COMPARISON OF EFFICACY OF HONEY VERSUS SILVER SULFADIAZINE AND ACETATE MAFENID IN THE TREATMENT OF CONTAMINATED BURN WOUNDS IN PIGGIES

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ABSTRACT

Introduction: Heat injury, with creation of conclusive necrosis in skin layers, prepares an environment suitable for bacterial infection as a result of low tissue perfusion and high protein content. Gram negative bacteries especially Pseudomonas Auroginosa have been recognized as the main creative organisms of wound infection mortality. Mankind has been interested in remedial role of honey since long.

Materials and Methods: Sixty Indian piggies were categorized in three equal groups. A part of their body, approximately 8.5cm^2, was burned with water steam (3 degree of burn). Then, a number of 10^8 microorganisms of Pseudomonas Auroginosa were inoculated in the wound area. Each group was treated with group-specialized drug for a period of one month. (Honey- silver sulfadiazine 1%-acetat mafenid 8.5%). In special days, according to determined schedule, animals' weight, as well as burn condition and extent were recorded and quantitative and qualitative cultural specimens were prepared periodically. The results were analyzed by statistical software of SPSS10.

Results: Out of three groups, the group of honey had the mortality at least equal with two other groups(30% with comparison of 40% and 45%), the most formation of granulation tissue in a time of 10 days (90% with comparison of 35% and 44%), the smallest remaining wound at the end of study(percent of dwindle in size 62% in honey group with comparison of 29% and 22%) and the least of contamination in prepared specimens(20% in 10th day of burn with comparison of 95% and 100%).

Conclusion: Utilization of topical honey in treatment of deep and infectious burn in piggies not only accelerates the healing procedure but has antimicrobial effect at least equal to valuable acetate mafenid drug.

KEY WORDS: Conclusive necrosis, inoculation, granulation tissue, contamination.

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INTRODUCTION

Superficial burns comprise a spectrum of injury severity depending on the depth of the wound and the proportion of the body affected. A burn may be superficial, involving just the epidermal layer of the skin. Partial thickness burns involve damage to more structures within the skin, and full thickness burn involves all layers of the skin and may involve structures beneath.[1]

Heat injury, with creation of conclusive necrosis in the skin layers, prepares an environment that is a suitable for bacterial infection as

a result of low tissue perfusion and high protein content. Wound infection, in addition to changing low degree burn into complete thickness necrosis, facilitates the microbe penetration into vital tissues and infection spreading as a result of skin barrier injury. So infection is the most important effective topical factor in healing procedure and causes prolongation of treatment period[2].

Since late 1950s, gram negative bacteries especially Pseudomonas Auroginosa have been recognized as the main creative organisms of wound infection mortality.

Although, antimicrobial drugs have had significant effects in reducing wound infection, but infection of massive burns is still one of the most important causes of mortality. The permanence rate of generalized burn wound infections is lower than 10% hence to heal burn wounds as quickly as possible and adequate control of dermal infections are most important treatment issues in these patients.

Currently three topical antimicrobial drugs are available (silver sulfadiazine, silver nitrite, and acetate mafenid).Before bacterial massive assembling, administration of each of these drugs, will have equal effects[3]. The usage of honey in medicine is referred to in the most ancient records. Honey was prescribed by the physicians of many ancient races of people for a wide variety of ailments. The ancient Egyptians, Assyrians, Chinese, Greeks and Romans all used honey, in combination with other herbs and on its own, to treat wounds and diseases of the gut.[4] Egyptian papyruses related to 3500 years ago, have mentioned remedial properties of honey. Such ancient documents have been found not only among old time Egyptians but by the side of Hebrews related to 3000 years ago, Greeks related to 2000 years ago, ancient Chinese civilizations and Hindus[4]. In the books of Aristotle, Hippocrates, Avicenna and other wise men of that time have mentioned the role of honey. In Avicenna medical book Kanoun, there are some examples based on honey and wax bee. Avicenna believed that honey prepared poultice is very helpful in healing of infectious wounds.[5] The Muslim Prophet Muhammad (PBUH) recommended the use of honey for the treatment of diarrhea. Creator God in chapter Nahl, miracle 68, 69 says: "and God voiced to honey bee to lodge in mountains and elevated trees and roofs and then to nourish from sweet fruits and sweet-smelling flowers' nectars and to obey from God way. Afterwards a sweet, variously-colored sherbet comes out of them that cure of human is in it. Sign of God's power for reflectives is obvious in this work, too".[6]

The use of honey as a medicine has continued into present-day folk-medicine. Currently there are some lectures based on cural role of honey in healing of wounds such as burn wounds in reputed medical journals. In two separate studies, beneficial effect of honey in superficial and non-infectious burns has been better than placental membranes and pomade silver sulfadiazine and honey has been introduced as ideal cover of burn wounds.[7-10] In India lotus honey is said to be a panacea for eye disease.[11] The ancient usage of honey for coughs and sore throats has also continued into the traditional medicine of modern times.[12] Other examples of current day usage of honey in folk medicine are: as a traditional therapy for infected leg ulcers in Ghana;[13] as a traditional therapy for earache in Nigeria;[14] as a traditional therapy in Mali for the topical treatment of the measles, and in the eyes in measles to prevent corneal scarring.[15] Honey also has a traditional folklore usage for the treatment of gastric ulcers.[16]

However, there is a tendency for some practitioners to dismiss any suggestion that treatment with honey is worthy of consideration as a remedy in modern medicine. An editorial in Archives of Internal Medicine assigned honey to the category of "worthless but harmless substances".[17]

For understanding the effect of honey on deep burn wounds, this study was performed on animal groups and its beneficial effects in wound healing with disinfectant properties was compared with silver sulfadiazine and acetate mafenid, with a view to disinfectant wound healing power.

MATERIALS AND METHODS

Sixty Indian piggies were categorized into 3 groups randomly. Each group had containing 20 piggies. Then these groups were recognized as honey, acetate mafenid 8.5% and silver sulfadiazine 1% based on lottery. In the beginning, animals were weighed and skin of right groin was shaved, then animals were anaesthetized with ketamin and the area was sterilized by betadin solution and alchohl and some performed special lidded boxes were fixed in the place with nylon string number 0. After renewed washing of place with physiologic serum, this limited area with width 8.5 cm^2 was exposed to boiling water steam within a period of 10 seconds. 10^8 microbes of Pseudomonas Aeuroginosa were inoculated in the wounds after the area getting cold. These microorganisms were isolated from one of patients of burn department of Khatamolanbiae Hospital of Zahedan. 4-6 hours after inoculation, wounds were dressed by special determined drugs. The honey used in this study was prepared from beehives in pastures of Taftan Mountain in Sistan-Balochistan state and no additional procedures were performed. All wounds were dressed daily and weight of animals, burns condition and extent were recorded according to determined schedule and quantitative and qualitative cultural specimens were prepared from piggies' wounds. Daily wound dressing was continued for 30 days after renewed weighting of animals, residual wound extent was measured at the end to the period. The results were analyzed with the usage of NPar tests and chi-square tests and frequency table. (SPSS 10)

RESULTS

Average weight of animals in three groups of honey – Mafenid – Silver sulfadiazine before beginning of study was 640,638 and 628gr that after 30 days of burning, it decreased to 491,482 and 505gr. (on the average 22% decrease in weight in 3 groups). There wasn't any significant differences between honey group and two other groups in this aspect. (p-value =0.658)

Table-I: Amount of average weight changes in mentioned groups

Weight changes / *Drug*	*Average weight before burn*	*Average weight at 30th day after burn*	*Weight loss %*
Acetatmafenid	638	482	25
Silver sulfadiazine	628	505	19
Honey	640	491	23

Within treatment period (30 days) 23 piggies died (total mortality was equal 38%) except 2 cases in silver sulfadiazine group, there wasn't any mortality within first two days after burn. Fewer deaths were related to honey group, although it was not statistically different. (p-value=0.610)

Table-II: Amount and distribution of mortality in mentioned groups

Day / *Drug*	*0-5*	*6-10*	*11-15*	*16-20*	*21-25*	*26-30*	*Total*	*Mortality(%)*
Silver sulfadiazine	2	0	1	1	1	3	8	40
Mafenidacetat	0	0	2	2	2	3	9	45
Honey	0	0	0	2	1	3	6	30

Wounds condition on 10th day after burn was assessed clinically in all groups for facilitation of classification of wounds according to amount of granulation tissue, two groups as G1 and G2 were defined, conventional. Group G1 consists of the wounds with good granulation tissue that covers major part of the graft and group G2 consists of the wounds that granulation tissue doesn't cover major part and the bed isn't prepared for graft (table-III). There was a significant difference between honey group and two other groups in this aspect. (p-value =0.003)

At the time of assessment, two of piggies of silver sulfadiazine had died, so percents of this group (Silversulfadizin) have been calculated on the basis of remaining eighteen.

After daily wound dressing for 30 days, wounds were measured and its ratio to first day of burn was evaluated. Surface of residual wounds was covered by granulation tissue in

Table-III: Granulation tissue condition in 10th day after burn

Drug	*G1*	*G2*	*%*
Silver sulfadiazine	0	8	44
Mafenidacetat	0	7	35
Honey	10	8	90

Table-IV: Average size of wound and reduction on 30thDay

Wound condition	*Acetatmafenid*	*Silver sulfadiazine*	*Honey*
Average size	6/59cm2	6cm2	3cm2
Dwindle in size	22%	29%	62%

all groups but honey group wound extents were obviously smaller than other groups. Average size of wound after 30 day was 6.59cm in Mafenid group, 6cm in Silver group and 3cm in honey group (table-IV). There was a significant differences between honey group and two other groups in this aspect. (p-value =0.000)

At the end of 30th day of wound dressing, there was hair loss in 10 cases of the 12 alive piggies of Silversulfadizin group (83%) and it was sever in 4 cases (33%). There was no evidence of hair loss in other groups.

Microbial cultural specimens were prepared from wounds of piggies in three groups periodically qualitative culture (sampling from wound surface by swap) was performed. The purpose of these tests was determination of existence of wound surface contamination as negative results of these tests are valuable.

Quantitative microbial cultures were performed atleast two times. Tissue specimens were prepared from wound area by scalpel. Number of existing organisms in each gram of tissue was distinguished by this test. If presence of microbes in tissue was more than 10^5 microorganism/gram, it may be due to wound infection.

Quantitative cultures were prepared at 6th day from acetatemafenid and silver sulfadiazine groups, too. In 45% of acetatemafenid group cultures and 100% of silver sulfadiazine ones there was more than 10^5 microbe/gram.

Table-V: Percent of positing microbial cultures of groups according to days after burn

Kind of culture	*Qualitative*		*Quantitative*	
Day of culture perform / *Drug*	*4*	*10*	*14*	*17*
Honey	100%	20%	5%	5%
Mafenidacetat	100%	95%	12%	12%
Silver sulfadiazine	100%	100%	90%	50%

Unfortunately, 6th day culture wasn't performed for honey group because the cultural environments weren't prepared. So these cultures were performed on 9th day and in 10% of cases they were positive. As shown in table-V, conditions of honey group wounds was better than other groups except at 4th day of burn and all qualitative cultures have been positive. Whereas 80% of honey group wound had been sterilized in 10 days this percent was 5% for Malefic- acetate group and 0% for silver group. (p-value = 0.000)

DISCUSSION

The purpose of this study was to highlight the beneficial effects of honey in deep and infectious burn wounds. Although benefical use of honey has been known to mankind since long, its role in treatment of burns is also discussed. In most of these studies superficial and non-infectious wound, were considered. However majority of our patients were suffering from deep burns wherein resistance to antibiotics is very common. Whether this antimicrobial properties of honey is compatible with silver sulfadiazine and acetate mafenid, and if honey is able to accelerate wound healing in such infectious environment was not known.

This study indicates that there were not major differences between three groups as regards mortality and weight loss. It further indicates that honey has beneficial effect on mortality and weight loss of piggies at least com-

parable two other antibiotics. It has been pointed out in another study that statistically there would have been no reliable difference in the mortality rates when honey is used as the wound dressing.[18] In honey group, the granulation tissue formation is better than others at 10th day after burn and it's possible to leave graft in 50% of wounds in this group, whereas in other groups it was not possible. In one experimental study[19], comparisons were made between honey and silver sulfadiazine, and between honey and sugar, on standard deep dermal burns, 7*7cm, made on Yorkshire pigs. Epithelialisation was achieved within 21 days with honey and sugar whereas it took 28-35 days with silver sulfadiazine. Granulation was clearly seen to be suppressed initially by treatment with silver sulfadiazine. In all honey-treated wounds the histological appearance of biopsy samples showed less inflammation than in those treated with sugar and silver sulfadiazine, and a weak or diminished actin staining in myofibroblasts suggesting a more advanced stage of healing. Histological and clinical studies of wound healing have been made on comparable fresh partial thickness burns with honey dressing or silver sulfadiazine (SSD) in two groups of 25 randomly allocated patients. Of the wounds treated with honey 84 percent showed satisfactory epithelialization by the 7th day, and in 100 percent of the patients by the 21st day. In wounds treated with silver sulfadiazine, epithelialization occurred by the 7th day in 72 percent of the patients and in 84 percent of patients by 21 days. Histological evidence of reparative activity was seen in 80 percent of wounds treated with the honey dressing by the 7th day with minimal inflammation. Fifty two percent of the silver sulfadiazine treated wounds showed reparative activity with inflammatory changes by the 7th day. Reparative activity reached 100 percent by 21 days with the honey dressing and 84 percent with SSD.[20] Condition of all honey group cultures was better than other groups, especially there is significant difference between honey and acetatmafenid groups with silver sulfadiazine group. In another study 104 cases of superficial burn injury were studied to assess the efficiency of honey as a dressing in comparison with silver sulfadiazine gauze dressing. In 52 patients treated with honey, 91 percent of wounds were rendered sterile within 7 days. In the 52 patients treated with silver sulfadiazine, 7 percent showed control of infection within 7 days.[21] In other study, a total of 15 bacterial strains (7 Pseudomonas & 8 Klebsiella species) isolated from various samples which showed multi-drug resistance were studied to verify in vitro antibacterial action of honey on the principle of Minimum Inhibitory Concentration (MIC) & its synergism with 3 common antibiotic—Gentamicin, Amikacin & Ceftazidime. The MIC of honey with saline for both organisms was found to be 1:2.[22] In another experimental study on buffalo calves[23] full-thickness skin wounds, 2*4 cm, were made after infecting the area of each wound by subcutaneous injection of Staphylococcus aureus two days prior to wounding. Topical application of honey, ampicillin ointment, and saline as a control were compared as treatment for the wounds. Clinical examination of the wounds and histomorphological examination of biopsy samples showed that honey gave the fastest rate of healing compared with the other treatments, the least inflammatory reaction, and the most rapid fibroblastic and angioblastic activity in the wounds, the fastest laying down of fibrous connective tissue, and the fastest epithelialisation.

At the end of 30th day, wounds size in honey group was less than others. Speed of wound healing was at least two times faster than others. In another study the possible therapeutic effect of topical crude undiluted honey in the treatment of severe acute postoperative wound infection was studied. Fifty patients having postoperative wound infection following caesarean sections or total abdominal hysterectomies with gram positive or gram negative bacterial infection were allocated in two groups. Twenty-six patients (group A) were treated with 12 hourly application of crude honey and 24 patients (group B) were treated with local antiseptics: spirit (70% Ethanol) and povidine-

iodine. Both groups received systemic antibiotics according to culture and sensivity. Complete wound healing was evident after 10.73±2.5 days in group A and after 22.04±7.33 in group B ($p<0.05$). Size of postoperative scar was 3.62±1.4 mm after using topical honey and was 8.62 ±3.8mm after local antiseptics ($p<0.05$). After using honey 22/26 patients (84.4%) showed complete wound healing without wound disruption or need for re-suturing and only 4 patients showed mild dehiscence. In group B 12/24 patients(50%) showed complete wound healing and 12 patients showed wound dehiscence, six of them needed re-suturing under general anesthesia.[24]

There were seven randomized trials[7,8,10,21,25-27], six performed in India by the same researcher[7,8,10,25-27] and one[21] performed in united Arab Emirates .Two of the studies involved superficial burns[27], three partial thickness burns[7,8,26], one moderate to severe burns that included full thickness injury[25] and one infected postoperative wounds[21]. All the controls were active comparisons, though these included potato peelings[26] and amniotic membrane[7] as well as conventional treatments. The main outcomes were the effect of honey and controls on healing time and infection rate, though antibiotic use and hospital stay were also noted in some studies.[1]

CONCLUSION

This experimental study shows that use of topical honey in treatment of deep and infectious burn not only accelerates the healing procedure but has antimicrobial effect at least equal to valuable acetatmafenid drug.

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