ORIGINAL ARTICLE

A Prospective Randomized Study to Compare the Effectiveness of Honey Dressing vs. Povidone Iodine Dressing in Chronic Wound Healing

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Abstract To compare the healing of chronic wounds with honey dressing vs. Povidone iodine dressing in adult subjects with chronic wounds of ≥ 6 weeks of duration, attending wound care clinic in Surgical Out Patient Department of All India Institute of Medical Sciences, Surgical Out Patient Department of Jai Prakash Narayan Apex Trauma center, New Delhi. Forty five subjects were randomized into two groups i.e., Honey & Povidone iodine dressing group. Dressing was done on alternate day basis for 6 weeks of followup period. Main outcome measure was complete healing at 6 weeks. Wound healing status was assessed at 2 weekly intervals till 6 weeks. Seven out of 22 subjects in honey treated group achieved complete healing as compared to none out of 20 subjects in Povidone iodine treated group. There was a significant decrease in the wound surface area, pain score & increase in comfort score in Honey dressing group in comparison to the Povidone Iodine group at 0.05 level of significance. Honey dressing is highly effective in achieving healing in chronic wounds as compared to Povidone iodine dressing.

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A. B. Ji Patanjali Yogpith, Haridwar, India Keywords Honey dressing \cdot Povidone iodine dressing \cdot Chronic wound healing \cdot Occlusive dressing \cdot Randomized trial

Introduction

Honey is used as a wound dressing in traditional Indian medicine [1]. In recent times this has been rediscovered as a topical antibacterial agent for the treatment of wounds, burns, and skin ulcers [2]. It quickly reduces the inflammation, swelling, pain, and unpleasant odors. It also facilitates separation of necrotic tissue without the need for debridement [3]. The honey dressings can be removed painlessly without causing damage to regrowing tissue [4, 5].

Honey may provide nutrients needed for regenerating tissue because it contains large quantities of readily assimilable sugars, many amino acids, vitamins, and trace elements. Its high vitamin C content may prove beneficial by promoting collagen synthesis [6].

In India, most physicians and nurses use povidone iodine solution or ointment for dressing the wounds. Since there is no randomized controlled trial comparing the effect of honey with povidone iodine, we conducted this study to compare the effect of honey with povidone iodine.

Patients and Methods

Settings This study was conducted in the wound care clinic, surgical outpatient department (OPD), All India Institute of Medical Sciences (AIIMS) Wound Care Clinic, at Jai Prakash Narayan Apex Trauma Centre from June to December 2008. The ethics committee, AIIMS, approved the study. Inclusion Criteria A total of 45 subjects, age ≥ 18 years, with chronic wounds of duration ≥ 6 weeks were enrolled after informed written consent. Only clinically clean wounds without signs of acute inflammation, purulent discharge, or malodor were included. Patients presenting with infected wounds were initially treated with daily dressing—cleansing with normal saline and dressing with paraffin gauge along with surgical debridement and oral antibiotics based on bacterial wound culture report.

Pretherapy Assessment All patients were assessed by a consultant surgeon. Patients suffering from leg or foot ulcer were evaluated with color duplex scan to assess the arterial/venous insufficiency. An X-ray of the region was also carried out to rule out any underlying osteomyelitis. A wound bacterial culture swab was collected before inclusion in the study. Washout period of 1 week was given to all the subjects before randomization. During 1 week of washout period, chronic wounds were cleansed with sterile normal saline (0.9 %) and covered with sterile paraffin gauze, cotton pads, and bandages.

Exclusions Criteria Patients with postoperative wounds, burns, and skin grafts donor sites, wound size >5 cm in maximum diameter, known allergy to honey, povidone iodine, and Tegaderm.

Methods of Wound Care Computer-generated random numbers using block randomization were used to develop the randomization schedule. The subjects were randomized into two groups—the honey dressing group and the povidone iodine dressing group—with the help of numbered opaque sealed envelopes.

The honey was prepared by experienced ayurvedacharya of Patanjali Yogpeeth, Haridwar, by collecting it from a beehive on a neem tree (Azadericta indica). In the ayurvedic text, this honey is regarded as having special wound-healing property. The honey was sterilized by gamma-irradiation and was applied on 23 wounds in the experimental group. Ten percent povidone iodine solution was applied on 22 wounds. The wound surface was cleansed with normal saline followed by application of honey or povidone iodine (1–2 ml), just sufficient to fill the wound cavity. The wound was covered with a transparent sterile polyurethane semipermeable membrane sheet (Tegaderm 3M, USA) (Figs. 1 and 2). The Tegaderm sheet served as an occlusive dressing and retained the honey or povidone iodine in the wound cavity. The wound dressings were changed on alternate days for 6 weeks of follow-up period or till complete healing. Dressing in patients suffering from venous leg ulcer was reinforced by elastic compression garments. The observations of wound healing status were made at 2-week intervals at second, fourth, and sixth weeks. Wound swab for bacteriological culture was taken at each visit. The pain and overall comfort were recorded on a visual analog scale (VAS). Wound tracings were made on a transparent acetate sheet on each visit. From these tracings wound surface area (in cm²) was determined by computer image analysis with software package IMAGE-Pro plus (version 4.1). An adverse reaction form was filled in to record adverse reaction to povidone iodine or honey on each visit.

Outcome Variable The main outcome of interest was complete healing at the end of the sixth week. Secondary outcomes were reduction in wound *surface area* measured in cm², *pain* during dressing change measured on a VAS of 0–10 (0 meaning no pain and 10 indicating very severe pain), and *overall comfort* of subjects with dressing measured on the VAS of 0–10 (0 indicating no comfort and 10 indicating maximum comfort).

Statistical Analysis Friedman test and Wilcoxan rank sum (Mann–Whitney) test were used to find out the differences between the two groups. Data analysis was performed on STATA software (version 9.1). A P value of <0.05 was accepted as significant.

Results

Forty-two subjects completed the follow-up period. Two subjects developed adverse reaction to povidone iodine and were excluded from outcome analysis. One subject was lost to follow-up. Table 1 describes the baseline characteristics. Mean age was 42.27 (SD=16.24) years in the honey group and 42.95 (SD=13.58) years in the povidone iodine group. There was male preponderance in both the groups. Both the groups were comparable in terms of demographic characteristics, duration, etiology, and location of wounds. Similarly, both groups were comparable in terms of concomitant disease, previous medical and surgical therapy. The duration of existence of chronic wounds ranged from 2 to 180 months. Most cases had chronic wounds of venous etiology. Majority of the subjects in both the groups had chronic wounds located on the leg and ankle. Two groups were comparable in terms of wound surface area, pain score during dressing change, and overall comfort score of dressing at baseline (i.e., at 0 week) (P > 0.05).

Proportion of Complete Healing at 6 Weeks In the honey group, 31.82 % of the subjects achieved complete healing of chronic wounds at the sixth week. None of the subject attained complete healing with povidone iodine in 6 weeks.





Surface Area Reduction Median surface area of chronic wounds was 4.25 cm^2 at baseline (0 week) in the povidone iodine group, which reduced to 1.95 cm^2 at the sixth week. In the honey group, baseline median surface area was 4.35 cm^2 , which reduced to 0.55 cm^2 at the sixth week. This difference was significant at 0.05 levels (Tables 2 and 3).

Pain Score on Visual Analogue Scale (VAS) Median pain score at baseline was 7 on an 11-point scale of 0–10. This reduced to 1 at the sixth week in the honey dressing group. Patients in the povidone iodine group experienced a reduction in pain score from 7 at baseline to 5 at the sixth week (Table 3). Overall Comfort Score on Visual Analogue Scale (VAS) Median overall comfort score at baseline was 4, which markedly increased to 9 at the sixth week in the honey dressing group (Table 2). Patients in povidone iodine experienced increase in overall comfort score from 4 at baseline to 6 at the sixth week (Table 3).

Discussion

Majority of the subjects—54.55 % in the honey dressing group and 45 % in the povidone iodine dressing group—were having chronic wounds of venous etiology. Luciana et al. also support that 70 % of chronic wounds

Fig. 2 (a) Transparent sterile polyurethane occlusive dressing for retaining honey in the wound cavity and (b) complete healing of wound after 6 weeks of honey dressing



Variables	Honey dressing $(n=22)$	Povidone iodine Dressing $(n=20)$
Age in years	Mean - 42.27	Mean - 42.95
	Standard deviation - 16.24	Standard deviation -13.58
Gender	Male - 19(86.36 %)	Male - 17(85.00 %)
	Female – 3(13.64 %)	Female -3(15.005)
Body mass index (BMI)	Mean - 25.3	Mean - 24.5
	Standard deviation - 6.4	Standard deviation – 2.97
Diabetes	4(18.18 %)	6(30.00 %)
Smoking	7(31.82 %)	6(30.00 %)
Alcohol	8(36.36 %)	7(35.00 %)
Haemoglobin gm%	Mean - 12.3	Mean - 12.5
	Standard deviation - 1.6	Standard deviation – 1.4
Serum protein gm%	Mean - 8.19	Mean - 7.8
	Standard deviation - 0.68	Standard deviation - 0.64
Duration of chronic wounds (in months)	Median – 27	Median – 30
	Range – 2–180	Range – 2–180
Types -Venous ulcer	12(54.55 %)	9(45.00 %)
Arterial ulcer	1(4.55 %)	0(0.00 %)
Diabetic ulcer	3(13.64 %)	5(25.00 %)
Pressure sore	1(4.55 %)	1(5.00 %)
Traumatic ulcer	4(18.18 %)	5(25.00 %)
Site -Leg wound	8(36.36 %)	6(30.00 %)
Ankle wound	7(31.82 %)	7(35.00 %)
Foot dorsum wound	1(4.55 %)	1(5.00 %)
Foot sole wound	4(18.18 %)	5(25.00 %)
Thigh wound	1(4.55 %)	0(0.00 %)
Forearm wound	0(0.00 %)	1(5.00 %)
Back wound	1(4.55 %)	0(0.00 %)

Table 1 Baseline characteristics of honey and povidone iodine dressing groups

The data for categorical variables are given as numbers with percentages in brackets.

of the lower limbs are caused by chronic venous insufficiency [7].

Several authors have reported that honey enhances wound healing rate, compared to other conventional or topical applications in a variety of clinical conditions, namely, burns, chronic wounds, infected surgical wounds, and pressure ulcers [8-14].

In 1999 Kramer conducted a review of the clinical trials in which povidone iodine was used for cleansing, irrigating, and dressing wounds. He concluded that povidone iodine did not effectively promote good wound healing and did not reduce bacteriological wound infection [15].

Our results with honey were similar to reports in literature showing rapid healing with the application of honey

Tahla 🤉	Outcome	of honey	dressing	aroun
Table 2	Outcome	of noney	uressing	group

Variables	Median (Range) Honey dressing Group (N=22)				P value
	Surface area of wounds	4.35 (1.8–12.1)	3.7 (0.9–12.1)	1.9 (0.4–12.1)	0.55 (0-12.1)
Pain score during dressing change	7 (0–10)	5 (0-10)	2.5 (0-6)	1 (0-4)	0.000
Overall comfort score of dressing	4 (3–7)	6 (4–9)	8 (4–10)	9 (7–10)	0.000

Table 3 Outcome of povidone iodine dressing group

Variables	Median (Range) Povidone Iodine dressing Group (N=20)				P value
	0 weeks	2nd week	4th week	6th week	
Surface area of wounds Pain score during dressing change	4.25 (0.8–8.6) 7 (0–10)	3.55 (0.6–8.8) 5 (0–10)	3.2 (0.3–8.1) 5 (0–9)	1.95 (0–7.8) 5 (0–9)	0.000
Overall comfort score of dressing	4 (2–7)	5 (3-8)	6 (4–7)	6 (4-8)	0.000

[16]. Moreover, honey caused no adverse skin reaction. Hamdy et al. reported that the number of microorganisms and bacterial species decreased by 50-100 % by application of honey on chronic infected wounds [17].

Various authors reported mild or no pain at all during dressing change with honey as compared to other treatments [12, 18, 19].

In our study, 31 % of the subjects in the honey dressing group achieved complete healing of chronic wounds at the sixth week. Medhi et al. reported similar findings by conducting a meta-analysis to evaluate the efficacy of topical application of honey in observational studies as well as in clinical trials in the treatment of wounds. Most of the subjects reported complete healing within 4–12 weeks in clinical trials and within 2–9 weeks in observational studies [20].

The present randomized trial is unique in the sense that the salutary effects of honey have been combined with those of "moist occlusive" dressing. Occlusion of a wound cavity with the help of a semipermeable membrane retains the moisture of wound exudates and serves as a moisture-retentive dressing [21]. Evaporation of wound exudates through an open dressing, namely, gauze or cotton pads, leads to cooling, desiccation, and dehydration of surface cells. The mitotic rate of healing cells is diminished at lower body temperatures [22]. Moreover, the layer of dehydrated dead cells on the top of wound cavity serves as a good food for microbes hampering healing. These adverse effects of open dressing are averted with the application of occlusive dressing. The occlusion can be achieved with the help of a semipermeable polyurethane or hydrocolloid dressing [22].

A meta-analysis on trials comparing hydrocolloid occlusive dressing versus paraffin gauze and cotton dressings demonstrated significantly better healing with occlusive dressing. The odds ratio for healing with hydrocolloid dressing was 1.72 compared to the conventional paraffin gauze dressing (i.e., 72 % more wounds healed completely with hydrocolloid dressing than with conventional paraffin gauze dressing) [22]. This meta-analysis confirmed the beneficial effects of moisture-retentive occlusive dressing in terms of complete healing of chronic wounds.

The good results observed in the honey treated group may be a combined effect of honey and Tegaderm occlusive dressing. Tegaderm offered an opportunity to inspect the wound cavity without the need for disturbing the dressing. It provides an occlusive environment in which honey could exert its full beneficial effects as the entire honey poured into the cavity remained available to the healing cells. When honey application to a wound is covered with gauze or cotton, most of it gets absorbed in the gauze and is not available to healing cells. Moreover, polymorphs and macrophages immigrating into the wound cavity liberate growth factors essential for healing (e.g., epidermal growth factor, fibroblast growth factor, and vascular endothelial growth factor). These are retained in the wound cavity by an occlusive film like Tegaderm allowing them to exert their full biological activity [23]. In the conventional dressings with gauze and cotton, the wound cavity is deprived of large fractions of these essential molecules as they get absorbed in gauze and cotton, losing their biological activity.

In the Western world, most wound clinics do not recommend the use of povidone iodine application on clean wounds. However, in India many physicians and nurses frequently use povidone iodine even in clean wounds. The present study demonstrates that the rate of wound healing with povidone iodine and Tegaderm was much slower than that achieved by the honey-treated group.

Limitations of Study It was a short study with small sample size. All the subjects were not followed till complete healing. There was no blinding and no attempt was made to quantify the microorganisms (colony-forming unit per gram tissue).

Conclusion

Honey dressing is more effective as compared to povidone iodine dressing in achieving complete healing, reducing wound surface area and pain, and increasing comfort in subjects with chronic wounds.

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