EFFECTS OF SILVER SULFADIAZINE AND ACTILITE® HONEY ON BACTERIAL WOUND COLONISATION AND WOUND HEALING IN CHILDREN UNDER TWELVE YEARS WITH PARTIAL SUPERFICIAL BURN WOUNDS AT UNIVERSITY ADULT TEACHING HOSPITAL IN LUSAKA, ZAMBIA

By

Emmanuel Liche

A dissertation submitted to the University of Zambia in partial fulfilment of the requirements for the award of Master of Medicine in General Surgery

The University Of Zambia

Lusaka

2019

COPYRIGHT

DECLARATION

I, Emmanuel Liche, declare that this dissertation, being presented for Master of Medicine in General Surgery, represents my own work and that it has not been previously submitted either wholly or in parts for a degree, diploma or other qualification at this or any other university.

Signed……..

Date……..

APPROVAL

This dissertation of Emmanuel Liche is approved, fulfilling part of the requirements for the award of the degree of Master of Medicine in General Surgery by the University of Zambia.

Examiner 1……Signature……..…….Date……

Examiner 2……..Signature……Date……

Examiner 3……...Signature……Date……..

Chairperson

Board of Examiners…….. Signature……Date……..

Supervisor…….Signature……...Date……..

ABSTRACT

Burn wounds are a global public health concern and Zambia has not been spared. Burn wounds account for 6% of surgical admissions yearly and yet are amongst the common causes of mortality at University Teaching Hospitals (UTH). Burn wounds seen at UTH affect children more than adults and the common size is ≤ 20 per cent and partial superficial thickness in depth. The hospital has no burns unit and as such patients are admitted in general wards where cross infection is not uncommon. With high infection and mortality rates at UTH this study is of importance as it examined the effects of honey and SSD on bacterial wound colonisation and wound healing in paediatric partial superficial burn wounds of ≤ 20 per cent TBSA. This two-arm open label randomised trial was done at UTH over a period of seven months (July 2017-January, 2018). Children under twelve years with ≤ 20% partial superficial burn wounds were recruited. They were then randomly allocated to either honey or SSD group. Demographics were noted on recruitment. Swabs for microbiological evaluation were collected on day 0, 3, 7 and 10 and wounds were assessed for healing. The University of Zambia Biomedical Research and Ethics Committee approved the research. Of the 64 patients, 32 were allocated to each group and showed 1:1 ratio in both groups. The modal age distribution was 1-2 years and the percentage burn wound surface area was 6-10 percent in both age groups. At baseline there was no significant difference in bacterial wound colonisation (80% in honey group and 83% in SSD group; p = 0.74). However, by day 10 on treatment, there was significant reduction in bacterial wound colonisation (Honey Vs SSD; P = 0.026). Wounds treated with Actilite® honey healed quicker than those treated with SSD (Mean 11± 4, 15±6, P=0.0049).The study showed that treatment of children under 12years with partial superficial burn wounds of ≤ 20 per cent TBSA using Actilite® honey significantly reduced levels of bacterial wound colonisation by day 10. It was further demonstrated that wounds treated with Actilite® honey healed at a faster rate compared to those treated with SSD.

Keywords: honey, silver sulfadiazine, burn wounds, wound healing, wound infection

DEDICATION

To my wife, Elizabeth Kabwe, my progenies, Wongani and Temwani and my parents, Wilson Liche and Elizabeth Timilile Nkhoma for the constant support through this process.

'*A great part, I believe, of the art of medicine is the ability to observe'. - Hippocrates*

ACKNOWLEDGEMENTS

I would like to extend my gratitude to my supervisors, Dr. Robert Zulu and Dr. Zachariah Kasongo for nurturing this idea from infancy to its maturity. Indeed they have been good mentors. To all academic staff in the school of medicine and department of surgery, I say thank you for your comments. Special mention goes to Dr. James Munthali, Head of Department, Surgery, Dr. Jovic Goran, Dr. Nenad Spasojevic, Professor Bellington Vwalika and Professor Christian Ezeala for reading through my work and their encouragement through this academic journey.

To my sponsors, Advancis Medicals, UK for supplying me with Actilite® honey, Shalina Pharmaceuticals, Zambia for providing the silver sulfadiazine and the Moses Sinkala Award, I am greatly indebted for translating a brisk idea into reality. Your contribution to this research is highly valued.

To my hard working research assistants, Limata and Ben, this work would not have come to reality without your hard work. I am indeed thankful.

My sincere gratitudes to my wife, Elizabeth Kabwe, my progenies, Temwani and Wongani and my parents, Wilson and Timilile for the support rendered in this academic journey. To my siblings, Evaristal and Dominic together with their spouses Taonga and Patricia, your support has been overwhelming. To my late grandmother, Valentine Negi Mgifwile and late brother, Fatson Liche, your inspiration has brought me this far, how I wished you could witness this academic maturity.

Moreover, this work would not have been accomplished without the patients and their guardians who voluntarily and passionately contributed to the findings presented herein.

Above all, may glory and honour be to God my creator for his abundant blessings upon me through my academic life.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF APPENDICES

ACRONYNS

CI	Confidence Interval
FDA	Food and Drug Administration
GPPF	Graduate Proposal presentation Forum
HIV	Human Immuno-deficiency Virus
NHS	National Health Services
RCT	Randomised Controlled Trial
SPSS	Statistical Package for Social Sciences
SSD	Silver Sulfadiazine
TBSA	Total Body Surface Area
TGA	Therapeutic Group Administration
UK	United Kingdom
UNZABREC	University of Zambia Biomedical Research and Ethics Committee
UNZA	University of Zambia
USA	United States of America
UTH	University Teaching Hospital
WHO	World Health Organisation
ZAMRA	Zambia Medicines Regulatory Authority

CHAPTER ONE: INTRODUCTION

1.1 Background

Burns are traumatic injuries caused by coagulative destruction of the skin due to thermal injury (Dune, 2014). Due to its oxidative nature, release of free radicals is seen and these further injure important cells of life.

Burn wounds are a global public health concern. It is reported that about 300,000 deaths yearly are due to burn wounds and 90% of this burden occur in middle and low-income countries like Zambia. In Africa between 17,000-30,000 children less than five years die each year due to burn wounds. It is said that in Africa, infants succumb to burns three times more than the global average (Ringo and Chilonga, 2014)

Zambia has not been spared of the circumstances. Studies done at UTH acknowledge that burn wounds account for about 6% of all yearly surgical admissions and yet it is the commonest cause of mortality in the surgical wards. Whereas general mortality in surgical wards is less than 5%, burn wounds contribute about 15-30% mortality (Sheyo, 2010; Maimbo *et al.*, 2014). True to the global picture, burn wounds at UTH are chiefly a paediatric condition. In studies at UTH, it was demonstrated that most patients who sustained burn wounds were children less than 12 years and they presented commonly with burn wounds of $\leq$ 20 percent. And those who succumbed showed similar pattern in terms of age and percentage of wounds (Sheyo, 2010; Maimbo *et al.*, 2014 and Ziwa, 2016).

Moreover, burn wound complications like infection entails prolonged stay in hospital and attached to it are numerous costs both on the hospital and the patient. With only 403 out of 1254 beds designated to surgical wards, there is need to look into treatment modalities which will accelerate wound healing thereby reducing hospital stay.

The management of burns is not only challenging at UTH but even globally as wounds tend to be infected. However with no dedicated isolated wards managing burn wounds and unavailability of protocols it even becomes more difficult as seen in high infection rates due to cross contamination (Ziwa, 2016). At UTH the

challenge is evident as in 2010 the department requested guidance to better manage burns from the American Burns Association. Strides to improve management of burns at UTH have been made. In one study results showed reduction in wound infection using gamma irradiated amniotic membranes (Katebe, 1996). However, it was a pilot study and acceptability among patients and guardians was among issues on utilisation.

Treatment methods for partial superficial burn wounds at UTH currently range from use of Silver sulfadiazine, Povidone Iodine, saline soaks, and Pawpaw, as topical agents after washing wounds with soap and water, depending on the general surgical unit managing the patient. However, the Zambia National Formulary recommends use of Silver sulfadiazine yet its use at UTH is as it is available.

In literature, currently, there is controversy on the antimicrobial and wound healing properties of SSD that has ubiquitously been used on burns. Moreover, safety and resistance issues have been highlighted. Thus, the world is searching for alternatives like use of honey that has sparked its own debate. Honey has been used from antiquity and Africa pioneered its use yet there have been very little research emanating from Africa on role of honey in partial superficial burn wounds.

With high bacterial wound contamination and infection rates, retrospectively pegged around 30-40 percent and that children under 12 years with burn wounds ≤ 20percent are mostly affected (Sheyo, 2010 and Maimbo *et al*., 2014), this study might offer a solution on reduction of bacterial wound colonisation and promotion of wound healing. Moreover, this study seeks to add knowledge in the Zambian context as whether Actilite® honey could be an alternative to SSD in managing burn wounds. Currently, we don't know whether what other studies in Europe, Asia, Latin America, Australia and New Zealand have found can be similar or not in Zambia.

1.2 Statement of the problem

Most of patients presenting with burn wounds at UTH are children under 12 years with partial superficial burn wounds of ≤20% total body surface area and local bacteria wound colonisation and infection (30-40%) are the commonest complication culminating into mortality (Maimbo et al., 2014, Sheyo, 2010 and Ziwa, 2016). Partial superficial burn wounds in children are therefore of public health concern as

they are a commonest cause of mortality amongst surgical patients admitted to UTH (Peck *et al.*, 2010). Thus, this study intends to find out whether use of Actilite® honey compared to SSD would help in managing partial superficial burn wounds of ≤ 20 percent of total body surface area in children at UTH.

1.3 Significance of the study

As the current management of partial superficial burn wounds of ≤20 percent of total body surface area in children is none standardised amongst general surgical units and complicated by lack of special wards for burn wounds, it's imperative to conduct a study that might help in reducing bacteria wound colonisation and promote wound healing. Current methods of treating partial superficial burn wounds in children has significant wound infections rates of about 30-40 percent and mortality rates of 15-30 percent (Maimbo *et al.,* 2014; Peck *et al.,* 2010). Actilite® honey has been seen as having antimicrobial properties and ability to facilitate wound healing (Vandamme, 2015). If no intervention is done with the current trend, most wounds might continue having a high bacterial bio-burden and slow wound healing rates.

1.4 Objectives

1.4.1 Main Objectives

To compare effects of Actilite® honey and Silver Sulfadiazine on bacteria wound colonisation and wound healing in children under 12 years with partial superficial burn wounds of ≤ 20% TBSA at UTH.

1.4.2 Specific Objectives

1. To determine the occurrence of bacteria wound colonisation in patients being treated with Actilite® honey and silver sulfadiazine.
2. To determine the rate of wound healing in patients being treated with Actilite® honey and silver sulfadiazine

1.5. Research Question

In children under 12 years with partial superficial burn wounds of ≤20 percent TBSA what are the effects of Actilite® honey and Silver sulfadiazine on bacteria wound colonisation and wound healing?

CHAPTER TWO: LITERATURE REVIEW

2.1 Epidemiology

Burn Wounds are a common form of trauma globally. In a document released by World Health Organisation (WHO) in 2004, a global incidence of 110/100,000 per year with an annual mortality rate of 4.8/100,000 was reported. In Africa, burn wounds account for about 17,000-30,000 deaths per annum in children (Ringo and Chilonga, 2014). . In Subsaharan Africa, burn wounds are second among common causes of accidental death in African children younger than 5years. Due to low socioeconomic status, burn wounds associated mortalities were higher in low and middle-income countries than developed countries. In Africa, studies have reported mortality rates of 20% in Nigeria, 22% in Zimbabwe, 27% in Malawi and 9% in South Africa (Olaitain, 2006; Mzezwa *et al.,* 1999; Samuel *et al*., 2011; Allorto *et al.,* 2009). In all these studies the burden was higher in children and more so in those less than 5years of age. The presence of burn centres and improved health services could explain the lower mortalities seen in South Africa. Mortality rates secondary to burn wounds have been reported as 2.7% in USA and 1% in Canada (William, 2009). This shows that with dedication and resources it is possible to achieve lower mortality rates from burn wounds

In a Tanzanian study, it was found out that children less than 5 years were the most affected with burns and mortality rate was at 27% and 53.7% of the burns under study developed wound infection. The majority of the burn wounds were partial thickness of 15% and less body surface area (Ringo and Chilonga, 2014). This disputes earlier notion that most mortalities in burns were due to hypovolaemia.

In Zambia, burns also contribute significantly to mortality and morbidity. In a report by the American Burns Association International Outreach Committee and Children's Burns Foundation in 2010, reported burns as the commonest cause of mortality in surgical patients. The mortality rate was found to be 27% using departmental audits and most of the patients affected were children more so under the age of 5years.

Studies done at UTH have shown that most patients affected with burn wounds were children. In a study by Sheyo (2010) only 4% of the participants were aged above 16

years. Subsequent studies by Maimbo (2014) and Ziwa (2016) also demonstrated that burn wounds presenting to UTH affected paediatric patients more than adults. In all the above studies, most burn wounds were ≤ 20% of total body surface area. Similarly, children, more so less than five years old, were the most affected in terms of wound infection and mortality. Contrary to the global notion that the larger the percentage of the burn wound in comparison to total body surface area the more the patients are prone to mortality, at UTH, it was found that most children who died from burn wounds had 20 percent or less. This variation could be explained by the increased rates of wound colonisation and later on infection due to lack of isolation of patients and locally generated protocols.

2.2 Challenges in Managing Burn Wounds

Management of burn wounds is challenging. It is difficult to find an ideal dressing apart from skin. The ideal topical preparation for wounds should have certain characteristics. Firstly, it should have antibacterial and fungicidal effects of rapid onset and broad spectrum. Moreover, it should enhance and accelerate the physiological process of wound healing. In addition, it should have no local and systemic adverse effects. Finally, it should be cost effective, able to offer patient comfort and compliance. As such there has been a quest by human beings both in antiquity and contemporary society for a better topical preparation in burn wounds.

Currently at UTH, burn wound management is challenging due to a number of factors. Firstly, there are no separate dedicated wards for burn wound admission. As such, burns are admitted in side wards of general surgical, orthopaedic, urological and neurosurgical patients; thereby increasing propensity for wounds to get infected due to cross contamination (Ziwa, 2016). Moreover, there are no standardised protocols for all units to follow based on local evidence and finally non-availability of topical agents at UTH such as the recommended silver sulfadiazine.

In Zambia, few attempts have been made to research on the effectiveness of the various treatments employed in management of burn wounds. In a study done at UTH, it was demonstrated that burn wounds dressed with gamma irradiated amniotic membranes had less infection rate than those treated conventionally with SSD (Katebe, 1996). Moreover, when he looked at wound healing, it was found that wounds treated with SSD took longer to heal than those dressed with amniotic

membranes. However, there was no mention on mortality levels prospectively. Concerns included acceptability of patients and their guardians hence proving difficult for utilisation.

2.3 Pros and Cons of Use of Silver Sulfadiazine

In current literature, despite the pervasive use of SSD on burn wounds, there seem to be a body of knowledge for and against use of SSD.

The popularity of SSD is due to its antimicrobial effects against both gram positive and negative organisms (Rashaan *et al.,* 2016). Antimicrobial properties of SSD are described four fold. Firstly, silver ions have been postulated to interfere with microbial respiration as it inhibits electron transport. Moreover, it has been shown that silver ions interact with microbial cell wall and membrane leading to rupture of bacteria. In addition, silver ions bind to microbial DNA thereby preventing replication. Finally, sulfadiazine inhibits addition of para-aminobenzoic acid into folic acid thereby preventing DNA formation.

Whereas results from a single research showed excellent result with SSD against all pathogens isolated, a Cochrane review demonstrated a statistically increase in burn wound infection with SSD use (Gunjan *et al.,* 2012; Lóper-Alcade *et al.,* 2013). This contradiction could have been due to different study designs. In the earlier study it was SSD versus isolated organisms and in later review, human studies were analysed. In most of the individual studies, sample size was hardly calculated. In another study it was found that wounds got more infected in the SSD group than the honey group (Malik *et al.,* 2010).

It has been shown that no dressing was able to show superiority and benefit over SSD regarding infection control (Heynmane, 2016). Earlier preclinical evaluation of SSD and honey demonstrated reduced bacterial counts with SSD use than honey (Guthrie, 2014). Moreover, it was concluded that SSD prevented biofilm formation in burn wounds better than honey (Halstead, 2015). In this research what seemed obvious was that SSD did well in vitro studies but worse in vivo studies. In another Cochrane review of 26 RCT found insufficiency evidence whether SSD was better than non-silver containing topical agents. Moreover even in the silver containing

topical agents, meta- analysis showed that nano-crystalline silver reduced wound infection and hospital stay more than SSD (Nherera, 2017).

The debate of SSD promoting wound healing is even more versatile. It is agreed that SSD has no significant effect on wound healing (Storm *et al.,* 2010; Aziz *et al.,* 2012). Moreover, negative effects of SSD on wound healing have been demonstrated (Magsoudi, 2013). What seems to be uniform is that SSD is cytotoxic to keratinocytes. Moreover, it up-regulates pro-inflammatory cytokines that delay wound healing. However, some studies disagreed and noted positive effects of SSD on wound healing. SSD was found not to be toxic to both fibroblasts and keratinocytes and promoted wound healing (Olson, 2000; Landsdown 2010). However, these were animal studies.

In terms of cost effectiveness and resistance, it is agreed that as a rule of thumb it takes 10 grams of SSD per percent of burns per 24 hours and has multi-resistance to *Pseudomonas aureginosa* and *Enterobacter ssp* (Mason, 1986; Ita *et al.,* 2002) This could be costly especially if the burnt area is large and SSD needs to be applied more frequently for effectiveness. However, some researchers have demonstrated positive effect against Methicilin Resistant *Staphylococcus aureus* (MRSA) and *Enterobacter ssp* (Bowler, 2004; Ip 2006)

In the quest for alternatives to SSD, researches emanating from New Zealand, India, USA and Europe looked at honey as an alternative. Honey use on wounds is ancient as Hippocrates himself used it.

2.4 Properties and Antimicrobial Effect of Honey

Honey is a highly saturated viscous which contains carbohydrates, amino acids, vitamins enzymes and water. It has proline as the most abundant amino acid. Honey has a pH of 3.2 and water activity of 0.5-0.62(Vandamme, 2015). It has enzymes like glucose oxidase that lead to release of hydrogen peroxide at 1% which stimulates fibroblasts growth. It also helps in killing bacteria as it stimulates neutrophils to release Tumour Necrosis alpha (TNFα), Interleukin 1 and 6. Moreover bacteria cannot proliferate in the presence of honey, as it needs a pH of 7.2-7.3, which is higher than that of honey. Moreover at water activity of 0.5-0.62, bacteria cannot grow, as it requires higher water activity of 0.94-0.99 for colonisation. Microscopic

analysis showed that honey treated *Staphylococcus aureus* arrested at cell division level (Henrique *et al.*, 2005)

Manuka honey from New Zealand has been well studied and is considered as an appropriate therapeutic standard in treatment of burns. The USA-FDA, Australian Therapeutic Group Administration and the NHS in UK have approved use of honey. Honey is described as the nectar of life and is recommended for use on burn wounds in India (Nagane, 2004)

2.5 Pros and Cons of Honey Use on Burn Wounds

Whereas there is some evidence of low infection rates with use of honey on burn wounds compared to SSD, others disagreed in that honey was unable to prevent biofilm formation compared to SSD (Malik, 2010; Halstead 2015). It could be that the later study did not use honey concentrated enough to cause mitotic inhibition. In fact 1% honey was used. In contrast to the latter study, it was shown that honey was effective in aggregated bacterial biofilms where SSD proved ineffective (Hill *et al.,* 2010).

In a Cochrane review, it was stated that honey might be superior to some conventional dressing, but there was uncertainty about reproducibility of the evidence (Jull *et al.,* 2008). Systemic review showed moderate quality of nine randomised controlled trials in which honey rendered bacteria colonised burn wounds sterile in less days than SSD (Aziz, 2016). However quality of individual studies was questionable and most of studies emanated from similar regions in Asia and Europe. Moreover, Studies showed that honey dressing maintains wound sterility and if applied on infected wounds, sterility is achieved at a faster rate compared to conventional dressings (Habibullah *et al.,* 2013; Wijesinghe *et al.,* 2009). Furthermore, when used as a graft fixator, significant reduction in infection rate was noted by day five (Maghsoudi and Moradi, 2015). Resistance to honey has not been documented and no cytotoxicity to either fibroblasts or keratinocytes has been recorded (Cooper, 2014)

In terms of wound healing, it has been demonstrated than honey facilitated wound healing in about 15-18 days as compared to SSD which achieved healing between 18 and 32 days (Bhagel, 2009; Hill, 2010). This could be due to honey's ability to

improve phases of healing especially inflammation, proliferation and remodelling. It is further agreed that honey reduces the activities of cyclo-oxygenase 1 and 2 thereby reducing excessive production of inflammatory markers such as prostaglandins (Raynaud *et al.,* 2013; Vallianou *et al.*, 2014). Honey also acts as an oxidant. In burn wound there is excessive activity of free radicals. Hydroxyl radicals and hypochlorite anions impair wound healing (Fahmida *et al.,* 2014). Honey treatment, through ascorbic acid, phenolics and catalases excite a positive effect on the oxidative stressful state in burn trauma by effectively mopping up free radicals. This ultimately improves wound healing (Subramanyam *et al.,* 2003).

Honey has been noted to be safe despite a hypothetical fear of contamination especially if it's not medical honey. Although use of gamma irradiated medical honey is recommended, it is argued that real risk of bacterial contamination on wounds due to dressing with non medical grade honey is not significant (Al Waili *et al* 2015).

Honey is safe, could be cost effective as it can be applied once daily and beneficial for wound management (Oryan *et al.,* 2016). It has been found that allergy to honey has rarely been observed in studies (Molan, 1998).

From literature, it is not clear on effectiveness of SSD and honey on bacterial wound colonisation and wound healing. Therefore, this study might help to add to the body of knowledge. Moreover, there are very few studies emanating from Africa as most of them are from Asia, Europe, USA, New Zealand and Australia. As such, it would be important to find out how results obtained elsewhere will compare with this study done in an African population.

CHAPTER THREE: RESEARCH METHODOLOGY

3.1 Research Methods

In this part of the dissertation detailed descriptions of methods used in the study are presented. Cardinal aspects include data collection techniques, study type, sampling methods and procedures, data collection and analysis, ethical considerations.

3.1.1 Study Design

The study was a two-arm open label randomised trial

3.1.2 Study Site

The study was conducted in the Department of Surgery at the University Teaching Hospital. Patients were recruited from the surgical admission ward (G01) upon presentation. Follow up was done in subsequent surgical wards (G02 and G12). Upon discharge guardians were reminded for reviews in Clinic 4 at UTH and patients were reviewed on a particular day in clinic 4.

3.1.3 Target population

Children with burn wounds

3.1.4 Study population

Burn wound patients satisfying the inclusion criteria.

3.2 Inclusion Criteria

- Children under 12 years (common age seen with burn wounds at UTH)
- Burns less than 24hrs, admitted to UTH (more than 24hrs burn wounds tend to be more colonised)
- Burns of 20% or less body surface area (common burn wound size presenting to UTH)
- Partial superficial thickness burns (common burn wounds seen at UTH)

3.3 Exclusion criteria

- Co-morbidities like Diabetes and HIV (wound healing is poorer in diabetics and compromised immunity like HIV)
- Clinically infected burn wounds (would be difficult to compare clinically infected wounds with those presumed to be clean)
- Known malnourished children (malnutrition has negative effect on wound healing)

It should be noted that both inclusion and exclusion criteria put forward is in order to exclude confounding factors in data analysis and is representative of the population as most wounds seen at UTH are in children under 12 years with partial superficial burn wounds of ≤ 20% TBSA and without obvious co-morbidities.

3.4 Sample size

Previous data, in paediatric burns patients; demonstrated re-epithelialisation within 15 days (Sd= 4) and minimally clinically important difference (d) is 3 days (Miller *et al.*, 2011). The power of the study was at 80%(which is globally acceptable statistically), with type 1 error at 0.05, 95% significance and 0.20 type two error.

The formula used to calculate the number of patients is $f(\alpha,\beta)x\ \frac{2xsd^2}{(d)^2}$

Where $f(\alpha,\beta)\ at\ 80\% = 7.85$

Thus $number\ of\ patients\ in\ each\ group = 7.85\ x\ \frac{2x4^2}{3^2}$

This gives 28 patients in each group and a total of 56 patients.

Using the other outcome, which is infection, previous data noted 40% infection with SSD and 10% with honey and using formula

$$n = \frac{\left(Z\,{}^{\alpha}/_{2} + Z\beta\right)^2 \times (P1(1-P1) + P2(1-P2))}{(P2-P1)^2}$$

Where

$$Z\frac{\alpha}{2} \text{ at } 0.05 = 1.96, Z\beta \text{ at } 80\% \text{ power} = 0.84, P1 = 0.40 \text{ and } P2 = 0.10$$

Substituting in the equation we get n = 29 in each group. And total sample size =58. Literature has found 10% loss to follow up and adjusting for the loss, sample size of **64** was adequate for both outcomes.

3.5 Sampling strategy

Simple randomised sampling of the patients meeting the inclusion criteria was used to allocate patients to honey or SSD groups. Even numbers translated to honey group and odd number translated into SSD group.

3.6 Procedure

Patients that presented with burns were recruited and subjected to thorough history taking and examination for determination of percentage and location of the burns. Enrolment was done using the inclusion and exclusion criteria and data was collected using data collection sheets

After detailed patients' guardian counselling, all enrolled patients' guardians were required to sign a written informed consent. Then they were required to pick a number from one to hundred and the intervention was assigned to them based on whether they had picked an even or odd number. Swabbing of the wound was done on day 0 before any intervention, day 3, day 7 and day 10. Wounds were thoroughly washed with carbolic soap and tap water once a day and either honey or SSD was applied, then wounds were dressed. The size of the wound was assessed on day 0, day 7, day 14 and day 21.Treatment failure was defined as deepening wound, presence of slough and consistent positive bacterial colonisation beyond day 10. If treatment failure occurred, patients would be crossed over to conventional dressing (SSD). Patients upon being discharged were reminded by phone to come for reviews. If patients in either group got wound infection, they would get systemic antibiotic treatment as guided by sensitivity results. If partial superficial thickness deepened whilst on treatment, wounds would be grafted with skin. Treatment failure was

defined as persistent fever associated with dirty wounds despite use of honey and by day 10 cross over to SSD was done.

3.7 Variables

Outcomes

- Number of days taken for a wound to fully re-epithelise (i.e. 95% re-epithelialisation)
- Bacterial wound colonisation on day 0, 3, 7 and 10

Dependent (outcome) variable: microbiological culture result and size of the wound at particular day of assessment.

Independent variables: sex/age of patient

Categorical variable: sex (Male/Female), treatment outcomes (discharged, mortality), wound colonised or not, burn wounds healed or not

Continuous variable: age, percentage of TBSA, percentage of wound re-epithelised

Potential confounders: admission of patients to general wounds wound affect wound colonisation and patients were being cared for by unit doctors (UTH has five firms)

3.8: Data Management

3.8.1 Data Collection

The burn percent was estimated with the aid of Lund and Broader chart and rest of data was collected using the attached data collection sheet. Estimation of burnt surface area was done using a $1cm^2$ chart.

3.8.2 Data entry

Data collected was entered into Excel spreadsheet for analysis

3.8.3 Data analysis

The characteristics of patients enrolled in the study were summarized using tables and charts. The clinical outcomes at specific moments were compared using t-test for continuous variable with normal distribution. For categorical variables, association was detected using chi-squared test.

3.9 Ethical Considerations

- This was a comparative effectiveness research (CER) as the two topical drugs used were already approved and established methods in management of partial superficial burn wounds in children
- Permission was obtained from University Teaching Hospital Management and Department of Surgery. Ethical approval was obtained from the University of Zambia Biomedical Research Ethics Committee (UNZABREC).
- Participation in this study was voluntary. Refusal to participate in this study didn't affect the patient's management at UTH. Guardians who consented for their children to participate in the study were at liberty to have their children withdrawn without demand for reasons. Patients were not remunerated. All information obtained was kept confidential. However the findings of the research would be shared with the public through journal publication.

- All the investigations done were by qualified personnel. Pus swab was a non-invasive procedure. The only anticipated risk to the patient was minimal discomfort. No reaction was documented towards honey being used in this research. A written consent was obtained from every guardian.

- There was no risk or discomfort for the patients in this study compared to daily practice. Since most of the measurements used in the study were also implemented in daily care of burn patients at UTH, participation did not involve any burden for patients

- Septic patients whilst on these treatment modalities benefited from antibiotics as guided by sensitivity reports. If wounds deepened, treatment with split thickness skin graft was done.

- No adverse reactions were reported according to the pharmaceutical pharmaco-vigilance unit protocol and UNZABREC would be notified.

- Permission to import Actilite® honey was sought from Zambia Medicines Regulatory Agency (ZAMRA). Moses Sinkala award of $2000 was received for research.

CHAPTER FOUR: RESULTS

4.1 Enrolment

In this study, 70 patients were assessed and only 66 met the inclusion criteria. Four patients could not meet the inclusion criteria. The reasons included known positive HIV status, inhalation burns and obvious malnutrition. Details are as shown in Figure 1. Of those who met the inclusion criteria, two fell out as their parents/guardians declined consent.

64 patients were enrolled in the study. Randomisation was done to allocate 32 participants to either honey dressing or silver sulfadiazine groups. Participants whose guardians picked even numbers were allocated to honey dressing group and odd numbers to silver sulfadiazine group. Patients were then followed up to the endpoint of the study, which was full re-epithelialisation of the wound.

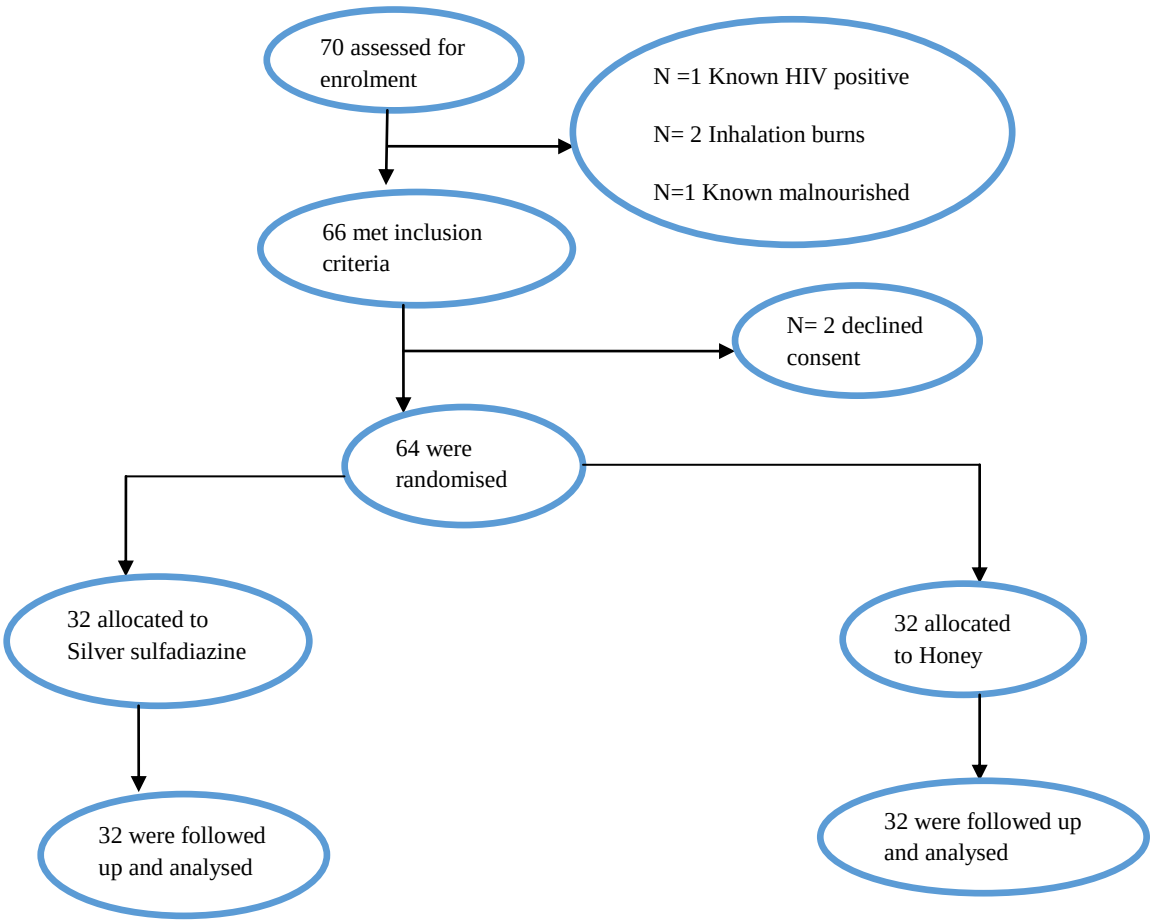


Figure 1: Flow diagram of study participants

4.2: Characterisation of patients in the study

Patients enrolled in the study were characterised based on sex, age, firms, burn percentage of total body surface area, mechanism of burns and time taken to reach the hospital.

4.2.1: Sex distribution of the patients enrolled in the study

In both groups the ratio of male to female was almost 1:1. In the honey group 54 %(n =18) were males and 46 %(n = 14) were females. In the Silver sulfadiazine group 50 %(n =16) was for either male or female. There was no significant difference in sex between the two groups as shown below in Table 1.

Table 1: Sex distribution of patients enrolled in the study

	Male	Female	P-value
Silver sulfadiazine	16 (50%)	16(50%)	0.62
Honey	18(54%)	14(46%)	

4.2.2: Age distribution of the patients enrolled in the study

The modal age distribution in both groups was 1-2 yrs. There were few patients aged less than a year. The least in both groups were seen in patients aged between 7-12 yrs as shown in Figure 2.

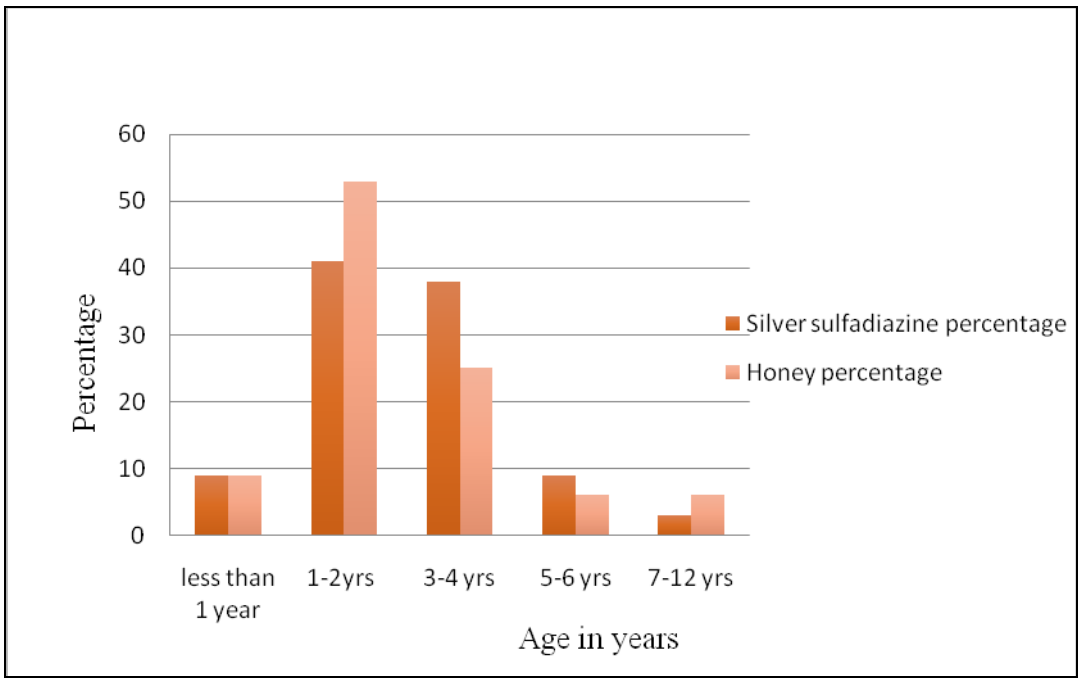


Figure 2: Age distribution of patients

4.2.4: Firm distribution of enrolled patients

Patients were recruited from all the five General Surgical firms as shown in Figure 3. Most patients were recruited from Red and Green Firms. In the honey group no patient was recruited from Blue Firm.

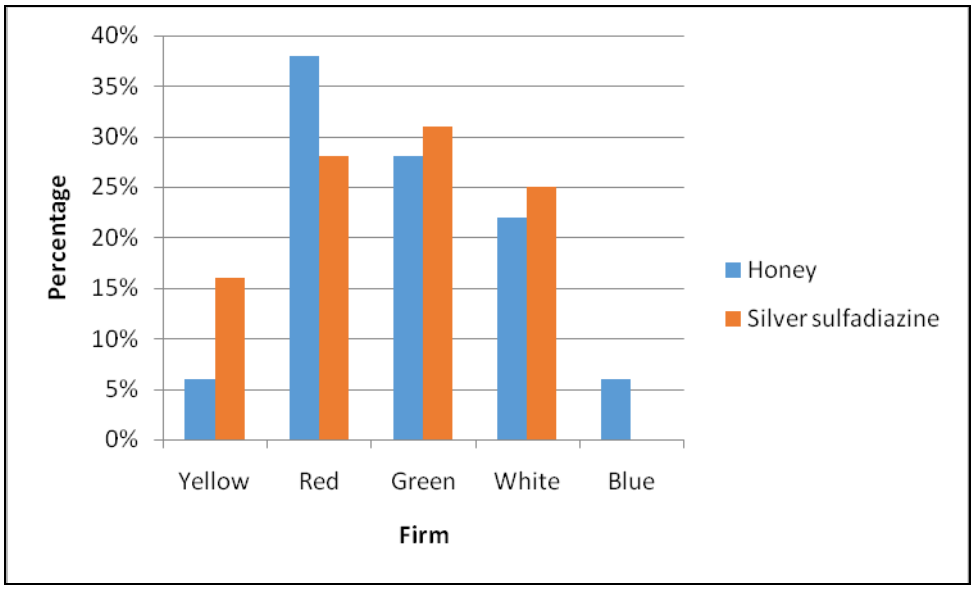


Figure 3: Firm distribution of patients

4.2.5: Burn Percentage of total body surface area

The modal burn percentage in both groups was 6-10% (n =15; n = 11 respectively). There were few patients in both groups with burn percentage of 1-5% as shown in Figure 4.

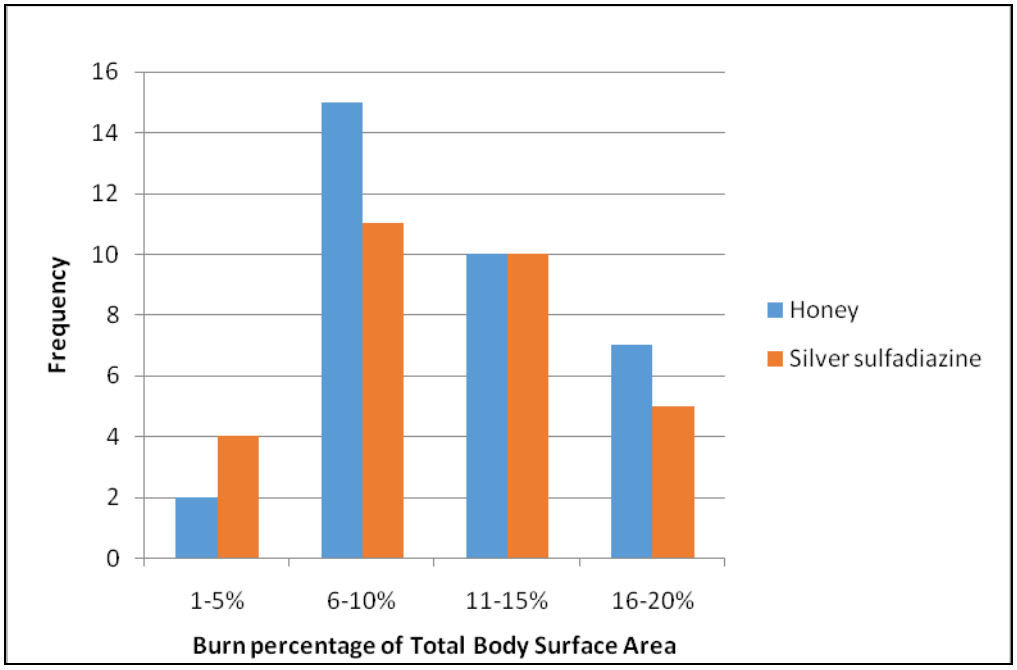


Figure 4: Burnt percentage of total body surface area

4.2.6: Common causes of burns in patients under study

Most of the patients in both groups were burnt by hot water (n = 26; 80%). Other causes were as shown in figure 5. There were no patients in Silver sulfadiazine group burnt by cooking oil.

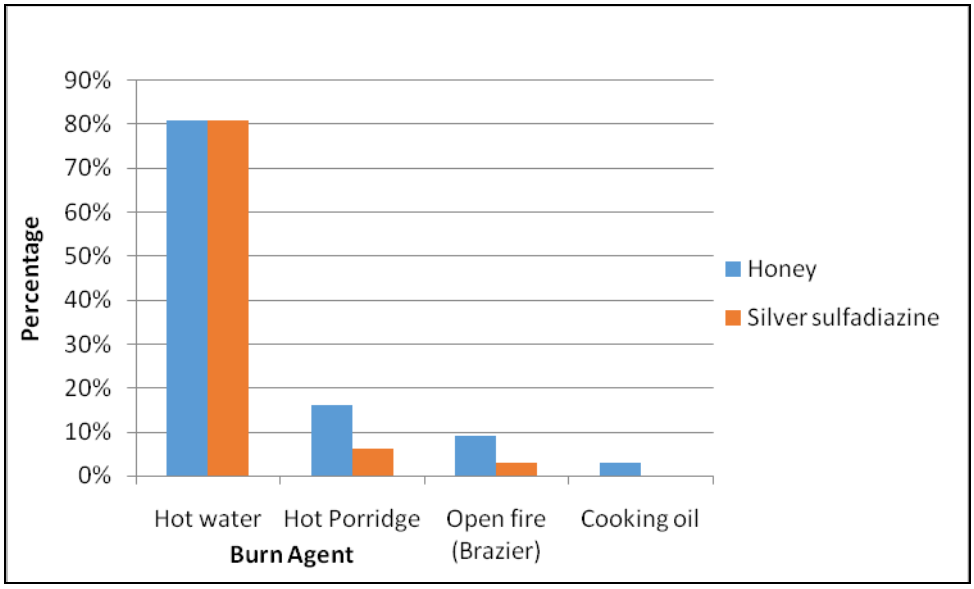


Figure 5: Causes of burns in patients under study

4.2.7: Time taken to reach hospital

The modal time taken for patients to reach the hospital was 1-2hrs (53% and 50%) as shown in Figure 6. Only a few in the honey group reached the hospital in 30minutes.

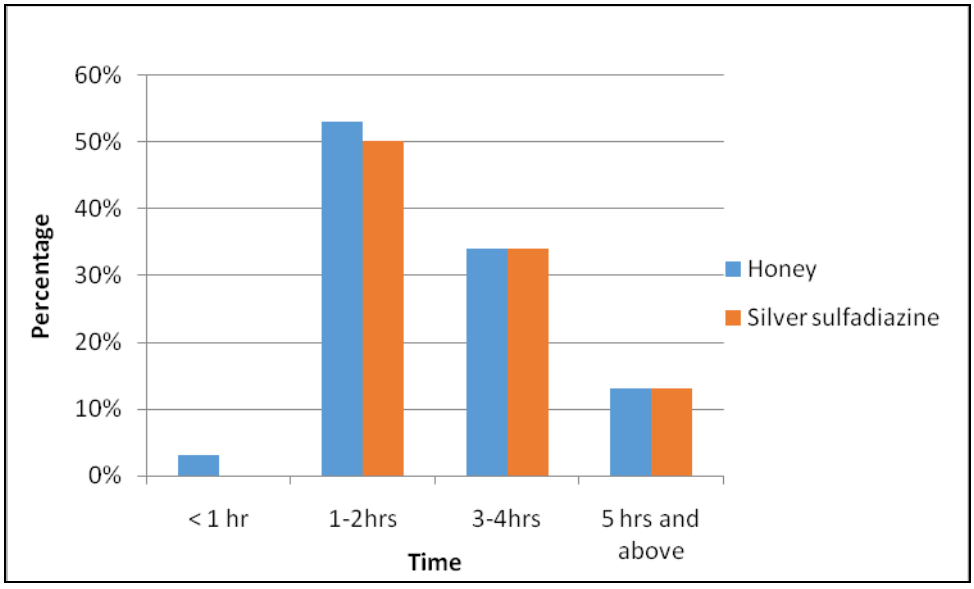


Figure 6: Time taken to reach the hospital

4.3: Outcomes

The outcomes in this study included bacteria wound colonisation on day 0, 3, 7 and 10 and average duration for the wound to reach full re-epithelisation.

4.3.1: Bacteria Wound Colonisation in both treatment groups

In both groups most of the wounds came in with bacterial colonisation (80% and 83%) as shown in Figure 7. On admission, there was no statistical difference in wound colonisation (p=0.74) as shown in Table 2. In the honey group the reduction in bacteria wound colonisation was more than in the Silver sulphadiazine group at day 10(16% and 41%). When subjected to further statistical analysis for day 10, the p value was 0.026 as shown in table 3.

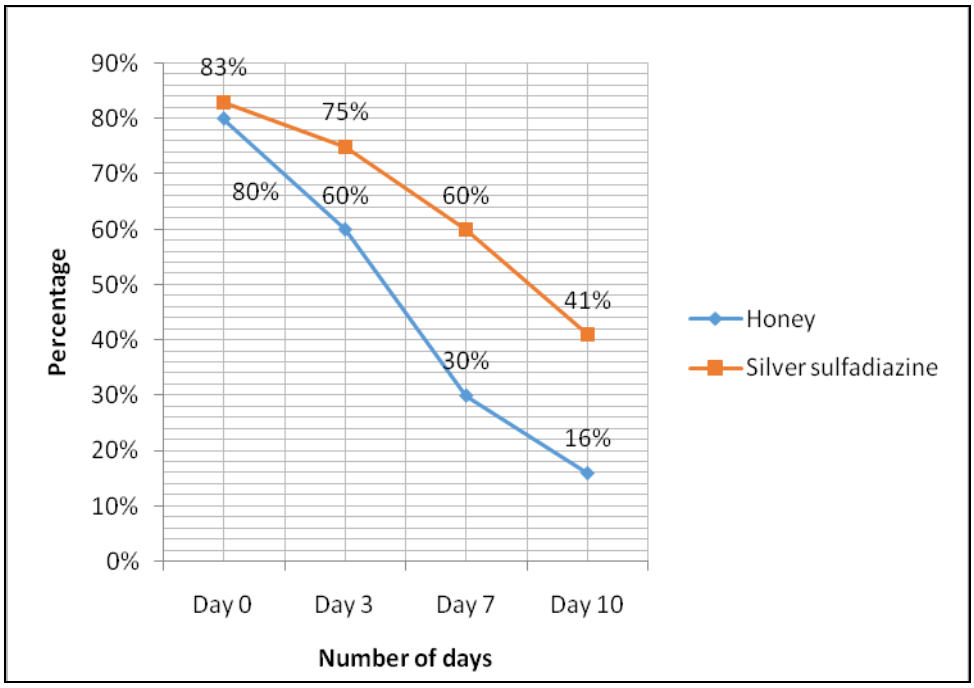


Figure 7: Bacteria wound colonisation in both treatment groups over 10 days

Table 2: Statistical analysis of bacterial wound colonisation on admission

Group	Positive	Negative	X^2	P value
Silver sulfadiazine	27	5	0.11	0.74*
Honey	26	6		

*Chi-square test

Table 3: Statistical analysis of bacterial colonisation on day 10

Group	Positive	Negative	X^2	P- value
Honey	5	27	4.95	0.026*
Silver sulphadiazine	13	19		

*Chi-square test

4.3.2: Mean time taken for wounds to reach full re-epithelialisation

The mean times taken for wounds to heal in honey and Silver sulfadiazine groups were 11(CI: 10-12 at 95% significance) and 15(CI: 13-17 at 95% significance) days respectively. The p value was 0.0049 as shown in Table 4.

Table 4: Statistical analysis of the average days for full re-epithelisation

Group	**Number of observations**	**Mean (days)**	**Standard Deviation**	**CI**	**P-Value**
Honey	29	11.41	3.95	11±1	0.0049*
Silver sulfadiazine	29	15.24	5.92	15±2	

*Student t-test

CHAPTER FIVE: DISCUSSION

A total of 64 patients were recruited in this study and this figure was within the sample size calculated based on primary outcomes. There was homogeneity in the distribution of sex in both groups. The ratio of male: female in the silver sulfadiazine group was 1:1 and in the honey group was 1.3: 1. This was similar to sex distribution reported in previous studies done at UTH (Ziwa, 2016).

The modal age distribution in both groups was 1-2 years and there were fewer patients who were above 5 years of age. In a Tanzanian study similar epidemiological findings, that is burn wounds affected under fives more than any other childhood age group, were made (Ringo and Chilonga,2014). In this age group there is disproportionate maturation between motor and cognitive development. Therefore their zeal to play and experiment does not correspond with their perception of danger. In circumstances where the child is left unattended to, a catastrophe like being burnt might ensue. Mostly in low and middle-income countries like Zambia, such circumstances are rather common.

The commonest cause of burns in both age groups was hot water. Most of these burns occurred at home or by the neighbours once the child was not tended to. Previous research done at UTH showed similar distribution in terms of mechanism of burns (Maimbo *et al.,* 2014). In a study done in the rural part of Zambia in Katete, it was shown that open fire was the commonest cause of burn wounds (Edwards *et al*., 2011). This demonstrates that mechanism of burn wounds in children varies from one geo-location to another even within the same country.

In this study, most of the patients were brought to the hospital within 1-2hrs. In a study done in Malawi it was found that most patients presented to the hospital after 24hrs of burn injury (Tyson *et al*., 2013). This could be due to the fact that most patients in this study came from peri-urban areas and hospitals and clinics were within reach.

Despite presenting early to the hospital, it was surprising to note high percentages of bacterial wound colonisation. In the Honey group 80% of the patients had positive swabs and 83% in the SSD group had positive swabs. However, the difference was not statistically significant and as such did not influence the results henceforth after

commencement of treatment. Similar results of early bacterial colonisation were reported in a study done in Pakistan, that is 83% in Honey group and 75% in silver sulfadiazine group (Habibullah *et al*., 2013). Common isolation included gram-positive bacteria with *Staphylococcus aureus* being the commonest in both groups in the first week. In subsequent weeks gram-negative bacteria became prominent like *Klebsiella pneumonia*, *Pseudomonas aureginosa* and *Enterobacter ssp*. These findings are similar to an earlier study done by Ziwa (2016) at UTH. Moreover, a study by Duin (2016) noted similar pattern of bacterial isolation in burn wounds.

There was significant reduction of wound colonisation in the honey group compared to SSD group by day 10. The P-value was 0.026 and OR of 4 demonstrates that the difference was not only statistically significant but also clinically significant. Studies by Habibullah et al (2013) and Subramanyam (1998) noted similar findings in that most partial superficial burn wounds in children treated by honey became sterile by day seven compared to those treated with Silver sulfadiazine. Generally, honey achieved wound sterility at a faster rate compared to conventional topical dressings, SSD inclusive (Wijesinghe *et al*., 2009).

Honey has a water activity that creates unfavourable environment for bacterial growth. Moreover, the low pH of honey impairs enzymatic function thereby inhibiting bacterial survival and proliferation. Glucose oxidase in the honey facilitates release of one percent hydrogen peroxide that is bactericidal. Moreover honey up regulates the activity of neutrophils through nuclear transcription factor. Unlike use of prophylactic antibiotics, which does not permeate bacterial biofilm, honey as a topical antibiotic prevents formation of biofilms. Evaluation of three trials in a systematic review showed no reduction in bacterial colonisation in burn wounds with prophylactic antibiotic use. Moreover, in 11 trials in the same systematic review reported rather an increase in wound infection in burn wounds treated with SSD(Lopez-Alcade *et al*., 2013)

In terms of wound healing, wounds dressed with honey re-epithelised at a faster rate than those treated with SSD. Wounds in the honey group re-epithelised in 11±4 days compared to 15±6 in the SSD. This difference when subjected to statistical analysis proved to be significant with a p value of 0.0049. The effective size (Cohen's d = 0.6) showed that the difference was observable clinically by the observer. Systematic

review of six randomised controlled trials reported that honey was more effective in promoting wound healing on days 15 and 21 than its comparators (Wijesinghe *et al.*, 2009)

Wound healing is a complex cascade that is usually described under the following phases: inflammation, re-epithelialisation and remodelling (Goljan, 2014). Benefits of honey use are seen in all the phases of wound healing. Use of honey has been shown to reduce inflammation by inhibiting cyclo-oxygenase 1 and 2(Raynaud *et al*., 2013; Vallianou *et al*., 2014). As burn wounds generate free radicals which are cytotoxic, honey through its anti oxidant properties mops up the free radicals. Antioxidants found in honey include ascorbic acid and catalases(Subramanyam *et al., 2003).*

One percent hydrogen peroxide is not only antimicrobial but also stimulates angiogenesis. As a result, re-epithelialisation is facilitated. The low PH in honey stimulates growth of fibroblasts and accelerates epithelial cell migration (Barui *et al*., 2013). Rushton (2007) demonstrated that acidification of wounds not only reduced bacterial colonisation but also accelerated wound healing.

One key factor that negatively affects wound healing is local infection. The presence of infection on the wound elongates the inflammatory phase of wound healing and has negative effects on the proliferative phase. As discussed above, honey treated wounds yielded fewer bacteria on day 10. Moreover, honey up regulates plasmin, which digests fibrin. Fibrin plays a cardinal role in attachment of slough to the wound surface(Molan, 1998). Hence honey has debridement properties on the wound. It should be emphasised however that honey is not toxic to newly formed collagen. Honey is rich in proline, an amino acid key in collagen synthesis.

The study had limitations in that patients were admitted in general wards and therefore cross contamination could attribute to bacterial wound colonisation. Moreover, SSD was in paste form and Actilite honey was in dressing form and this could influence both wound colonisation and wound healing as studies have shown better outcomes with silver based dressings like Merpilex Ag compared to SSD (GeeKee *et al*., 2015).

CHAPTER SIX: CONCLUSIONS AND RECOMMENDATIONS

This study has elucidated that treatment of partial superficial burn wounds of ≤ 20 percent TBSA with honey significantly reduced the level of bacterial colonisation on burn wounds by day 10 in children under 12 years. The longer the patient was on treatment the less colonised their wounds were with bacteria. It was also clear that wounds treated with honey healed quicker than those treated with SSD. The demographic characteristics of the two groups were similar and allowed comparison to be made fairly. Therefore the findings of this research suggest better outcomes of partial superficial burn wounds of ≤ 20 percent TBSA in children at UTH with use of honey compared to silver sulfadiazine.

This study recommends the following

1. Use of Actilite® honey on partial superficial burn wounds of ≤ 20 percent TBSA in children under 12 years should be considered in hospital protocols just like silver sulfadiazine.
2. Routine swabs of wounds on day 0, 3, 7 and 10 should be done to monitor effect of topical dressings used in managing partial superficial burn wounds of ≤20 percent TBSA in children.

It will be good to do more studies to compare effects of Actilite® honey with local honey on partial superficial burn wounds of ≤ 20 percent in paediatric patients at UTH so that if results are comparable patients can easily acquire the honey. Moreover, the results from this study should not be generalised to all burn wounds. Further study with a bigger and more inclusive sample size should be done for generalised conclusions to be drawn.

REFERENCES

Allorto, N.L., Oosthuizen, G.V., Clarke, D.L., & Muckart, D.J (2009), 'The spectrum and outcome of burns at a regional hospital in South Africa', Burns, Vol. 35, pp.1004-1008

Al-Waili, N.S.,Salom,K.,Butler,G., & Al Ghamdi,A.A(2011), 'Honey and Microbial Infections: A Review Supporting the use of Honey for Microbial Control', Journal of Medicinal Food, Vol. 14, No.10, pp.1079-1096

Aziz, Z, Abu, S.F. & Chong, N.J (2011), 'A systematic review of silver-containing dressings and topical silver agents for burn wounds', Burns, Vol.38, No. 3: pp 307-318

Barui,A., Mandal,N., Majumder,S., Das,R.K., Sengupta,S., Banerjee,P., Ray,A,K., RoyChaudhuri,C., Chatterjee,J(2013), 'Assessment of molecular events during in vitro re-epithelialization under honey-alginate matrix ambience', Materials science and engineering C, Vol.33, pp.3418-3425

Bhagel, P.S., Shinkla, S., Mathur, R. K., & Randa, R(2009), 'A comparative study to evaluate the effect of honey dressing and Silver Sulfadiazine on wound healing in burn patients', Indian Journal of Plastic Surgery, Vol.42, No. 2: pp.176-181

Bowler, P.G., Duerden, B.I., & Armstrong, D.G (2001), 'Wound microbiology and associated approaches to wound management', Clinical Microbiology Reviews, Vol. 14: pp. 244-269.

Edwards, D., Heard, J., Latenser, B.A., Quin, K.Y & Jovic, G (2011), 'Burn Injuries in Eastern Zambia: Impact of multidisciplinary teaching teams', Journal of Burn Care and Research, Vol.32, No.1: 31-38.

GeeKee,E.L.,Kimble,R.M.,Cuttle,L.,Khan,A. & Stocktorn, K.A(2015), 'Randomised controlled trial of three dressings for partial thickness burns in children', Burns 41:946-955.

Goljan, F.E (2014) Rapid Review Pathology, 4th Edition, Elsevier saunders, Philadelphia, USA.

Gunjan, K., Chamania, S., Sheetal, C.,Nanda, H., Chitnis, U.& Chitnis, D.S(2012), 'A comparative study of the effects of different topical agents on burn wound infections', Indian Journal of Plastic Surgery, Vol.45, number 2: pp.374-378.

Guthrie, H.C., Martin, K.R., Taylor, C., Spear, A.M., Whiting, R., Malcidowie,S., Clasper, J.C & Watts, S.A(2014), ' A pre-clinical evaluation of silver, iodine and Manuka honey based dressings in a model of traumatic extremity wounds contaminated with Staphylococcus aureus, Injury, Int.J. Care Injured, Vol.45: pp.1171-1178.

Habibullah, S., Neemullah,D., & Mansour,K(2013), 'Effectiveness of honey dressing and silver sulfadizine dressing on wound healing in Burns Patients', The journal of Bioscience and Medicine(JBM), Vol.3, No.1: pp 23-28.

Halstead, F. D, Rauf, M.,Bamford, M., Wearn, C.M., Bishop, J.R.B, Burt R., Fraise, A.P.,Moiemen,N.S., & Oppenheim, B.A, & Webber, M,A(2015), 'Antimicrobial dressings: Comparison of the ability of a panel of dressings to prevent biofilm formation by key burn wound pathogens', Burns, Vol.41, pp. 1683-1694.

Heyneman, A., Hoeksema, H., Vanderkerckhove, D.,Pirayesh,A & Monstrey, S (2016), 'The role of silver sulfadiazine in the conservation treatment of partial thickness burn wounds: A systemic review, Burns, Vol.42, No.7:pp.1377-1386.

Hill, K.E., Malic, S. & McKee, R(2010), 'An in vitro model of chronic wound biofilms to test wound biofilms to test wound dressing and assess antimicrobial susceptibilities, Journal of Antimicrobial Chemotherapy, Vol.65, No. 6: pp. 1195-1206.

Ip M, Lui SL, Poon VK, Lung I, & Burd, A (2006), 'Antimicrobial activities of silver dressings: an in vitro comparison', J Med Microbiol., Vol.55, No.1: pp.59-63.

Jull, A.B., Rodgers,A.& Walker,N(2008), 'Honey is a topical treatment for wounds', Cochrane Database Systemic Review, Vol.4(October,8):CD005083.

Katebe, K. R.C (1996), 'The use of amniotic membrane in the treatment of burns in children: A clinical trial at the University Teaching Hospital', MMed (Gen.Surgery) dissertation submitted to the University of Zambia.

Lansdown, A.B., (2010), ‘A pharmacological and toxicological profile of silver as an Antimicrobial agent in medical devices’, Advanced Pharmacological Sciences, Vol.2010: pp. 1-16.

Lopez-Alcade,J., Roquei, F.M., Sola,I & Bonfill, L.X(2013), ‘Antibiotic prophylaxis for prevention of burn wound infection’, Cochrane database systemic review, Vol. 6(June 6): CD008738.

Magsoudi, M., Nezami, N & Mirzajanzadeh, M (2013), ‘Enhancement of burn wounds healing by platelet dressing’, International Journal of Burns and Trauma, Vol.3,pp. 96-101.

Maimbo, M., Jovic, G. & Odimba, B.F.K(2014), ‘A comparative study of early-delayed skin grafting and late or non-grafting of deep partial thickness burns at the University Teaching Hospital’, Medical Journal of Zambia, Vol. 41, No.1, pp.32-36.

Malik, K.L., Malik, M.A & Aslam, A (2010), ‘Honey compared silver sulfadiazine in the treatment of superficial partial thickness burns, International Wound Journal, Vol. 7 No. 2: pp. 413-417.

Mason, A.D, McManus, A.T, Pruitt, B.A (1986), ‘Association of burn mortality and bacteraemia: a 25 year review’, Archives of Surgery, Vol. 121**:** pp**.** 1027-1031.

Miller K, Rodger S, Kipping B, & Kimble RM (2011), ‘A novel technology approach to pain management in children with burns: a prospective randomized controlled trial’, Burns, Vol.37, pp.395–405.

Molan, P.C(1998), ‘A brief review of the use of honey as a clinical dressing’, The Australian Journal of Wound Management, Vol.6, No.4, pp. 148-158.

Mzezewa S, Jonsson K, Aberg M & Salemark L(1999), ‘A prospective study on the epidemiology of burns in patients admitted to the Harare burn units’, Burns, Vol. 25(September (6)), pp. 499–504.

Nagane, N.S., Ganu, J.V.,Bhagwat, V.R & Subramanyam, M (2004), ‘Efficacy of topical honey therapy against silver sulfadiazine treatment in burns: A biochemical study, Journal of clinical Biochemistry, Vol.19, No. 2:pp.173-176.

Nherera,L.M., Trueman, P.,Roberts, C.D.& Berg, L(2017), 'A systematic and meta-analysis of clinical outcomes associated with nanocrystalline silver use compared to alternative silver delivery systems in management of superficial and deep thickness burns', Burns, Vol.43, No.5: pp 935-948.

Olaitan, P.B & Jiburum B.C(2006), 'Analysis of burn mortality in a burns centre,' Annals of Burns and Fire Disasters, Vol.19, No. 2: pp 59- 62.

Oryan, A, Alemzadeh, E & Moshiri, A (2016), 'Biological properties and therapeutic activities of honey in wound healing: A narrative review and meta-analysis', Journal of tissue Viability, Vol.25, No. 2: pp 98-118.

Peck, M., Kardos, P., Farrar, N., Grissom, K., Peck, J (2010), 'Consultative Report from American Burn Association: International Outreach Committee and the Children's Burns Foundation', unpublished data.

Rashaan, Z.M., Krijnen, P, van den Akker-van Marle, M.E., van Baar, M.E., Vloemans, A.F., Dokter ,J., Tempelman, F.R., van der Vlies, C.H., Breederveld, R.S(2016), 'Clinical effectiveness, quality of life and cost-effectiveness of Flaminal® versus Flamazine® in the treatment of partial thickness burns: study protocol for a randomized controlled trial', Trials, Vol.17, No.122:pp 1-9.

Raynauld, A., Ghezali, L., Gloaguen,V., Liagre ,B., Quero, F. & Petit, J.M(2013), ' Honey-induced macrophage stimulation: AP-1 and NF-κB activation and cytokine production are unrelated to LPS content of honey, International Immunopharmacology, Vol. 17: pp. 874–879.

Ringo, Y & Chilonga, K (2014), 'Burns at KCMC: Epidemiology, presentation, management and treatment outcome', Burns, Vol.40, pp.1024-1029.

Rushton, I (2007), 'Understanding the role of proteases and PH in wound healing', Nurs. Stand, Vol.21, No.32, pp.68-70.

Samuel,C, Campbell ,L.P, Mjuweni, S., Muyco, A.P, Bruce, C. & Antony, C (2011). Epidermiology, Management,outcomes and areas of improvement of burn care in central Malawi: An observational study. The Journal of International Research, Vol.39: pp 873-879.

Sheyo, M (2010), 'Clinical outcomes of burns in HIV positive patients in Lusaka, Zambia', Medical Journal of Zambia, Vol.39, No.4: pp. 1-6.

Storm-Vesloot, M.N.,Vos, C.G., Ubbinki,D.T. & Vermeulen, H(2010), 'Topical Silver for Preventing Wound infection', Cochrane Database Systematic review, Vol.17, No.3:CD006478

Subramanyam,M.,Shahapure,A.G.,Nagane, N.S.,Bhagwat,V.R. & Ganu,J.V(2003), 'Free radical Control- The main mechanism of action of honey in burns', Annals of Burns and Disasters, Vol.16, No.3, pp.135-138.

Tyson,A.F., Boschini,L.P., Kiser,M.M., Samuel,J.C., Mjuweni ,S.N., Cairns,B.A. & Charles, A.G(2013), 'Survival after burn in a sub-Saharan burn unit: Challenges and opportunities', Burns, Vol. 39: pp.1619-1625.

Vallianou,N.G., Gounar,P., Skourtis,A., Panagos, J.& Kazazis, C(2014), 'Honey and its Anti-Inflammatory, Anti-Bacterial and Anti-Oxidant Properties', Gen Med(Los Angel), Vol.2, No.2, pp. 1-5.

Vandamme, L., Heyneman, A., Hoeksema, H.,Verbelen, J & Monstrey,S(2013), 'Honey in Modern Wound Care: A Systemic Review', Journal of Burns, Vol.6, No.14, pp.1-13.

Wijesinghe, M., Weatherall, M.,Perrin, K. & Beasley, R(2009), 'Honey in the treatment of burns: A systematic review and metanalysis of its efficacy', New Zealand Medical Journal, Vol.122, No.1295, pp. 47-60.

Williams, F.N., Herndon, D.N., Hawkins, H.K., Lee, J.O., Cox, R.A., Kulp, G.A., Finnerty, C.C., Chinkes, D.L., Jeschke, M.G (2009), 'The leading causes of death after burn injury in a single pediatric burn center', Critical Care Vol.13, No.6: pp. 1-7.

Ziwa, M., (2016), 'Common Hydrotherapy Practices and Prevalence of Burn Wound Bacterial Colonisation at the University Teaching Hospital in Lusaka, Zambia', Master of Medicine Dissertation Submitted to UNZA, Unpublished data.

APPENDICES

APPENDIX 1: ASSENT FORM

ASSENT TO PARTICIPATE IN A RESEARCH STUDY FOR CHILDREN AGED 7 YEARS AND ABOVE

A COMPARATIVE STUDY ON EFFECTS OF HONEY AND SILVER SULFADIAZINE ON BURN WOUND OUTCOMES IN PEDIATRIC PATIENTS AT UNIVERSITY TEACHING HOSPITAL, ZAMBIA

My name is Emmanuel Liche and I am a Master of Medicine student in the Department of Surgery at the University of Zambia. I am doing a research study as part fulfilment of my degree and I am working with my teachers, Dr. Robert Zulu and Dr. Zachariah Kasongo. I'd like to tell you about this study and ask if you will take part in it.

What is a research study?

A research study is when people like me collect a lot of information about a certain thing to find out more about it. Before you decide if you want to be in this study, it's important for you to understand why we're doing the research and what's involved.

Please read this form carefully. You can discuss it with your parents or anyone else. If you have questions about this research, just ask me.

Why are we doing this study?

We are doing this study to find out how use of honey in treatment of burns in children compares with the traditional silver sulfadiazine.

Why are we talking to you about this study?

We're inviting you to take part because our research involves pediatric burns in the age group of 12years and below as they are the most affected.

What will happen if you are in this study?

If you agree to be in the study and your parents give permission, we will do the following

Measure the size of your wound and collect swabs to check if there are bugs on the wound on admission day, days 3, 7.10,14 and 21 from first contact.

Depending with the group allocated, your wounds will be treated with either silver sulfadiazine or honey and both are known treatment methods which are safe.

If you don't want to be in the study, what can you do instead?

You have the right to refuse participation and you will still be treated like any other patient who comes with burns at the University Teaching Hospital.

Are there any benefits to being in the study?

There are personal benefits as your wounds will be taken care of and you and your parents will not be asked to buy silver sulfadiazine or honey as might be the case in routine care. Moreover, we hope that the results of this research will improve the management of paediatric burns at UTH

Are there any risks or discomforts to being in the study?

There are very minimal risks of reacting to the topical agents; both SSD and honey.

Who will know about your study participation?

Apart from yourself, your parents and researcher, no one will know about your participation and results as the information will be kept confidential. Group results however will be communicated to you and will get published in journals

Will you get paid for being in the study?

You will not get paid for participating in this study

Do you have to be in the study?

No, you don't. Research is something you do only if you want to. No one will be annoyed with you if you don't want to be in the study. And whether you decide to participate or not, either way will have no effect on the routine treatment you get at UTH

Do you have any questions?

You can contact us if you have questions about the study, or if you decide you don't want to be in the study any more. You can talk to me, or your parents, or someone else at any time during the study.

Dr. Liche Emmanuel
University Teaching Hospital,
Private Bag 1X RW,
Lusaka.
Phone +260977531328
Email: emmanuelliche@gmail.com

OR

The University of Zambia Biomedical Research Ethics Committee (UNZABREC),
School of Medicine,
Ridgeway Campus,
Nationalist Road,
Lusaka

If you decide to participate, and your parents agree, we'll give you a copy of this form to keep for future reference.

If you would like to be in this research study, please sign your name on the line below.

_____	_____
Child's Name/Signature (*printed or written by child*)	Date
_____	_____
Signature of Investigator/Person Obtaining Assent	Date
----------	----------
Witness	Date

KUBVOMEREZANA KUTENGAKO MBALI KU PHUNZIRO KWA ANA ADZAKA CHISANU NDI CHIWIRI KUPITA PATSOGOLO

PHUNZIRO LOYANGANA PAKASEBENZEDWE KA MANKHWALA A UCHI NDI *SILVER SULFADIAZINE* PA ZILONDA ZAKUPSA NDI MOTO PAKATI PA ANA PA CHIPATALA CHOPHUNZITSILA ZAUMOYO MUMUZINDA WA LUSAKA MUZIKO LA ZAMBIA

Ine dzina langa ndine Emmanuel Liche, mwana wasukulu wophunzira za ukaswiri ochita maopaleshoni pasukulu la UNZA. Ndikuchita Phunziro londithandiza kufika kumapeto a maphunziro anga. Muphunziroli ndili in aziphunzitsi awiri, a dotolo a Robert Zulu ndi a dotolo Zachariah Kasongo amene ndi aphungu onithandiza kuti zonse ziyende bwino. Ndifuna ndikuunikileni paphunziro limeneli ndipo ngati simunamvetsese osachedwa kundifunsa.

Kodi Phunziro ndi Ciani?

Phunziro ndipamene anthu monga ine tikufufuza zinthu kwa anthu zamene zingatithandize kupeza zimene tifuna. Mukalibe kubvomela kutengako mbali, ndikwabwino kumvetsesa cholinga chaphunziro. Welengani bwino bwino ndipo mungafunse makolo anu kapena ali yense ndipo osachita mantha kufunsa mafunso.

Cifukwa Ciani Tikuchita Phunziroli?

Tikufuna kuona kapena uchi uchilitsa bwino zilonda zamoto kopambana mankhwala ochedwa *Silver sulfadiazine*.

Cifukwa Ciani Tikulankhula ndi Inu?

Tikulankhula ndi inu popeza phunziro lathu likhuza ana ofika dzaka khumi limodzi chichiwiri amene ali ndi zilonda zamoto monga inuyo.

Ndiciani chizachitika Mukabvomeleza Kutengako Mbali?

Ngati mwabvomeleza kutengako mbali, tizapima ukulu wazilonda zanu ndipo zilonda zisatsukidwa ndi manzi ndi sopo. Tizaika mankhwala a uchi kapena Silver sulfadiazine kulingana ndi gulu limene muzapatsidwa. Tizapititsa katonje pazilonda

zanu ndi kupeleka kwa anzathu a zasainsi kuti apime ngati pali tulombo. Zimenezi zizachitika patsiku loyamba, lachitatu, lachisanu ndi chiwiri ndiponso lachikhumi.

Ngati Simubvomeleza Kutengako Mbali ndi Ciani Cizachitika?

Kutengako mbali kapena kukana ndi ufulu wanu. Osachita mantha kuti tizakuthamangitsani mukakana. Muzalandilabe thandizo bwino bwino monga odwala aliyense.

Kodi kuli Phindu Lanji Lotengako Mbali?

Potengako mbali mutitandiza ife akafukufuku a zaumoyo kupeza njira yabwino yothandizira zilonda zamoto. Simuzapatsidwa malipilo akhobili koma mankhwala onse amene muzalandila ndi aulele.

Kodi kuli Chiopsezo Potengako Mbali?

Mankhwala awiriwa ndiwophikidwa bwino kotero kuti alibe chiopsezo chilli chonse.

Ndani Azadziwa kuti Mwatengako Mbali?

Ife akafukufuku, inuyo ndi makolo anu ndi amene azadziwa kuti mwatengako mbali. Padera pa awa chinsinsi chizasungidwa. Zotuluka muphunziroli zizalembeka mumabuku aakulu a sainsikugawana nzeru ndi anzathu koma maina anu sazachulidwa.

Kodi muli ndi Mafunso?

Nthawi ili yonse muli ndi zakukhosi mungathe kufunsa ine kapena akulu a gulu loyangana kuti maphunziro achitika potsata malamulo. Mungathe kuwonana nafe kapena kuyimba lamya.

Emmanuel Liche Biomedical	OR	University of Zambia
Department of Surgery		Research and Ethics Committee
University Teaching Hospital		Nationalist Road
P/B RW1X		School of Medicine
Lusaka.		Ridgeway Campus
Lamya: 0977531328 Email: emmanuelliche@gmail.com		Lamya: 260-1-256067 Email: unzarec@zamtel.zm

Ngati mwamvetsesa ndipo ndinu wokonzeka kutengako mbali sainani apa

…….	…….	……
Dzina	Chizindikiro	Tsiku
…….	…….	……..
Dzina la opeleka umboni	Chizindikiro	Tsiku

APPENDIX 2: CONSENT FORM

A COMPARATIVE STUDY ON EFFECTS OF HONEY AND SILVER SULFADIAZINE ON BURN WOUND OUTCOMES IN PEDIATRIC PATIENTS AT UNIVERSITY TEACHING HOSPITAL, ZAMBIA

I, ……., do hereby confirm that the nature of this clinical study has been sufficiently explained to me. I am aware that my child's personal details will be kept confidential and I understand that I may voluntarily, at any point, withdraw my child's participation without suffering any consequences. I have been given sufficient time to ask questions and seek clarifications, and of my own free will declare my child's participation in this research. I have also received a signed copy of this agreement.

…….....	…….	…….
Name of Participant (Print)	Signature/ Thumb print	Date
……	…….	……
Witness (Print name)	Signature/ Thumb print	Date

PEPALA LACHIVOMELEZO

PHUNZIRO LOYANGANA PAKASEBENZEDWE KA MANKHWALA A UCHI NDI *SILVER SULFADIAZINE* PA ZILONDA ZAKUPSA NDI MOTO PAKATI PA ANA PA CHIPATALA CHOPHUNZITSILA ZAUMOYO MUMUZINDA WA LUSAKA MUZIKO LA ZAMBIA

Ine…….ndikusimikidza kuti zonse zokhudza kutengako mbali ku phunziroli andifotokozela bwino bwino. Ndikudziwa kuti zonse zomwe zingalenge mwana wanga kudziwika zizasungwida mwachinsinsi. Ndiponso ndikudziwa kuti ndabvomeleza kutengako mbali mosakakamizidwa ndipo ndili ndi ufulu wochokako ku phunziroli kopanda zifukwa. Ndapatsidwa nthawi yokwanila kuti ndifunse zonse zakukhosi ndipo mwaufulu ndikusimikidza kuti mwana wanga atengeko mbali kuphunziro.Ndisimikidzanso kuti andipatsa pepala lomasulira phunziroli.

…… …….. ……

Dzina la obvomekedza Chidzindikiro Tsiku

…… ……. ……

Dzina la opeleka umboni Chidzindikiro Tsiku

APPENDIX 3: DATA COLLECTION SHEET

AGE/SEX……DOB……. School going child: Yes/No Grade:……

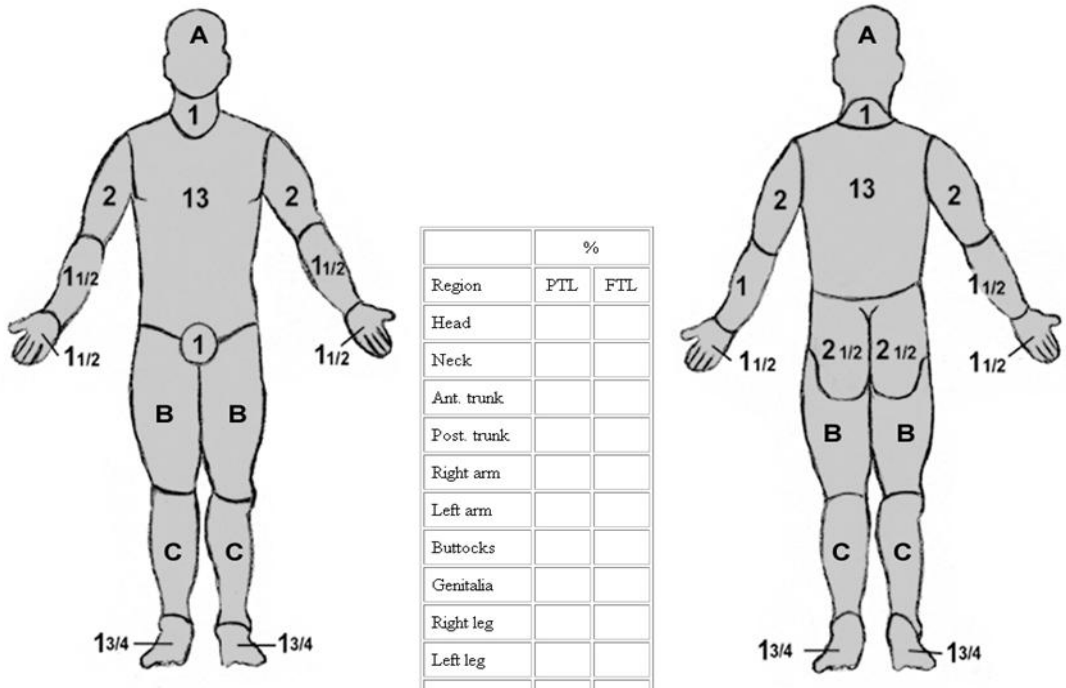
File # …….. Firm…… Date…… Time……

Time from burns to hospital…… Allocation number……

Honey ☐ Silver Sulfadiazine ☐

% Total body surface area burn

Be clear and accurate, and do not include erythema.



	%	
Region	PTL	FTL
Head		
Neck		
Ant. trunk		
Post. trunk		
Right arm		
Left arm		
Buttocks		
Genitalia		
Right leg		
Left leg		
Total burn		

AREA	Age 0	1	5	10	15	Adult
A = 1/2 of head	9 1/2	8 1/2	6 1/2	5 1/2	4 1/2	3 1/2
B = 1/2 of one thigh	2 3/4	3 1/4	4	4 1/2	4 1/2	4 3/4
C = 1/2 of one Lower leg	2 1/2	2 1/2	2 3/4	3	3 1/4	3 1/2

Partial Thickness ☐ Burn Agent …….

Admission Day

Lab Number…….

Microscopy result: Positive ☐ Negative ☐ Culture results…….

Sensitivity……..

Size of wound in cm^2 …….

Day 3 post Admission

Ward admitted to…… Lab number……

Microscopy result: Positive ☐ Negative ☐ Culture results……

Sensitivity……

Day 7 post admission

Status of patient: Admitted/Discharged

Ward/clinic reviewed:…….

Lab number……

Microscopy result of swabs: Positive ☐ Negative ☐ Culture results…….

Sensitivity……..

Wound size in cm^2…….. Percentage healed……

Description of the wound: Healed ☐ Not Healed ☐

Day 10 post Admission

Status of patient: Admitted ☐ Discharged ☐

Ward/clinic reviewed……

Lab number……..

Microscopy results: Positive ☐ Negative ☐ Culture results……

Sensitivity…….

Wound size in cm^2…….. Percentage healed…….

Description of wounds: Healed ☐ Not healed ☐

Day 14 post admission

Status of patient: Admitted ☐ Discharged ☐

Ward/ Clinic reviewed……..

Wound Size in cm^2……Percentage Healed ……

Description of wounds: Healed ☐ Not Healed ☐

Day 21 post admission

Status of patient: Admitted ☐ Discharged ☐

Ward/Clinic reviewed ……..

Wound size in cm^2……..Percentage Healed……

Description of wounds: Healed ☐ Not Healed ☐

APPENDIX 4: PATIENT INFORMATION SHEET

A COMPARATIVE STUDY ON EFFECTS OF HONEY AND SILVER SULFADIAZINE ON BURN WOUND OUTCOMES IN PEDIATRIC PATIENTS AT UNIVERSITY TEACHING HOSPITAL, ZAMBIA

Introduction

I, Emmanuel Liche, Master of Medicine (M.Med) in General Surgery student in the School of Medicine at The University of Zambia, hereby request your child's participation in the above mentioned research study. This study is part of the requirement for me to become a doctor who does operations. I kindly request you to carefully read this document and ask me anything you do not understand. I would like you to understand the purpose of the study and what is expected of you. Kindly remember that participation in this study is absolutely voluntary. If you agree to take part in this study, you will be asked to sign consent form in the presence of a witness.

Aim of the study

The purpose of the study is to compare effects of honey and Silver Sulfadiazine on outcomes in burn wounds

Procedure of the study

If you agree to participate in this study, information will be obtained from you and entered into the burns chart. The patient (your child) will be examined to ascertain the site of the burns, depth and percentage of the burnt surface area. A swab (a cotton wool mounted on a stick for collecting specimens from wounds) specimen will be collected from the burns on your first presentation to hospital. A follow-up swab specimen will be collected again from the burns on day 3, 7 and 10 of your admission or clinic visit. Moreover, the size of the wound will initially be assessed and subsequent assessments will be done on day 7, 14 and 21 from the day of initial presentation to assess healing. There will be two research assistants who will be trained on collection of swabs and measurement of wound size using a graduated 1 cm^2 paper .Once admitted, the patient's guardian will pick a number corresponding to the type of intervention (honey Vs silver sulphadiazine) and dressings will be changed once a day. If infection sets in, both groups will benefit from systemic antibiotics.

Possible risks and discomfort

Participation in this study will not expose your child to any risk as the honey used is sterile. However minor reaction might be seen and further during collection of the swab, your child might experience slight pain as the swab is being taken from the burn wound itself. Kindly note that as routine management of all burns patients, adequate medication to relieve pain will be given to your child.

Benefits

There are no monetary benefits attached to your child's participation in this study. However your child will benefit from frequent reviews whilst in the hospital and you will be reminded for follow up reviews in the clinic. Moreover your participation will be of help to the institution to manage burn wounds better

Confidentiality

All the information collected is strictly confidential. Data that will be collected, analysed and reported on will not include your name and therefore cannot be traced to you and the data collected is strictly for the purposes of academia and clinical benefit

Refusal and Withdrawal

You are free to refuse participation in this study as it is your right and it has no negative impact on the quality of health care your child will receive. Even upon giving consent you are still at liberty to withdraw your child from the study.

Consent

Your Child's participation is absolutely voluntary. Thus you are free to withdraw the child from the study at any time for any reason without any consequence to your child. If you agree for your child to participate in the study, you will be required to sign a consent form in the presence of a witness. A copy of this information sheet will be given to you.

I am grateful to you for considering participation in this study. For any concerns and clarifications, please contact Dr. Liche Emmanuel or The University of Zambia Biomedical Research Ethics Committee on the following respective addresses:

Dr. Liche Emmanuel

University Teaching Hospital,
Private Bag 1X RW,
Lusaka.
Phone +260977531328, email: emmanuelliche@gmail.com

OR

The University of Zambia Biomedical Research Ethics Committee (UNZABREC),
School of Medicine,
Ridgeway Campus,
Nationalist Road,
Lusaka.
Phone: 260-1-256067, email: unzarec@zmtel.zm

PEPALA LA CHIDZIWITSO KWA ODWALA OTENGAKO MBALI KUPHUNZIRO

PHUNZIRO LOYANGANA PAKASEBENZEDWE KA MANKHWALA A UCHI NDI *SILVER SULFADIAZINE* PA ZILONDA ZAKUPSA NDI MOTO PAKATI PA ANA PA CHIPATALA CHOPHUNZITSILA ZAUMOYO MUMUZINDA WA LUSAKA MUZIKO LA ZAMBIA.

Malonje

Ine dzina langa ndi Emmanuel Liche mwana wasukulu wophunzira zaukaswili ochita maopaleshoni pa sukulu lapamwamba la UNZA. Ndifuna Kukupemphani kutengango mbali pa phunziro lomwe mutu wache ndanena kale. Phunziro limeli lizandithandiza kuti ndifike kumapeto a maphunziro anga. Mupemphedwa kuti mudekhe mutima ndi kuwelenga pepala ili ndipo ngati simvetsesa mungathe kundifunsa. Mumvetsese lingo la phunziroli ndi zimene mupemphedwa kuchita. Ngati muvomeleza kutengako mbali mungathe kuika chizindikilo chanu papepala lachibvomelezo ndipo munthu wochita umboni naye achite chimozimozi.

Cholinga cha Phunziro

Cholinga cha phunziroli ndi kusiyanisa kagwilidwe kanchito ka mankhwala a uchi ndi Silver sulfadiazine pochilitsa zilonda zakupsa ndi moto mu gulu la ana a zaka kuchoka kubadwa kufika khumi limodzi ndi chiwiri.

Ndondomeko ya Phunziro

Ngati ndinu wokonzeka kutengako mbali kuphunziroli, muzafunsidwa mafunso okhuza zochitika kuti mwana wanu apse ndi moto. Mwana wanu azapimidwa ndipo tizatsimikiza ukulu wa zilonda pogwilitsa nchito chipepa cholembedwa ndi *Lund* ndi *Browder*. Pachilondapo tizapitsapo katonje kamene kazapelekedwa kuzasainsi kuti apime ngati pali zilombo. Tizachita zimezi patsiku loyamba, lachitatu, lachisanu ndi chiwiri ndiponso lachikhumi.Tizapima ukulu wa zilonda patsiku loyamba, lachisanu ndichiwiri, lachikhumi chimodzi ndi chinayi ndiponso lamakumi awiri ndi chimozi. Mutafika kuchipatala poyamba muzafunsidwa kutenga pepala lomwe muzauzidwa mutundu wamamnkhwala pakati pauchi ndi Silver sulfadiazine omwe mwana wanu

azapatsidwa. Ngati zilonda z mwana wanu zapezeka ndi tulombo ngakhale ali pa mankhwalawo, azapatsidwa mankhwala ena omwe atha kupaya tulomboto.

Chiopsezo

Mwana wanu sazakhala ndi chiopsezo potengako mbali kuphunziro popeza mankhwala amene azapatsidwa ndi opimidwa bwino ndipo alibe bvuto lili lonse. Mwana wanu angathe kumvera kuwawa pamene tipititsa katonje pachilonda. Mufunika kudziwa kuti chisamalilo cha zilonda zamoto, odwala onse apasidwa mankhwala olekesa kuwawa. Kotero mwana wanu nayenso azapatsidwa mankhwala ameneyo.

Chinsinsi

Zonse zomwe tikambitsana ndi kuchita mu phunziroli zizasungidwa chinsinsi pakati pa inu ndi ife. Zonse zotuluta muphunziro ili ndizotithandiza kusamala ana bwino omwe akabwele kuchipatala.

Kuchokako ku mbali ya phunziro

Ngakhale mutabvomela kutengako mbali kuphunziroli, mungathe kuchoka popanda zifukwa zili zonse. Muli ndi ufulu wakukana kutengako mbali. Chikakamizo kulibe.

Phindu Lotengako Mbali

Mukatengako mbali kuphunziro, kulibe malipiro a khobili. Koma mwana wanu azasamalidwa bwino ndipo mankhwala onse muzapatsidwa mwaulele. Kutengako mbali kwanu nkotithandiza ife achipatala kupeza njila yabwino yotandizila odwala ndi zilonda za moto.

Chibvomelezo

Kuvomeleza kuti mwana wanu atengeko mbali ku phunziro ndi ufulu wanu; mungathe kuvomeleza kapena kukana. Ndipo ngakhale mutabvomereza kale, ngati zamukati zace za phunziro ndizododometsa mungathe kusiya kutengako mbali popanda kuopsedwa.

Ndine wokondwa ndiponso wothokoza kuti mwavomeleza kutengako mbali. Ngati muli ndi mafunso ali onse mungathe kundifika ine kapena akulu a gulu loona kuti phunziroli lili kuchitika potsata malamulo

Emmanuel Liche	OR	University of Zambia Biomedical
Department of Surgery		Research and Ethics Committee
University Teaching Hospital		Nationalist Road
P/B RW1X		School of Medicine
Lusaka.		Ridgeway Campus
Lamya: 0977531328		Lamya: 260-1-256067
Email: emmanuelliche@gmail.com		Email: unzarec@zamtel.zm