

# Effects of Silver sulfadiazine and Actilite® Honey on Bacteria Wound Colonisation and Wound Healing in Children with Partial Superficial Burn Wounds at University Teaching Hospital, Lusaka, Zambia.

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## ABSTRACT

**Background:** 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 Hospital (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 Actilite® honey and Silver sulfadiazine on bacteria wound colonisation and wound healing in paediatric partial superficial burn wounds of £20 per cent total body surface area.

**Methods:** 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. Simple randomisation was used to allocate patients to either honey or SSD group. Patients' clinical characteristics 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.

**Results:** Of the 64 patients, 32 were allocated to each group. 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 association between the two treatment methods and bacterial wound colonisation (80% in honey group and 83% in SSD group;  $p = 0.74$ ) using Chi-squared test. However, by day 10 on treatment, there was significant reduction in bacterial wound colonisation (Honey Vs SSD;  $P = 0.026$ ). Using Student T-test it was found that wounds treated with Actilite® honey healed quicker than those treated with SSD (Mean  $11 \pm 4$ ,  $15 \pm 6$ ,  $P = 0.0049$ ).

**Conclusion:** The study showed that treatment of children under 12 years with partial superficial burn wounds of £20 per cent TBSA using Actilite® honey significantly reduced levels of bacteria wound colonisation by day 10. Furthermore, wounds in the Actilite® honey group healed quicker than SSD group. Therefore, use of Actilite Honey on burn wounds could be explored as alternative to SSD in managing paediatric partial superficial burn wounds of 20% and below at UTH.

**Key words:** *Partial superficial burn wounds, bacteria wound colonisation, wound healing, Actilite® honey, Silver sulfadiazine, University Teaching Hospital.*

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## INTRODUCTION

Burn wounds which account for over 300,000 deaths globally are generally of public health concern. In Africa, between 17,000 to 30,000 children less than 5 years old die each year from burn wounds<sup>1</sup>. In Zambia, burn wounds account for 6% of all yearly surgical admissions yet are the commonest cause of surgical mortalities<sup>2,3</sup>. Whereas overall mortality in surgical wards is less than 5%, burn wounds contribute about 15-30% towards mortality<sup>2,3</sup>. True to the global picture, burn wounds at UTH are chiefly a paediatric condition. In studies at UTH, it was found that most patients who sustained burn wounds were children less than 12 years and they presented commonly with burn wounds of £ 20 percent. And those who succumbed showed similar pattern in terms of age and percentage of wounds<sup>3</sup>.

Management of burn wounds poses a challenge as it can be complicated by overwhelming wound colonisation and infection, more so in low- middle income countries (LMICs) like Zambia. Several studies have demonstrated that wound colonisation and infection prolongs wound healing.<sup>3-8</sup> Hospital environment might be a niche for wound infection. Whereas use of prophylactic antibiotics in prevention of wound infection in surgery is a success, such use in burn wounds is rendered ineffective due to biofilm formation.<sup>5,9</sup>

For centuries, burn wounds have been managed by a constellation of methods. Conventionally, use of silver sulfadiazine topically has been well documented. However, controversies have currently arisen pertaining to efficacy of silver sulfadiazine in preventing and controlling infection. Some studies have actually reported an increase in wound infection whilst on silver sulfadiazine.<sup>10-13</sup>

Use of honey, despite being ancient, has not been popularised in Africa. There is paucity of data on use of honey on an African population. Studies done in Asia, Europe and America on use of honey have shown benefits not only in prevention and control of infection but also in promoting wound reepithelialisation.<sup>14-17</sup> The purpose of this study was to demonstrate the occurrence of bacteria wound colonisation and rate of wound healing in partial superficial burn wounds being treated with silver sulfadiazine and Actilite® honey.

## METHODS

This open label randomised controlled study was conducted from August 2017 to February, 2018 at University Teaching Hospital, Lusaka, Zambia.

Previous data in paediatric burn patients demonstrated reepithelialisation within 15 days (Sd=4) and minimally clinically important difference (d) is 3 days.<sup>18</sup> The power of the study was at 80%, with type 1 error at 0.05, 95% significance and 0.20 as type 2 error. Sample size was calculated as 58 and accounting for 10% loss to follow up, the total sample size was 64.

Children below 12 years were eligible if they sustained 20% or less partial superficial burn wounds and presented to the hospital within 24hrs from injury. Patients with inhalation burns were excluded from the study.

Patients were allocated to either group by simple randomisation. Numbers from 1 to 100 were placed in a box and the guardians to the patients were asked to draw a number. If an even number was drawn, the child was treated with Actilite® honey and odd numbered patients were treated with silver sulfadiazine.

At enrolment into the study, clinical details were entered in a data collection sheet. Burnt surface area was estimated using the Lund and Browder chart. The burnt surface area was further evaluated using 1 cm<sup>2</sup> transparent graph till the wound reached 95% reepithelialisation. Wounds were cleaned daily with soap and water and dressed with either Flazine® (silver sulfadiazine from Shalina Pharmaceuticals, Zambia) or Actilite® (Advancis Medicals, UK) honey and dressed secondarily with crepe bandages. Pethidine was given intramuscularly to ease the pain when changing dressings.

Swabs were collected from the burn wounds on admission day, third, seventh and tenth day after admission for microscopy and culture. In both groups prophylactic antibiotics were not given. However, in the presence of systemic infection, antibiotics were prescribed based on the sensitivity pattern. Wound assessment was done on day 7, 14, 21, 28 using 1cm<sup>2</sup> and percentage of reepithelialisation was calculated. Full reepithelialisation was defined at 95%.

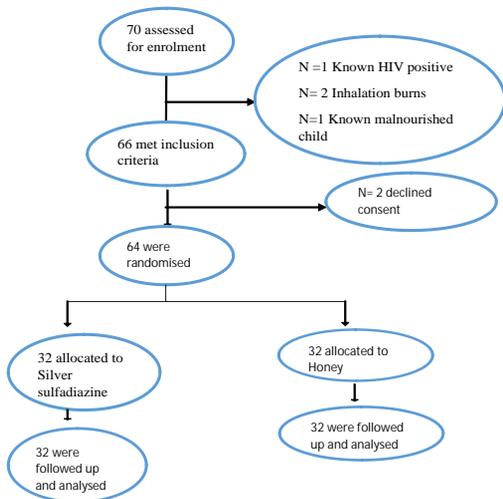
The outcomes were number of days taken for the wound to fully reepithelialise and degree of wound infection on day 0, 3, 7 and 10.

Statistical analyses were performed independent of the two pharmaceutical companies that provided silver sulfadiazine and honey for the study. Data was entered in Microsoft Excel and analysed using SPSS 22.0 software (IBM inc., USA). Demographic characteristics were summarised using tables. The clinical outcomes at specific moments were compared using t-test for continuous variables with normal distribution. For categorical variables, association was detected using chi-squared test.

The research was initiated and carried out in Zambia in conformity with the ethical principles from the 1975 Declaration of Helsinki. The University of Zambia Biomedical Research Ethics Committee (Ref: 012-3-17) approved the study.

**RESULTS**

In total, 64 patients were enrolled over a seven month period, i.e. from 8<sup>th</sup> July, 2017 to 10<sup>th</sup> February, 2018. Thirty two patients were allocated to each group. They were closely followed up closely. There were three patients who died before full reepithelialisation in each group and were excluded in analysing wound healing. The details in flow of patients are as shown in Figure 1.



**Figure 1: Flow diagram of study participants**

Key patient and wound characteristics are as elucidated in Table 1.

**Table 1: Key patient characteristics**

VARIABLE		TOTAL (n=64)	Honey (n=32)	SSD (n=32)
SEX	Male	34	18	16
	Female	30	14	16
AGE(Yrs)	< 1	6	3	3
	1-2	30	17	13
	3-4	20	8	12
	5-6	5	2	3
	7-12	3	2	1
TBSA(%)	1-5	6	2	4
	6-10	26	15	11
	11-15	20	10	10
	16-20	12	5	7
BURN AGENT	Hot water	52	26	26
	Hot porridge	7	5	2
	Open fire	4	1	3
	Cooking oil	1	0	1
TIME TO HOSPITAL(hrs)	< 1	1	1	0
	1-2	33	16	17
	3-4	22	11	11
	>5	8	4	4

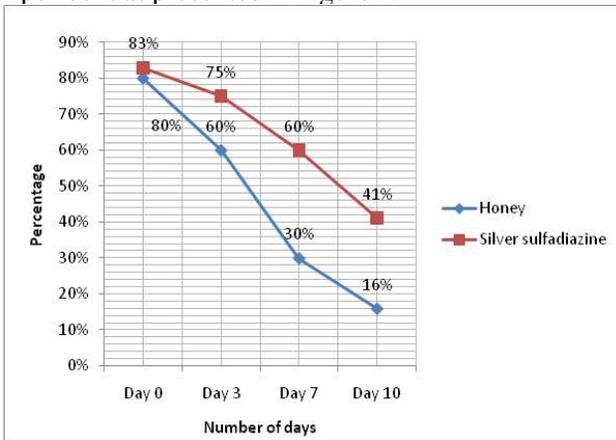
There were 54% male and 46% female patients in the honey group. There was equal sex distribution in the silver sulfadiazine group. Moreover, the modal age distribution in both groups was 1-2 years. Most patients had burns of 6-10% TBSA. The commonest causative agent was hot water (80% in both groups). It was also found that 53% and 50% of the patients in honey and silver sulfadiazine groups reached the hospital within 1-2 hours respectively. The groups were homogeneous with regard to baseline characteristics and thus suitable for comparison in main outcomes.

Two main outcomes assessed were wound colonisation over a ten day period and time taken for the wound to reach full reepithelialisation. On admission, 80% of the wounds in the honey group were positive for bacteria wound colonisation compared to 83% of wounds in the silver sulfadiazine group. There was no association between wound colonisation and treatment groups on admission as seen in table 2.

**Table 2: Statistical analysis of bacteria wound colonisation on admission**

Group	Positive	Negative	X <sup>2</sup>	P value
Silver sulfadiazine	27	5	0.11	0.74*
Honey	26	6		

The detailed evolution of results over a ten day period is as presented in Figure 2.



**Figure 2: Bacteria wound colonisation in both groups over 10 days**

By day ten, 16% of wounds in the honey group were positive for bacteria wound colonisation compared to 41% of the wounds in the silver sulfadiazine group. When subjected to chi square test to assess the association between treatment groups and the results, honey showed superiority ( $X^2 = 4.95$ ,  $P=0.026$ ) at 95% confidence level as shown in Table 3.

**Table 3: Statistical analysis of bacterial wound colonisation on day 10**

Group	Positive	Negative	X <sup>2</sup>	P- value
Honey	5	27	4.95	0.026*
Silver sulphadiazine	13	19		

\*Chi-squared test

The mean duration for wounds to attain full reepithelialisation was  $11\pm4$  in the honey group compared to  $15\pm6$  days in the silver sulfadiazine

group. When data was subjected to student t test, honey showed superiority over silver sulfadiazine ( $P=0.0049$ ) at 95% confidence level as shown in Table 4.

**Table 4: Statistical analysis of average days to reach full reepithelialisation**

Group	Number of observations	Mean (days)	Standard Deviation	CI	P- Value
Honey	29	11.41	3.95	$11\pm1$	0.0049*
Silver sulfadiazine	29	15.24	5.92	$15\pm2$	

\*Student T-test

## DISCUSSION

This randomised controlled trial conducted on partial superficial burn wounds in children less than 12 years is the first of its kind amongst the black African population. Most studies around Africa on honey dressing are laboratory experiments and not trials on human beings let alone comparisons with other conventional topical dressings.<sup>19-20</sup>

The study revealed the superiority of honey dressing in comparison to silver sulfadiazine in reducing bacteria wound colonisation by day 10. The difference was statistically significant at 95% confidence interval. Such a difference favouring honey in reducing bacterial colonisation and promoting wound sterility have been reported in other parts of the globe.<sup>22-25</sup>

Reduction of wound colonisation by honey is not only of statistical significance but is also of clinical and economic importance. Wound colonisation and subsequent infection prolong duration and quality of wound healing. Moreover, infection might convert a partial superficial burn wound to partial deep or even full thickness thereby altering the prognosis.

Wound colonisation and infection complicates burn wound management. Previous studies have demonstrated higher yields of antimicrobial resistant bacteria from burn wounds.<sup>7, 9, 26, 27</sup> Thus honey inhibit bacterial growth and its antimicrobial attributes include low pH, 1% hydrogen peroxide, up regulation of neutrophils through nuclear

transcription factor and a low water activity than what is required for bacterial growth.<sup>14, 28, 29</sup>

The ultimate goal of wound care is wound healing. Again wounds treated with honey reached full reepithelialisation faster than those treated with silver sulfadiazine. This significant difference is again in tandem with what studies across the globe have promulgated.<sup>9, 11, 30</sup>

Wound healing is a complex cascade of events which chiefly involve inflammation, reepithelialisation and remodelling. Honey has been shown to control prolonged inflammation through inhibition of cyclooxygenase 1 and 2. The major amino acid in honey is Proline, a molecule core in synthesis of collagen which is important in wound healing. Low pH coupled with 1% hydrogen peroxide stimulates fibroblasts formation resulting in accelerated epithelial cell migration.<sup>6, 31-33</sup>

## CONCLUSION

This study has elucidated that treatment of partial superficial burn wounds of £20 percent TBSA with Actilite® honey significantly reduced the level of bacteria colonisation on burn wounds by day 10 in children less than 12 years. It was also clear that wounds treated with honey healed quicker compared to wounds treated with SSD.

## LIMITATIONS

The patients were admitted in general wards where cross contamination was not uncommon and could attribute to high bacteria wound colonisation. Moreover, SSD was in paste form and Actilite® honey came as a dressing hence the open label study.

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