among study participants

Sex	Honey dressed Group(34)	povidine-iodine dressed group(34)	Total(68)
Female	4(11.8)	9(26.5)	13(19.1)
Male	30(88.2)	25(73.5)	55(80.9)

The mean age in honey group was 30.9 years while in the povidine-iodine group the mean age was 33.83 years. A relatively higher proportion 57.3% of patient was in the age group of 25-44 years. Those with old age > 65 were only 4.4% *(See table: 3)*

Table 3: Age Distribution among study participants

Age group years	Honey Dressing (34)%	Povidine-iodine (34)%	Total (68)%
<24	10 (29.4)	9 (26.5)	19 (28.0)
25-44	20 (58.8)	19 (55.9)	39 (57.3)
45-64	3 (8.8)	4 (11.7)	7 (10.3)
>65	1 (2.9)	2 (5.8)	3 (4.4)

Causes of wound/injuries.

Forty-three (63%) of the study participants the cause of their wounds was Road Traffic Accidents (RTA). Others causes were 6(9%) missiles, fall 10(15%) and crush injuries 8(12%) *(See Fig. 1)*

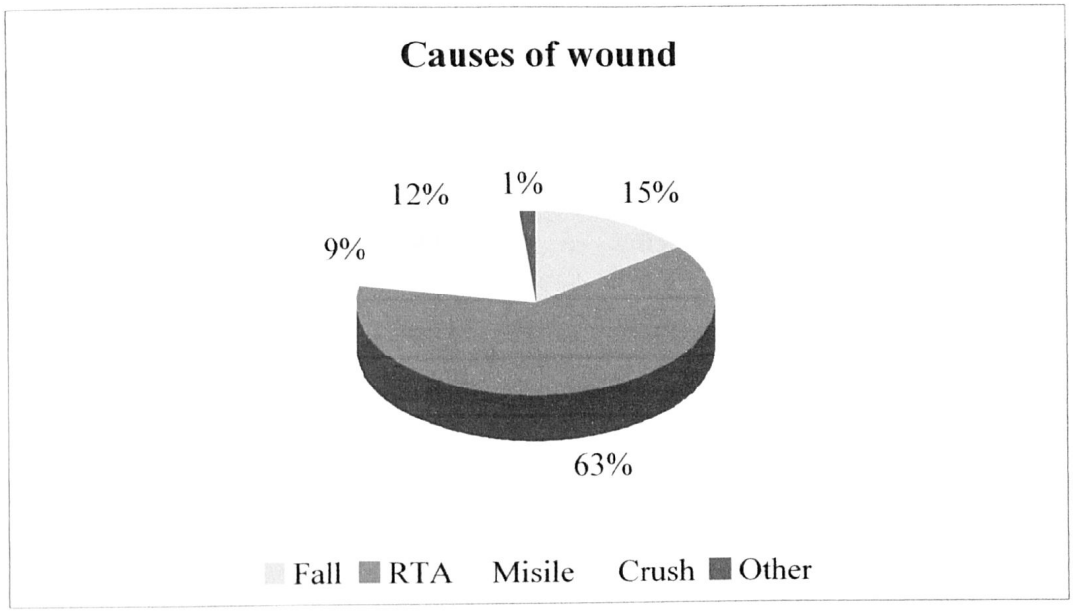


Figure 1.Causes of wound

Site of the Wound

Majority of patients had wounds on legs 63.2%. Wounds on the arm and hand were 10.3% respectively, foot 8.8%, thigh 4.4% and forearm 2.9%(*See Table 4)*

Table: 4 Wound site

Wound site	Frequency	Percent
Arm	7	10.3
Forearm	2	2.9
Hand	7	10.3
Thigh	3	4.4
Leg	43	63.2
Foot	6	8.8
Total	68	100.0

Wound diagnosis

Fifty two (76.5%) had Open Grade III fractures, Degloving Injury 4(5.8%), Crush injury 9(13.2%) and laceration 3(4.4%). Out of 34 patients dressed with honey 73.5% had open Grade III fracture, 11.8% –Degloving wound, 8.8% -crush injury and 5.9% had lacerations. For those dressed with povidine Iodine also out of 34; 79.4% had open grade III fracture, 17.6% -Crush injury, and 2.9% had lacerations and no one had degloving injury (*See table: 5).*

Table 5.Wound diagnosis by dressing category

Diagnosis	Honey dressed group (34)	Povidine Iodine dressed group (34)	Total (68)
Open Grade III fracture	25(73.5)	27(79.4)	52(76.5)
Degloving Injury	4(11.8)	0(0.0)	4(5.9)
Crush injury	3(8.8)	6(17.6)	9(13.2)
Laceration	2(5.9)	1(2.9)	3(4.4)

The rate of granulation tissue formation

The earliest healthy granulation tissue was observed on one patient being dressed with honey on 7th day. There was no patient with healthy granulation tissue in the control group at day 7. On 9th day there were 3 patients in honey group who had healthy granulation tissue and still none in control group. However this difference was not statistically significant between two groups. ($p > 0.05$). By day 11, 13, 15 and 17 of dressing, there was a higher proportion of patients whose wounds had healthy granulation tissue in the honey group compared to the povidine-iodine group. This difference was highly statistically significant ($p<0.0001$). Furthermore, on the 19th and 21st day there was a statistically significant difference between the two groups on the proportion of patients with healthy granulation tissue. ($p < 0.05$). However, from 23rd day of the treatment there was no significant difference between two groups ($p>0.05$)- *(see Table 6).*

Table 6.The rate of healthy granulation tissue formation

Day of dressing	Healthy granulation Tissue formation	Honey Dressing %	Povidine-Iodine Dressing %	P-value
day7	Yes	1 (2.9)	0 (0.0)	**p=1.0**
	No	33 (97.1)	34 (100.0)	
day9	Yes	3 (8.8)	0 (0.0)	**p= 0.24**
	No	31 (91.2)	34 (100.0)	
day11	Yes	13 (38.2)	0 (0.0)	**p<0.0001**
	No	21 (61.8)	34 (100.0)	
day13	Yes	25 (73.5)	3 (8.8)	**p<0.0001**
	No	9 (26.5)	31 (91.2)	
day15	Yes	34 (100.0)	8 (23.5)	**p<0.0001**
	No	0 (0.0)	26 (76.5)	
day17	Yes	34 (100.0)	15 (44.1)	**p<0.0001**
	No	0 (0.0)	19 (55.9)	
day19	Yes	34 (100.0)	23 (67.6)	**p-value=0.0004**
	No	0 (0.0)	11 (32.4)	
day21	Yes	34 (100.0)	26 (76.5)	**p-value=0.0049**
	No	0 (0.0)	8 (23.5)	

Bacteria Clearance rate

In both groups, all patients where given prophylactic antibiotic. Swabs taken on day 1 revealed bacteria growth in both treatment groups, though less proportion were in povidine-iodine group with a statistically significant difference ($p<0.05$). On 3rd and 5th day was a higher bacteria growth in povidine-iodine group, though it was not statistically significant between two groups ($p>0.05$). On day 7th, day 9th and day 11th the difference in proportion of bacteria growth between honey and povidine- iodine dressed groups were highly statistically significant with P values= 0.0004, $p<0.0001$ and $p=0.0005$ respectively. *(See table 7).*

Table 7.The rate of bacteria clearance

Day of dressing	Bacteria growth	Honey dressing(%)	Povidine dressing(%)	p value (p)
day1	Yes	12(35.3)	4 (11.8)	**P =0.0433**
	No	22(64.7)	30 (88.2)	
day3	Yes	12(35.3)	16 (47.1)	**P =0.46**
	No	22(64.7)	18 (52.9)	
day5	yes	10(29.4)	18 (52.9)	**P=0.084**
	No	24(70.6)	16 (47.1)	
day7	Yes	3(8.8)	17 (50.0)	**p =0.0004**
	No	31(91.2)	17 (50.0)	
day9	Yes	1(2.9)	18 (52.9)	**P <0.0001**
	No	33(97.1)	16 (47.1)	
day11	Yes	1(2.9)	13 (38.2)	**p =0.0005**
	No	33(97.1)	21 (61.8)	
day13	Yes	1(2.9)	4 (11.8)	**p =0.355**
	No	33(97.1)	30 (88.2)	
day15	Yes	0(0.0)	2 (5.9)	**p =0.493**
	No	34(100.0)	32 (94.1)	
day17	Yes	0(0.0)	1 (2.9)	**p =1.00**
	No	34(100.0)	33 (97.1)	

Bacteria isolated from patients dressed with Honey.

Two types of bacteria were isolated among honey group patients; these are *Staphylococcus aureas* and *Escherichia coli*. The most frequently isolated bacteria was *Staphylococcus aureas*. On the first day, bacterial was isolated on 12(35.3%) patients out 34 patients. Same number of patients had positive bacterial growth on third day. As treatment continued the frequency of *Staphylococcus aureas* declined and from 9th day seen in only 1 patient until day 13th where by bacteria growth was found in the same one patient. *Escherichia coli,* was seen in 4 patients on 1st day and from 7th day there was no further growth (See *Fig 2*).

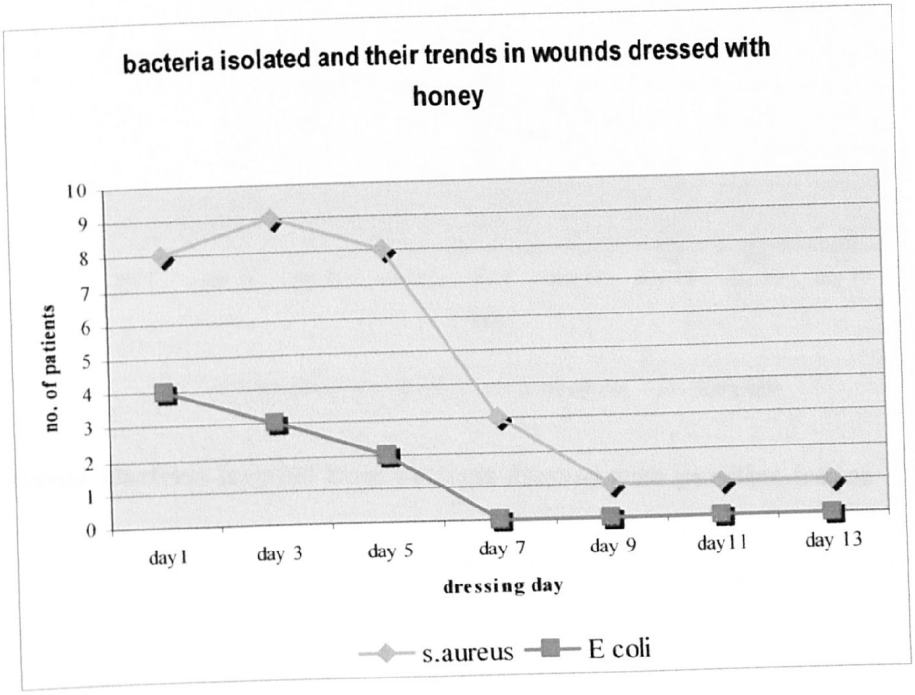


Figure2. Bacteria isolated from patient dressed with honey

Bacteria isolated from patient dressed with povidine-iodine

The isolated bacteria in povidine-iodine group were *Staphylococcus aureas*, *Escherichia coli, Streptococcus pyogenes* and *Klebsiella spp* . On the 1st day only *Staphylococcus aureas* was isolated .There were growths of Escherichia *coli* and *Klebsiella spp* on 3rd day, *Streptococcus pyogenes* on 11th day. From the 17th day there was one patient with Streptococcus pyogenes until 29th day. (See. *fig* 3)

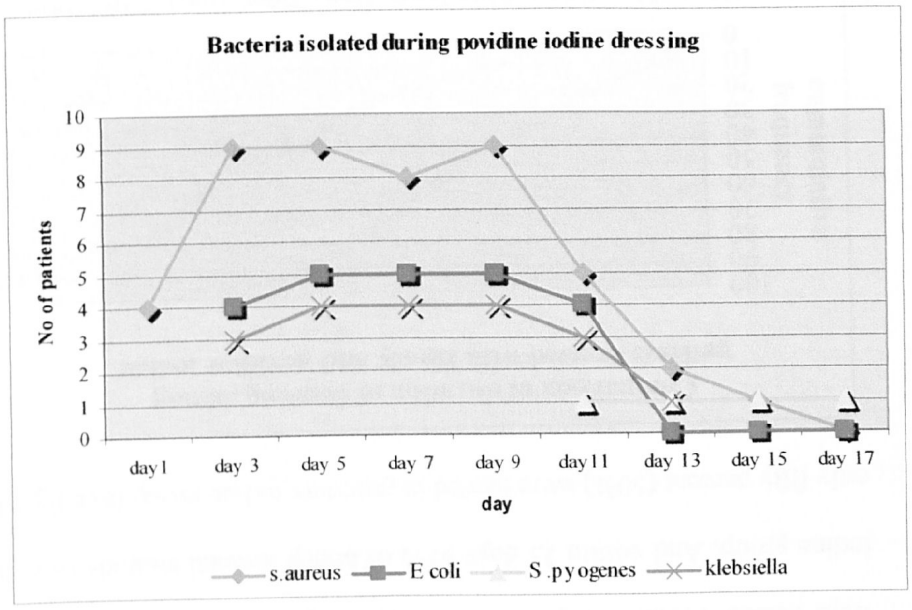


Figure3. Bacteria isolated from patients dressed with povidine-iodine

Duration of dressing

All 68 wounds were healed. In each group 29 (85.3) wounds healed primarily. Wounds which were grafted were 4(11.8) and 2(5.9) in povidine and honey group respectively while wounds which secondarily closed were 1(2.7) for povidine and 3 (8.8) for honey group.

The mean duration for wound healing in those dressed with Honey was 19days with Standard deviation ±4.15 while for povidine- iodine group was 25days with standard deviation of ±4.67. Of wounds treated/dressed with honey twenty one percent (21%) were healed within 15days of dressing as against zero percent (0%) in povidine iodine group. And within 25 days 97% of honey dressed wounds were healed while only fifty percent (50%) were healed in povidine Iodine group (See fig 4 below).

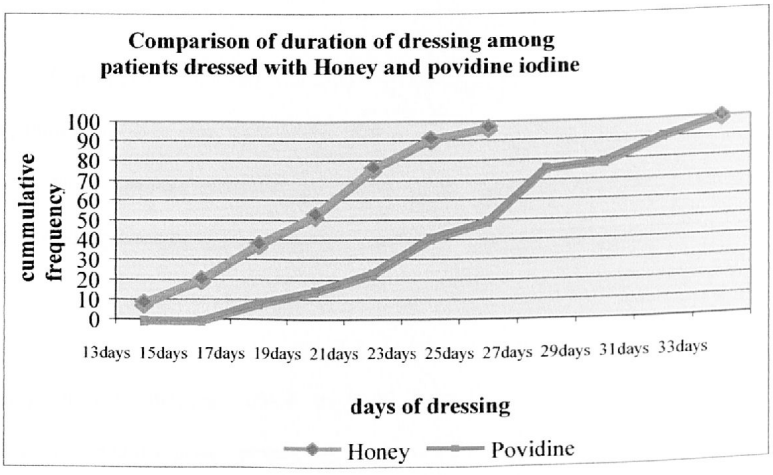


Figure 4. Comparison of duration of dressing in wound healing between Honey and povidine Iodine

7.0 DISCUSSION

This study was carried out in acknowledgement that injuries are an increasing surgical problem in most of the developing countries. The majority of these injuries result in open wounds.

Management of post-traumatic non infected open wounds still remain a matter of debate and an ideal or standard wound dressing material following surgical debridement has yet to be discovered.

A topically applied wound dressing material should have the benefit of preventing or reducing the infection rates and also to accelerate wound healing.
Presently many wound dressing agents have been used, including honey which for more than 100 years has been known to accelerate wound healing [9].

In this study of 68 patients 55(80.9%) were males and 13(19.1%) were females. The male to female ratio was 4:1. The majority of patients 57.3 % were in the age group of 25-44 years. These findings of male being predominant and involving the young energetic group were similarly to previous studies which showed the same young productive age group being predominant [41, 46, 47]

Predominance of the male population could possibly been explained by a higher tendency of them being in risky situations in both social and economic activities.

In this study the commonest cause of the wound injury was Road Traffic Accident which accounted for 63%. Similar findings have been shown in other studies done at Muhimbili Orthopaedic Institute [41, 46, 47].

Worldwide the incidence of trauma is increasing with more cases reported in developing countries, such as Tanzania . Reasons which have been given to account for the high incidence in developing countries include rapid and unplanned urbanization, the absence of adequate infrastructure and weakness in legal regulatory framework[43,44].

In this study falls from height was the second leading causes of injury accounting for 15 % being in the line with previous local studies [41, 46, and 47].

The commonest part of the extremities which was involved was leg; accounting for 63.2 % followed by hand and arm with 10.3 % each. This explains why open grade III fractures of the tibia were the most frequent diagnosis accounting for 76.5 % of cases. This was also observed in previous studies at Muhimbili Orthopaedic Institute [41, 46, 47, 48].

In this study the healthy granulation tissue was formed much earlier in honey dressed group as compared to control group. The earliest healthy granulation tissue was observed on a 7th day and by 15th day all patients in honey dressed group had developed healthy granulation tissue while by 15th day only 8 patients in a control group had healthy granulation tissue. This was in line with what was observed by Bergaman et al in a study of animal model [9]. In other series, formation of healthy

granulation tissue was observed by 7th day in patient treated with honey [7, 30]. Similar findings in a study done in Nigeria showed healthy granulation tissue was observed earlier and wounds healed faster [6]. This could be due to the properties of honey in stimulating proliferation of peripheral B-lymphocytes and T- lymphocytes, and also by stimulation of monocytes which in turn activate immune system by releasing cytokines[29, 30, 31, and 32]. The nutrient content of honey and presence of vitamins especially vitamin C make wounds heal faster [8, 9].

The results observed in the present study show that, by 15th day 100% of the patients from honey dressing group and only 23% of the patients from the control group had developed healthy granulation tissue, this meant that their wounds were ready for skin grafting.

During this study *Staphylococcus aureus* was the commonest pathogen isolated from patients wounds in both study groups. Similar results were reported by Mcharo C.N in Tanzania [49].

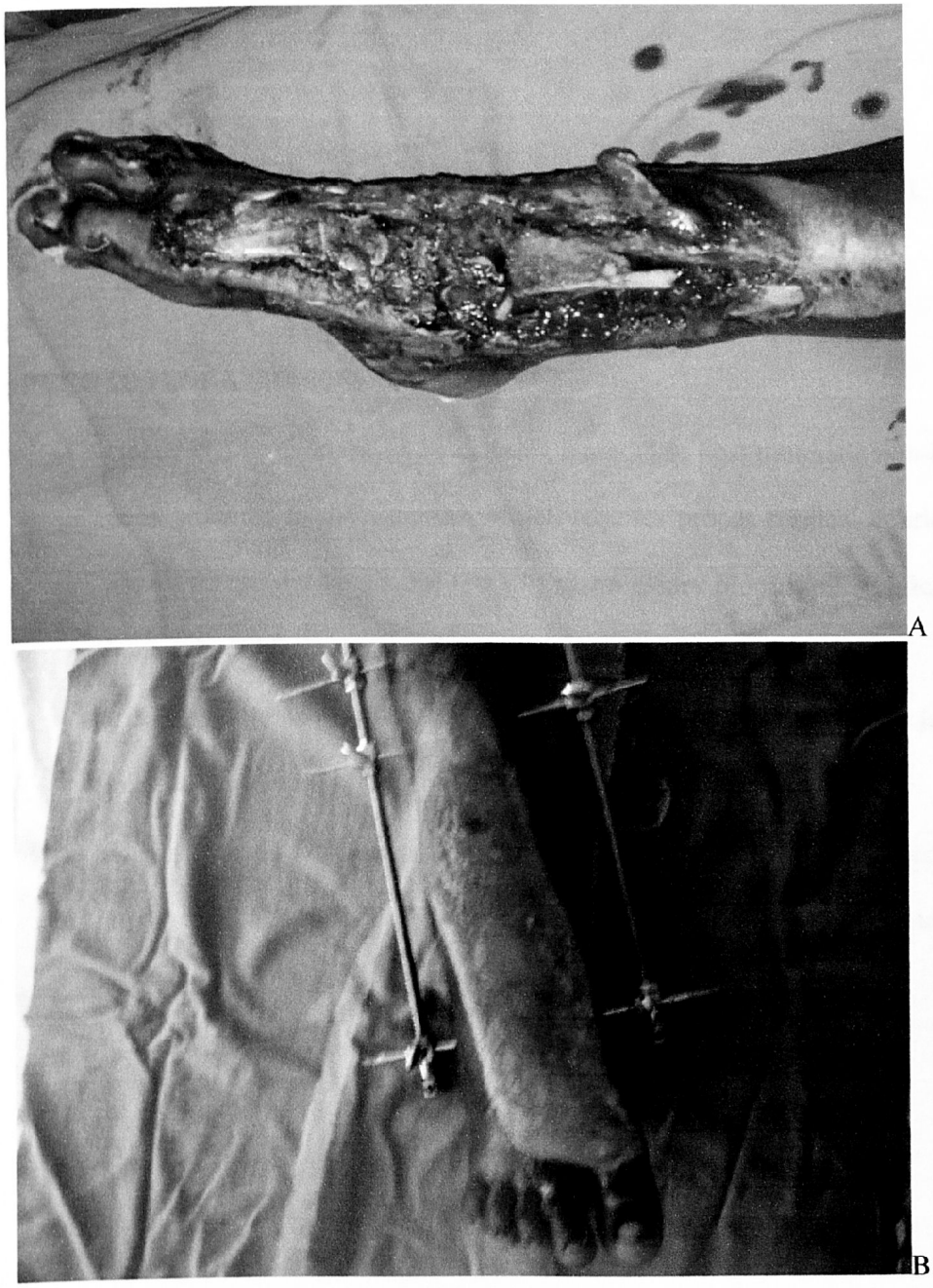
This study found out that only two types of bacteria were isolated from honey dressed wounds i.e. *S. aureus and E. coli* while in povidine iodine dressed wound the bacteria isolated includes the *Klebsiella and S.pyogenese*. This can be due antibacterial activities of honey, which are responsible for inhibiting bacteria growth [6,7,12,13,14,15,16,17,18,19,20,21,22,23,24,29,30,35] Furthermore honey's high viscosity act as a barrier, which prevent penetration of bacteria into the wound [10].

The study revealed that wounds dressed with honey became bacteriologically sterile within 5-10 days. Efem et al observed the same within one week of topical honey dressing [6]. In the study done at KCMC the wounds became sterile in seven to ten days of treatment [23]. Some authors reported about difference in antibacterial activities of honey depending on its origin. Allen K.L et al [50]. This was not observed in my study as I used honey from different parts of Tanzania and yet got the same results as other scientist.

In the present study the duration that patients needed to attend clinic for dressing was much shorter in honey dressed than in the control group. Similar results were observed in India [7, 30]. In this study wound healing was faster in honey dressed than povidine iodine dressed wounds. The same results were observed by Bergaman et al [9] Efem SE [6] Vardi A et al [29]

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The risk of wound infection with *Clostridium botulinum* after topical application of pure honey has been raised by some authors [51]. This might be rather theoretical than practical as so far there are no reported cases of wound botulism as a result of honey application. During this study pure unprocessed honey was used in all patients in honey group, and no patient developed signs of botulism infection.



A: On admission day B: 10 days after honey dressing

Figure 5: Patient's photograph before and ten days after honey dressing

8.0 CONCLUSION AND RECOMMENDATIONS

CONCLUSION

This study has proved that honey is an effective open wound dressing agent. It heals wounds faster and inhibits bacterial growth .

RECOMMENDATION

- Honey can be safely used as dressing material in post traumatic non-infected open wounds. In the situation, which requires proper surgical debridement, honey should not be a substitute of this necessary procedure! Application of honey should follow after all necessary procedure.
- Efforts should be made to categorize honey as formal dressing agent in health institutions like in other countries.
- There is need to conduct more studies concern honey dressing, especially in areas of Diabetic wounds, malignant wounds. Contaminated wounds and eradicating MRSA-bacteria.

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