

Original Research Article

One year randomized controlled trial to compare the effectiveness of honey dressing versus povidone iodine dressing for diabetic foot ulcer at Dr. Prabhakar Kore Hospital and MRC, Belagavi

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ABSTRACT

Background: The objective of the study is to find out the effect of honey dressing versus povidone iodine dressing for reduction of wound size in diabetic foot ulcer.

Methods: This randomized controlled trial was done in the Department of General Surgery, KLES Dr. Prabhakar Kore Hospital, Belagavi from January 2017 to December 2017. 64 patients were randomized into 32 group each undergoing unprocessed honey dressing and other group undergoing povidone iodine dressing.

Results: The mean wound size in honey dressing was 23.16 cm² and 23.03 cm² in povidone dressings at baseline, 23.16 cm² and 22.94 cm² at 1st day follow up, 23.16 cm² and 22.94 cm² at 3rd day follow up, 19.38 cm² and 20.28 cm² at 5th day follow up, 16.13 cm² and 17.06 cm² at 7th day follow up, 12.44 cm² and 16.13 cm² at 10th day follow up and the end of 15th day, it was 10.69 cm² and 15.06 cm² respectively in honey dressing group and povidone dressing group. The difference in the wound size in honey dressing group and povidone dressing group at 1st day, 3rd day, 5th day, 7th day, 10th day follow up period were statistically not significant ($p > 0.05$). The difference in the wound size in honey dressing group at 15th day follow up period were statistically significant ($p < 0.05$).

Conclusions: This study shows more favorable results with honey dressing for reduction of wound size in diabetic foot ulcers.

Keywords: Unprocessed honey dressing, Diabetic foot ulcers, Povidone iodine dressing

INTRODUCTION

Diabetes mellitus (DM) is chronic and progressive endocrine disorder that results in hyperglycemia. Globally, diabetes is considered one of the major health problems and there is increasing prevalence. The prevalence of diabetes worldwide was 2.8% and is estimated there may be increase 4.5% by 2030. At present, 200 million people worldwide are suffering from diabetes and predicted to increase up to 333 million by the end of 2025.^{1,2} Data of epidemiological studies have

indicated that the worldwide incidence of DM has been increasing by 3-6% with an approximate prevalence of one in 400 by 18 years of age.³

Diabetes is a growing challenge in India with estimated 8.7% diabetic population in the age group of 20 and 70 years. The rising prevalence of diabetes and other non-communicable diseases is driven by a combination of factors- rapid urbanization, sedentary lifestyles, unhealthy diets, tobacco use, and increasing life expectancy.⁴ The global prevalence of type 2 DM

(T2DM) has shown rapid growth over the past few decades. It is estimated that there will be 30-40 million diabetic patients in India, China by 2025.^{5,6} According to the statistics of the International Diabetes Federation, two will develop diabetes and two will die of it in every 10 seconds.⁷ Therefore, diabetes has become a serious health problem that causes a socioeconomic burden in many countries. Diabetic patients suffer from lower extremity complications which including neuropathy, arterial disease, ulcerations which may cause of diabetic foot infections.^{8,9}

Diabetic foot ulcers are one the reasons for major cause of morbidity and disability in diabetic patients. They are often the common cause for amputations when they are associated with ischaemia or neuropathy.¹⁰ 6.9% patients are affected with diabetes during their life time.¹¹ Ulcerations are the most common cause of amputations.¹² There was the resistant bacterial strains noted which hampers the healing moreover there was drug side effects and organ toxicity.¹³⁻¹⁵

Peripheral sensory neuropathy is one of the major reasons for ulcer formation. The decrease in sensation allows trauma to go unnoticed. Ulcers developing in such areas have increased pressure commonly to heel or toes. Sensory loss, motor deficits and muscle weakness may result due to injury or damage to the nerve.¹⁶ The neuropathy causes decrease in sensation of pain and temperature in the foot. This combination of motor and sensory loss causes a change in the mechanics of the foot causing for pressures ulcers. This increases the risk for ulcer formation.^{17,18} The other major factor in foot ulcer development is peripheral arterial disease. This is caused by plaque build-up in the arteries which eventually decreases blood flow to the small vessels in the periphery of the feet. There is decrease in blood flow, wounds are not able to heal due to the lack of oxygen, nutrients, and white blood cells all of which are carried in the blood.¹⁹ With the combination of peripheral neuropathy, change in foot mechanics causing an increase in trauma, and lack of blood flow to the lower extremity, diabetes patients are vulnerable to ulcers of the foot with an inability to heal these wounds in a usual time period.²⁰⁻²²

As of now there is no cure for diabetes so the goal is to treat the disease early by first changing patient's lifestyles by encouraging incorporation of a healthy diet, decreased sugar intake, and increased physical activity. After lifestyle changes the next step is to use oral medications to decrease blood sugars like metformin, sulfonylureas in addition to using injectable insulin.²³ Also, comorbidities such as hyperlipidaemia and hypertension are treated to avoid chronic complications. Ulcers are a common complication of diabetes, and their regular treatment includes debridement, irrigation, and application of some type of dressing including hydro gels, foams, iodine, absorbent polymers or skin replacements. These dressings help to keep the wound moist for autolytic

breakdown and healing as well as provide an antibacterial component.²⁴

Proper treatment is necessary if not, the amputation of the affected bone becomes unavoidable.²⁵ Wound healing is a complex process involving skin repair after injury.²⁶ it is also a long process in which devitalized and dead cellular structures and tissue layers are replaced. Many treatment approaches have been adopted that includes the use of topical and systemic antibiotics and ointments.²⁷ Many recent advances in antimicrobial therapy has been done though, diabetic foot ulcers remain a serious problem. Many numerous topical and systemic agents have been used either alone or in combination for the eradication of infections, but many have been eliminated because of resistance. These agents may lead to complications including drug side effects, and organ-specific toxicity.²⁸⁻³⁰ Diabetic wound infections caused by drug-resistant organisms are becoming more common and they have resistance to many commonly used antibiotics, that leads to increasing costs and morbidity.^{31,32} With an increasing frequency of antibiotic-resistant pathogens, modern medicine directs attention to natural products with increased antimicrobial property for clinical practice. Unprocessed honey is one such product which is a collection of nectar from many plants, which is processed by honey bees. Honey is well known for its high nutritional and medicinal value.³³ Honey has potent antibacterial activity which is useful in preventing and removing wound infections.³⁴ It has been used as a wound care product since decades, and its use as a wound healing agent was reported for treating venous leg ulcers, chronic leg ulcers, ulcers from many years due to burns.³⁵⁻⁴¹ Unprocessed honey has several natural substances that may contribute for antimicrobial activity including an low pH osmotic effect, and the production of hydrogen peroxide (H₂O₂).⁴²⁻⁴⁵ Many investigations have revealed that Unprocessed honey fights antibiotic-resistant strains of bacteria and helps preventing bacterial growth in spite of wounds been heavily infected.^{46,47} Furthermore, as unprocessed honey is a natural product, it does not induce microbial resistance, even if the honey is not able to kill the microbes.⁴⁸

Objective

The objective of this study was to find out the effect of honey dressing when compared with povidone iodine dressing for reduction of wound size in diabetic foot ulcer.

METHODS

This randomized controlled trial was done in the Department of General Surgery, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi, a tertiary care teaching hospital attached to KLE University's Jawaharlal Nehru Medical College, Belagavi, over a period, from January 2017 to December 2017.

Source of data were diabetic patients taking insulin or oral hyperglycaemic and suffering from diabetic foot ulcers which are not healed, over a period of >3 weeks and for which debridement is required for healing patients were enrolled.

The present study was comprised of 64 patients taking insulin or oral hyperglycaemic and suffering from diabetic foot ulcers which are not healed, over a period of >3 weeks and for which debridement is required for healing patients divided into two groups of 32 each. The patient will be randomly divided into 2 groups. First group (32 pt) with unprocessed honey dressing. Second group (32 pt) with povidone iodine dressing. Informed consent will be obtained from all the patients. Wound dressing will be changed on alternate days for 6 weeks of follow up or till complete healing. If there is soakage or discharge dressing will be changed every day with water soluble povidone iodine and unprocessed honey. Wound healing status to be monitored at 2 weeks interval. Same antibiotic will be used for both the groups to compare the exact status of wound in both the groups, there should be no difference in wound status by using different antibiotics in both groups.

As a part of assessment, ulcers were observed over a period of 15 days. Ulcer area was measured on days 1, 3, 5, 7, 10 and 15 using transparent graph paper. Each box of graph paper is counted and area is given in mm². Patient included in the study are those who are suffering from diabetic foot ulcers. Ulcers which are not healed, over a period of more than 6 weeks and for which debridement is required for healing, only clinically clean wounds without signs of inflammation, purulent discharge. Patients with grade 1 and 2 according to Wagners classification.

Wagner's classification

As per the classification, Grade 0 was no ulcer in a high risk foot, Grade 1 was superficial ulcer involving the full skin thickness but not underlying tissues, Grade 2 was deep ulcer, penetrating down to ligaments and muscle, but no bone involvement or abscess formation, Grade 3 was deep ulcer with cellulitis or abscess formation, often with osteomyelitis, Grade 4 was localized gangrene and Grade 5 was extensive gangrene involving the whole foot.

Patients with ischemic limb, associated osteomyelitis, cellulitis, diabetic ketoacidosis, exposed bone, Hb level less than 10 gm%, known allergy to honey or povidone iodine were excluded from the study.

The study was approved from the ethical and research committee, Jawaharlal Nehru Medical College, Belagavi. The eligible patients who fulfilled the selection criteria were informed in detail about the nature of the study and a written informed consent was obtained.

Method of data collection

The demographic data was obtained through an interview. Patients were asked for the past history, ulcer duration, diabetic history and treatment history. Further these patients were subjected to clinical examination. The wound observation was performed for ulcer characteristics such as site, size, shape, edge, margin, floor, base, discharge, surrounding skin and slough/necrotic tissue. These findings were noted on a predesigned and pretested proforma.

Investigations

The patients underwent investigations including fasting blood sugar, complete blood count, HbA1c, renal function test, urine R/M, wound discharge for C/S, X-Ray foot- antero-posterior and lateral view (as and when required), color doppler (as and when required).

Randomization

The patients were divided into two groups of 32 each viz., Group A and group B based on closed envelope method as: first group (Group A) with honey dressing, second group (Group B) with povidone Iodine dressing.

Treatment

All the patients underwent debridement of wound. Empirical antibiotics ceftriaxone and metronidazole were started and changed to sensitive antibiotics after culture and sensitivity report. For group A honey dressing was done and for group B povidone iodine dressing was done.

Dressings were done using same technique- cleaning and application of honey/povidone iodine and putting a dressing. Prior to application, the lesion was cleaned of debris and digested material by gently rubbing with gauze pad by normal saline. Unprocessed honey was applied on sterile gauze pad, which was then applied to the wound and properly secured. Povidone iodine soaked gauze was kept on the wound and dressing was secured. Wound dressing will be changed on alternate days for 6 weeks of follow up or till complete healing. If there is soakage or discharge dressing will be changed every day with povidone iodine and unprocessed honey. Wound healing status to be monitored at different days within 2 weeks interval. Same antibiotic will be used for both the groups to compare the exact status of wound in both the groups, there should be no difference in wound status by using different antibiotics in both groups.

Outcome variables

Debridement of slough/nonviable tissue, reduction in ulcer size, granulation. Discharge, odour, induration noted for overall response to treatment ulcer was assessed by the investigator at the beginning of the study. Ulcer mapping was made and size was recorded. Ulcers were

observed over a period of 15 days. Ulcer area was measured on days 1,3, 5, 7, 10 and 15 using transparent graph paper. Each box of graph paper is counted and area is given in mm².

Statistical analysis

The data obtained was coded and entered in Microsoft Excel spreadsheet. Study group (honey dressing, povidone iodine dressing) was considered as primary explanatory variable.

Wound size was considered as primary outcome parameter. Other wound related parameters like discharge, appearance of granulation tissue and status of edges etc were considered as secondary outcome variables.

Age, medication duration (in years), wound size in cm², hemoglobin (gm/dl), HbA1c (%), blood urea (gm/dl), serum creatinine (gm/dl) were as considered as potential confounders. All the quantitative variables were checked for normal distribution within each study group. Normally distributed quantitative variables were compared by mean and standard deviation using independent sample t-test.

Normality test using SPSS

A Shapiro- Wilk's test ($p>0.05$) and a visual inspection of their histograms, normal Q-Q plots and box plots showed that the study group (honey dressing, povidone iodine dressing) and wound size different follow up time periods was non-normally distributed.

Non-normally distributed quantitative variables were compared by median and inter quartile range using Mann-Whitney U-test. The categorical variables were compared between two groups using cross tabulation and Chi-square test/Fisher's exact test. P value <0.05 was considered statistically significant. IBM SPSS version 22 was used for statistical analysis.

RESULTS

Total of 64 patients were analysed among the honey dressing group, 26 (81.3%) participants were male, remaining 6 (18.8%) participants were female. Among the povidone iodine dressing group, 24 (75%) participants were male remaining 8 (25%) participants were female. Among the honey dressing group, 18 (56.3%) participants were farmer, 10 (31.3%) participants were worker and 4 (12.5%) participants were bus driver. Among the povidone iodine dressing group, 15 (46.9%) participants were farmer, 14 (43.8%) participants were worker and 3 (9.4%) participants were bus driver.

Table 1: Comparison of wound size in cm² within each group at different time follow up periods (n=64).

Wound size						
Days	Honey dressing		Povidone iodine dressing		P value	Inference
	Mean	S.D.	Mean	S.D.		
Base	23.16	10.94	23.03	11.57	0.9666	NS
Day 1	23.16	10.94	22.94	11.52	0.9415	NS
Day 3	23.16	10.94	22.94	11.52	0.9415	NS
Day 5	19.38	8.14	20.28	10.51	0.7139	NS
Day 7	16.13	7.37	17.06	10.22	0.6928	NS
Day 10	12.44	6.16	16.13	9.88	0.0868	NS
Day 15	10.69	5.13	15.06	8.97	0.0258	S

Table 2: Comparison of percentage reduction of wound size between each group at different time follow up periods (n=64).

Percentage reduction with respect to base line						
	Honey dressing		Povidone iodine dressing		P value	Inference
Days	Mean	S.D.	Mean	S.D.		
Day 5	9.87	24.44	11.79	18.34	0.7201	NS
Day 7	27.54	17.44	28.39	17.05	0.8429	NS
Day 10	42.58	18.91	32.73	15.74	0.0255	S
Day 15	49.87	20.24	36.30	14.05	0.0025	VS

Among the honey dressing group, 20 (59.4%) participants had left foot and 12 (37.5%) participants had right foot. Among the povidone iodine dressing group, 19 (53.1%) participants had left foot and 13 (40.6%) participants had right foot. The difference in the

proportion of sites between groups was statistically not significant ($p=0.785$). The difference in the proportion of shapes between groups was statistically not significant ($p=0.869$).

The mean wound size in honey dressing was 23.16 cm² at baseline, 23.16 cm² at 1st day follow up, 23.16 cm² at 3rd day follow up, 19.38 cm² at 5th day follow up, 16.13 cm² at 7th day follow up, 12.44 cm² at 10th day follow up and the end of 15th day, it was 10.69 cm². The difference in the wound size in Honey dressing group at 1st day, 3rd day, at 5th day, 7th day, 10th day follow up period with baseline value were statistically not significant ($p>0.05$). The difference in the wound size in honey dressing group at 15th day follow up period with baseline value were statistically significant (p value <0.05). The mean wound size in povidone dressing was 23.03 cm² at base line, 22.94 cm² at 1st day follow up, 22.94 cm² at 3rd day follow up, 20.28 cm² at 5th day follow up, 17.06 cm² at 7th day follow up, 16.13 cm² at 10th day follow up and the end of 15th day, it was 15.06 cm². The difference in the wound size in povidone Iodine at 1st day, 3rd day, at 5th day, 7th day, 10th day follow up period with baseline value were statistically not significant ($p>0.05$) and the difference in the wound size in honey dressing at 15th day follow up period was statistically significant ($p<0.05$).

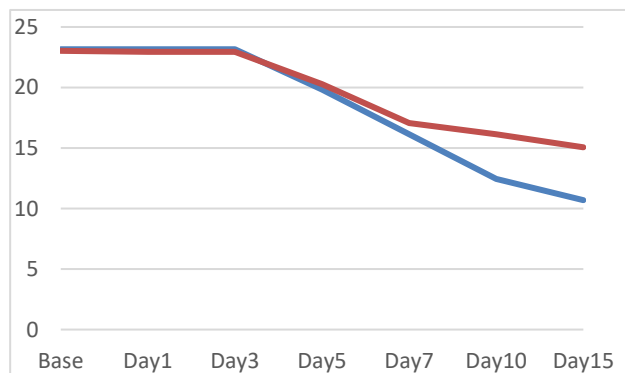


Figure 1: Comparison of area of the ulcer (in cm²) (n=64).

Sky blue- Honey dressings; Violet- Povidone dressings.

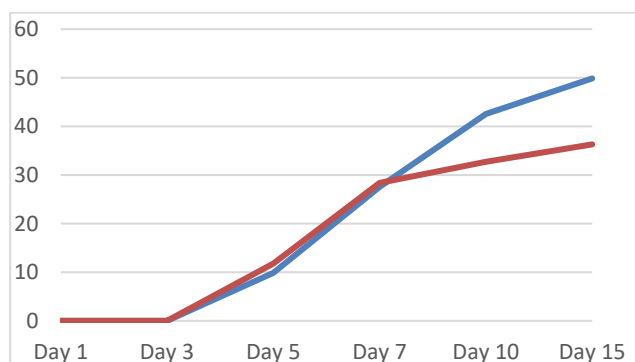


Figure 2: Percentage reduction of wound size (n=64).

Sky blue- Honey dressings; Violet- Povidone dressings.

The mean percentage reduction of wound size in both groups of day 1, 3 were almost same and statistically not significant, while in honey dressing group was 9.87 at 5th day follow up, 27.54 at 7th day follow up, 42.58 at 10th day follow up and the end of 15th day, it was 49.87. The

difference in the wound size in honey dressing group at 1st day, 3rd day, at 5th day, 7th day, 10th day follow up period with baseline value were statistically not significant ($p>0.05$). The difference in the wound size in honey dressing group at 10th and 15th day follow up period with baseline value were statistically significant ($p<0.05$). The mean percentage reduction in wound size in povidone iodine dressing group was 24.44 at 5th day follow up, 17.44 at 7th day follow up, 18.91 at 10th day follow up and the end of 15th day, it was 20.24. The difference in the wound size in povidone iodine at 1st day, 3rd day, at 5th day, 7th day, follow up period with baseline value were statistically not significant ($p>0.05$) and the difference in the wound size in honey dressing at 10th and 15th day follow up period was statistically significant ($p<0.05$).

DISCUSSION

The increasing prevalence of diabetes has resulted in concomitant illness. The critical effects of hyperglycemia include micro-vascular complications (nephropathy, neuropathy and retinopathy) and macro-vascular complications (coronary artery disease, stroke and peripheral arterial disease). Diabetes is a leading cause of non-traumatic lower extremity amputation, which is often preceded by a non-healing ulcer. The lifetime risk of foot ulceration in people with diabetes is 15-20%. More than 15% of foot ulcers result in amputation of the foot or limb. Several other population-based studies indicate a 0.5-3% annual collective incidence of diabetic foot ulcers. The prevalence of foot ulcers reported varies from 2-10%. Approximately 45-60% of all diabetic foot ulcerations are purely neuropathic, whereas 45% have both neuropathic and ischemic components. It has been estimated that around 15-27% patients with diabetes require lower limb amputations predominantly (50%) due to infection.⁴⁸

Dressing plays a major role in healing of wounds in combination with debridement. This study compared the effectiveness of honey dressing with povidone iodine dressing of grade 2 diabetic foot ulcers. In the present study male outnumbered females. That is majority of the patients in group A (81.3%) and group B were males (75%). However, the sex distribution pattern in group A and group B was not significant ($p=0.545$). Among the honey dressing group, 18 (56.3%) participants were farmer, 10 (31.3%) participants were worker and 4 (12.5%) participants were bus driver. Among the povidone iodine dressing group, 15 (46.9%) participants were farmer, 14 (43.8%) participants were worker and 3 (9.4%) participants were bus driver. The difference in the proportion of occupations between groups was statistically not significant ($p=0.582$). The difference in the wound size in povidone iodine at 1st day, 3rd day, at 5th day, 7th day, 10th day follow up period with baseline value were statistically not significant ($p>0.05$) and the difference in the wound size in honey dressing at 15th

day follow up period was statistically significant ($p < 0.05$).

Overall the present study showed that dressing with honey influences granulation and thereby promotes early healing compared to dressing with povidone iodine. However, we have less sample size compare these findings with other studies. We hypothesize that, dressing with honey might have multiple beneficial effects on wound bed preparation and healing, through the removal of necrotic plug by the enzymatic action.

There was one study conducted at AIIMS, New Delhi by Sonia Gulati et al which showed 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.⁴⁹

Shukrimi et al conducted a prospective study to compare the effect of honey dressing for Wagner's grade-II diabetic foot ulcers with controlled dressing group (povidone iodine followed by normal saline). Surgical debridement and appropriate antibiotics were prescribed in all patients. There were 30 patients age between 31 to 65 years old (mean of 52.1 years). The mean healing time in the standard dressing group was 15.4 days (range 9-36 days) compared to 14.4 days (range 7-26 days) in the honey group ($p < 0.005$). In conclusion, ulcer healing was not significantly different in both study groups. Honey dressing is a safe alternative dressing for Wagner grade-II diabetic foot ulcers.⁵⁰

CONCLUSION

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. 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. This study shows more favourable results with honey dressing as compared with povidone iodine dressing for reduction of wound size in diabetic foot ulcers.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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