

A CONTROL CLINICAL TRIAL OF HONEY-IMPREGNATED AND POVIDONE IODINE DRESSINGS IN THE TREATMENT OF DIABETIC FOOT ULCERS AMONG NORTHERN INDIAN SUBJECTS

**SARINA AGARWAL^{a1}, VINOD BHARDWAJ^b, ABHISHEK SINGH^c,
MOHD. HAROON KHAN^d, SHEWTANK GOEL^e, MASURAM BHARAT^f AND JAI KRISHNA^g**

^aDepartment of General Surgery, Maharishi Markandeshwar Institute of Medical Sciences, Mullana, Haryana, India

^bDepartment of Pharmacology, SHKM Government Medical College, Mewat, Haryana, India

^{cd}Department of Community Medicine, SHKM Government Medical College, Mewat, Haryana, India

^cDepartment of Microbiology, MSDS Medical College, Fatehgarh, Uttar Pradesh, India

^dDepartment of Pharmacology, MSDS Medical College, Fatehgarh, Uttar Pradesh

^eDepartment of Pharmacology, FH Medical College, NH-2, Tundla, Uttar Pradesh, India

ABSTRACT

To compare the effect of honey with povidone iodine as a dressing material in the management of diabetic foot ulcers among northern Indian subjects. Thirty six patients fulfilled the inclusion criteria hence data of 36 patients was collected and analyzed for various study parameters. The mean age of the patients was 52.4 ± 5.4 years (range 46-63 years). Males 24 (66.7%) outnumbered female patients 12 (33.3%). Wounds in the Group A took a mean duration of 14.2 days (range 6 - 25 days) to be ready for surgical closure. On the other hand, wounds in the Group B took a mean duration of 15.5 days (range 9 - 37 days) to achieve similar status. All patients in honey group experienced less pain during dressing. Oedema and foul smelling discharges resolved earlier as compared to the standard dressing group.

KEYWORDS : Clinical trial, Honey, Wound dressing, Diabetes mellitus, Povidone iodine

Diabetic foot ulcers (DFUs) are the consequence of multiple factors including peripheral neuropathy, decreased blood supply, high plantar pressures pose a significant risk for morbidity, limb loss and mortality. DFUs necessitate more hospital admissions than any other complication of DM (Abdelatif, 2008) and are the main risk factor for no-traumatic lower-extremity amputations (Reiber, 1992). The lifetime risk of foot ulceration in people with diabetes is 15%-20% (Singh, 2005). More than 15% of foot ulcers result in amputation of the foot or limb (Reiber, 2002). There is no conventional guideline regarding the selection of wound care materials in diabetic foot wounds. The successful management of diabetic foot wounds requires the multidisciplinary teamwork of specialists.

Honey dressing has been applied to clinical practice for many types of disease for centuries (Lipsky, 2004). It still being used as a dressing material for burn wounds, decubitus ulcers, gunshot wounds and wound dehiscence. As a wound dressing, honey dressing can provide a moist micro-environment with antimicrobial properties, has anti-inflammatory effects, reduces edema and exudates, promotes angiogenesis and granulation tissue formation, induces wound contraction, stimulates collagen

synthesis, facilitates debridement and accelerates wound epithelialisation (Al-Waili, 2011; Guo, 2013).

In terms of advantages, many researchers have studied the effects of honey dressing for the treatment of DFUs, and these conclusions are uncertainty. There is insufficient quality evidence available in the current literature regarding the effectiveness of honey dressing for the treatment of DFUs. Therefore the present study was planned to compare the effect of honey with povidone iodine as a dressing material in the management of diabetic foot ulcers among northern Indian subjects.

MATERIALS AND METHODS

The control clinical trial was planned and executed by the Department of General Surgery in collaboration with Department of Orthopedics, Maharishi Markandeshwar Institute of Medical Sciences And Research during February 2014 to September 2014. The study population consisted of non-Insulin dependent diabetes mellitus patients (NIDDM) with Wagner grade-II ulcers admitted for surgery in MM Institute of Medical Sciences. Inclusion criteria included patient's age between 35 – 65 years, transcutaneous oxygen tension of more than 30 mm Hg and serum albumin level of >35 g/dl. Exclusion criteria included

¹Corresponding author

multiple medical co-morbidity, steroid therapy, neutrophil count less than 2000/mm³.

Maharishi Markandeshwar Institute of Medical Sciences is a state of the art tertiary care teaching institution established in rural outskirts of Ambala to provide super specialty care to underserved population. Department of General Surgery is serving primarily patients mainly from lower socio-economic strata of community not only from whole of Haryana but also from neighboring states. On an average 150-200 patients seek care at Department of General Surgery and Orthopedics, MM Medical College on outpatient (OPD) basis per day. So this institution provided us a perfect base to plan and execute this study.

All the patients' full filling the inclusion criteria were randomized into two groups; Group A- honey impregnated dressing group and Group B- standard (povidone iodine) dressing group. Clean non-sterile pure honey which is commercially prepared for food was used for honey-impregnated dressing. Povidone iodine solution 10% (dilute with normal saline) was used in standard dressing group. All patients received appropriate antibiotics and the ulcers were debrided surgically by an orthopedic specialist doctor. Tissue specimen taken during the debridement were sent for culture and sensitivity testing. Blood glucose control was kept optimum under supervision. Wound dressing was started on the first post-operative day and it was carried by trained nursing staff.

In the honey-impregnated dressing group, the wound was initially cleansed with normal saline. A thin layer of honey was poured on the wound and the wound was then covered with sterile gauze and bandaged. In the control group, the wound was first cleansed with normal saline, followed by covering it with povidone-soaked gauze. Conversion to normal saline dressing was made once the wound was cleared from frank pus. The dressings were carried out on daily basis. Wounds were assessed on daily basis. The assessment terminated when the wound was either ready for surgical closure or needed further debridement. Duration from the initial debridement to the wound closure day was analyzed. If the wound required further surgical debridement, the treatment was categorized as failure and it will not be considered as the end result of the study. Swab for culture and sensitivity was taken when the

wound was ready for closure.

Data was captured on predesigned proforma. A total of thirty six patients fulfilled the inclusion criteria hence data of 36 patients was collected and analyzed for various study parameters like; mean duration for wound healing, duration for wound healing, mean pain while dressing, improvement in Oedema and discharge from wound. Permission of Institutional ethics committee (IEC) was sought before the commencement of the study. Informed consent was obtained from the study participants. All the questionnaires were manually checked and edited for completeness and consistency and were then coded for computer entry. After compilation of collected data, analysis was done using Statistical Package for Social Sciences (SPSS), version 21 (IBM, Chicago, USA). The results were expressed using appropriate statistical methods. Independent-Samples T Test was applied to compare means for Honey dressing group and Standard (Povidone Iodine) dressing group. A two-tailed P<0.05 was considered statistically significant.

RESULTS

Thirty six patients fulfilled the inclusion criteria hence data of 36 patients was collected and analyzed for various study parameters. The mean age of the patients was 52.4 ± 5.4 years (range 46-63 years). Males 24 (66.7%) outnumbered female patients 12 (33.3%). Mean transcutaneous oxygen tension was 38 mmHg (range 35-41 mmHg).

Culture report showed that following organisms were isolated prior to the treatment - *Streptococcus* sp. (32%), *Staphylococcus* sp. (18%), *Pseudomonas* (12%), *Enterococcus* (9%), *Bacteroides* (5%), *Acinobacter* (5%), *Proteus* (3%) and *Escherichia coli* (3%). Polymicrobial infections were encountered in (13%) of patients. In the Standard dressing group, wound infected with *Pseudomonas*, *Enterococcus* and mixed organisms remained infected until the end of the study; whereas in Honey dressing group, wound infected with *Bacteroides*, *Enterococcus* and mixed infections remained infected until the end of the study.

Wounds in the Group A - honey impregnated dressing group took a mean duration of 14.2 days (range 6 -

Table 1 : Comparative Analysis of Outcome Variables Between Honey Dressing Group and Standard (Povidone Iodine) Dressing Group

Variables	Groups	
	Group A Honey dressing group	Group B Stand ar d dressing group
Mean duration for wound healing *	14.2 days	15.5 days
Range	6- 25 days	9- 37 days
Mean pain score	5.3	6.6
Oedema	Less	More
Discharge from wound	Less	More
*P > 0.05, Non - Significant by Independent - Samples T Test		

25 days) to be ready for surgical closure. On the other hand, wounds in the Group B - Standard (povidone iodine) dressing group took a mean duration of 15.5 days (range 9 - 37 days) to achieve similar status. All patients in honey group experienced less pain during dressing. Oedema and foul smelling discharges resolved earlier as compared to the standard dressing group. (Table 1).

DISCUSSION

Diabetic foot ulcers are an important complication of diabetes. The integration of knowledge and experience through a multidisciplinary team approach promotes more effective treatment, thereby improving outcomes and early recovery (Shanmugam, 2013; Chahine 2013). Following specialists play their role- Endocrinologist/Diabetologist (optimize blood glucose control); Podiatrist (focus on the foot including prevention and treatment of diabetic foot wounds); Vascular surgeon (manage vascular issues); Microbiologist (look into microbiological etiology and antibiotic selection based on cultures); Orthotist (ensures that therapeutic or custom made footwear aids in minimizing pressure); and Nutritionist (concentrates on diet which helps in the management of diabetes as well as wound healing) (Basile, 2002).

The management of diabetic foot wounds needs timely detection of complications and frequent assessment of the wound. It is important to take into account all the related causes, identify the problem, and treat it. It was observed in this study that wounds in honey impregnated dressing group took 14.2 days to be ready for surgical closure whereas Standard (povidone iodine) dressing group took a mean duration of 15.5 days (range 9 - 37 days) to

achieve similar status. Wound healing involves formation of granulation tissue, epithelization and wound contraction. In this study these pathological parameters could not be assessed because of variable sizes of wounds. By focusing on whether the wound was clean and ready for closure, assessment of the wound of different size was done. A prospective randomized clinical and histological study of superficial burn wound observed that burn wound dressed with honey allowed early grafting on a clean clear base as compared with sulfur sulfadiazine dressing (Subrahmanyam, 1998). Honey dressing has been reported to promote formation of clean healthy granulation tissue (Subrahmanyam, 1991), accelerates wound healing and enhances graft taking (Bergman, 1983).

Our culture report showed that following organisms were isolated prior to the treatment - Streptococcus sp. (32%), Staphylococcus sp. (18%), Pseudomonas (12%), Enterococcus (9%), Bacteroides (5%), Acinobacter (5%), Proteus (3%) and Escherichia coli (3%). Polymicrobial infections were encountered in (13%) of patients. Another study reported a predominant gram negative infection in Wagner grade-II DFUs, and the type of organism correlate well with the severity of infection as determined by grading of the DFUs (Maria, 2002). No new organisms were found from the wound in both groups indicating both techniques were able to prevent cross-infection.

This study has several strengths. First, we have compared the effect of honey with povidone iodine as a dressing material in the management of diabetic foot ulcers. In-depth analysis of this aspect has not been closely investigated by many experts in the field. This study

becomes more important as sufficient quality evidences are not available in the current literature regarding the effectiveness of honey dressing for the treatment of DFUs. Second, in this study, strict inclusion criteria were adhered to standardized factors that may independently influence wound healing. Third, bias in selection and outcome evaluation were minimized with randomization of cases and single blinded assessment of the wounds. Lastly, all the investigations were conducted by authors of the study only, which creates a sense of uniformity. The study has some limitations as well. Some may argue that the results obtained may not be generalized as these findings are based on a single centre study. More multicentric studies need to be carried out. Second, sample size used in this study is small. Studies with bigger sample size are warranted to support our findings.

CONCLUSION

The findings of this study demonstrated that ulcer healing was not much different in both study groups. On the basis of generated evidences it can be said that honey-impregnated dressing can be considered safe alternative to povidone iodine dressing for Wagner grade-II diabetic foot ulcers. Further studies with bigger sample size especially randomized controlled trials are warranted to generate best quality evidences.

REFERENCES

- Abdelatif M., Yakoot M. and Etmaan M., 2008. Safety and efficacy of a new honey ointment on diabetic foot ulcers: a prospective pilot study. *J. Wound Care*, 17:108e10.
- Al-Waili N., Salom K. and Al-Ghamdi A., 2011. Honey for wound healing, ulcers and burns; data supporting its use in clinical practice. *Scientific World Journal*, 11:766e87.
- Basile P. and Rosenbloom B., 2002. Local care of the diabetic foot. In: Veves A., Giurini J.M., LoGerfo F.W., editor(s). *The Diabetic Foot*. New Jersey: Humana Press : 279-292
- Bergman A. and Yanai J., 1983. Acceleration of wound healing by topical application of honey. An animal model. *Am. J. Surg.*, 145: 374-6.
- Chahine E. B., Harris S. and Williams R., 2013. Diabetic foot infections: an update on treatment. *US Pharm*, 38: 23-26
- Guo C.L. and Fu X.Y., 2013. Research on effect evaluation of local treatment of patients with diabetic foot ulcers using honey dressing. *Med. J. West China*, 25:977e80.
- Lipsky B. A., Berendt A. R., Deery H. G., Embil J. M., Joseph W. S., Karchmer A. W., LeFrock J. L., Lew D. P., Mader J. T., Norden C. and Tan J. S., 2004. Diagnosis and treatment of diabetic foot infections. *Clin. Infect Dis.*, 39: 885-910
- Maria Fe P. R. and Mendoza M. T., 2002. The microbiologic features and clinical outcomes of diabetic foot infections among patients admitted at UP-PGH. *Phil. J. Infect Dis.*, 31(2): 51-63.
- Reiber G. E., 2002. Epidemiology and health care costs of diabetic foot problems. In: Veves A., Giurini J.M., LoGerfo F.W., editor(s). *The Diabetic Foot*. New Jersey: Humana Press, 2002: 35-58.
- Reiber G.E., Pecoraro R.E. and Koepsell T.D. Risk factors for amputation in patients with diabetes mellitus: a case-control study. *Ann. Intern. Med.* 1992; 117:97e105.
- Shanmugam P. and Susan S.L. The bacteriology of diabetic foot ulcers, with a special reference to multidrug resistant strains. *J. Clin. Diagn. Res.* 2013; 7: 441-445
- Singh N., Armstrong D.G. and Lipsky B.A. Preventing foot ulcers in patients with diabetes. *JAMA* 2005; 293: 217-228 [PMID: 15644549 DOI: 10.1001/jama.293.2.217]
- Subrahmanyam M. A prospective randomized clinical and histological study of superficial burn wound healing with honey and silver sulfadiazine. *Burns* 1998; 24(2): 157-61.
- Subramanian M. Topical application of honey in treatment of burns. *Br. J. Surg.* 1991; 78(4): 497-8