

IMPACT OF HONEY DRESSING IN CHRONIC ULCER*Santhosh Kumar S. S¹, Muhammed Sumarban Sharmad²**¹Assistant Professor, Department of Orthopaedics, Government Medical College, Trivandrum.**²Additional Professor, Department of Neurosurgery, Government Medical College, Trivandrum.***ABSTRACT****BACKGROUND**

This was an open label study. Although, honey has been used for centuries in wound care, now only it is being integrated into modern medical practice. The resurgence of interest in honey as a medicine for modern wound dressing offers opportunities for both patients and clinicians.

The aim of this study is to show the advantage of honey dressing over conventional saline dressing in the management of chronic non-healing ulcer. This property of honey is mentioned in papyrus traced to 3500 years ago among ancient Egyptians and the Hebrews 3000 years ago. Honey naturally contains small amounts of enzymes. The predominant enzymes in honey are diastase (amylase), invertase (alpha-glucosidase) and glucose oxidase. Honey has been proven to have significant antibacterial properties and is a useful constituent in wound and burn care. The stimulation of cell growth seen with honey is probably also responsible for 'kick-starting' the healing process in chronic wounds that have remained non-healing for long periods. Honey has a broad spectrum of activity against bacteria and fungi. Many randomised and non-randomised study has shown the efficacy of honey as a healing agent and excellent dressing material.

MATERIALS AND METHODS

Study was conducted in medical college, Trivandrum, which is a tertiary care centre. Patients are selected from orthopaedic and general surgical wards. The study period was one year extending from July 2014 to June 2015. Saline dressing was given for the patients admitted in the first 6 months of study. Honey dressing was given for the next 6 months of study. Outcome was assessed on duration of hospital stay, difference of outcome in different distribution of grades of ulcer, difference of outcome in patients with vascular compromise, which is found out by Doppler ultrasound and difference of outcome in patients with diabetes mellitus.

RESULTS

Most significant observations made were in regard to duration of hospital stay and better outcome in case of honey dressing compared to conventional saline dressing. Average duration of hospital stay in those dressed using normal saline was found to be 31.3 days. Mean duration in those dressed with honey was found to be 25.77 days. Difference in average duration of hospital stay in both groups was proven to be highly statistically significant with a p value of 0.000934.

The number of patients that could be grafted during their hospital stay was significantly more in those dressed with honey. 63% of patients who were dressed with honey could be grafted during their hospital stay, whereas only 17% of normal saline dressing group could be grafted. This difference was proven to be statistically significant with a p value of 0.004.

CONCLUSION

The rate of amputations was also very much less in patients dressed with honey dressing. It was also noted that honey dressing turned more number of unsterile cultures sterile than normal saline. This difference was also proved statistically significant. Doppler findings were also noted in the beginning of study to see whether the efficacy of honey dressing is lesser in patients with vascular impairment. But, it was noted that there is no significant difference in the efficacy of honey dressing in both groups. The difference in number of diabetic patients included in honey and saline dressing was also proved not significant; thus confirming efficacy of honey dressing in diabetic and nondiabetic individuals.

KEYWORDS

Honey Dressing, Chronic Non-Healing Ulcer, Diabetes.

HOW TO CITE THIS ARTICLE: Kumar SSS, Sharmad MS. Impact of honey dressing in chronic ulcer. J. Evid. Based Med. Healthc. 2018; 5(2), 140-146. DOI: 10.18410/jebmh/2018/31

Financial or Other, Competing Interest: None.

Submission 28-12-2017, Peer Review 31-12-2017,

Acceptance 04-01-2018, Published 06-01-2018.

Corresponding Author:

Dr. Santhosh Kumar S. S,

Assistant Professor, Department of Orthopaedics,

Government Medical College, Trivandrum.

E-mail: santhoshkumarss@gmail.com

DOI: 10.18410/jebmh/2018/31

**BACKGROUND**

A chronic non-healing ulcer is one of the most common cause of admission in the surgical and orthopaedic ward. Most common cause are diabetes mellitus, POVD, traumatic and venous ulcer. Most commonly, the lower extremity is affected.

Nearly, 1% of the adult population is affected by this morbidity of which 12% of chronic non-healing ulcer foot go for amputation. Even if the limb is saved, prolonged use of antibiotics, hospital stay, repeated wound debridement add

to the physical, mental and financial trauma of the patient. Still the line of management of chronic non-healing ulcer in our hospital is repeated wound debridement, saline washing, dry-to-moist gauze dressing and antibiotics.

Although, honey has been used for centuries in wound care. Now only, it is being integrated into modern medical practice. The resurgence of interest in honey as a medicine for modern wound dressing offers opportunities for both patients and clinicians.

Aim of this study is to show the advantage of honey dressing over conventional saline dressing in the management of chronic non-healing ulcer.

One of the oldest medical manuscripts known to man is a clay tablet that dates back to 2200 BC. This tablet describes, perhaps for the first time, the "three healing gestures" washing the wounds, making the plasters and bandaging the wound. Plasters were made of honey and oil.¹

This property of honey is mentioned in papyruses traced to 3500 years ago among ancient Egyptians and the Hebrews 3000 years ago. Greeks and ancient Chinese have mentioned it 2000 years ago.²

The fact that the antibacterial properties of honey are increased when diluted was clearly observed and reported in 1919. This antibacterial agent was referred to as 'inhibine' prior to its identification as hydrogen peroxide. The term 'inhibine number' was coined as a measure of the relative antibacterial potency of different honeys, it being the number of steps by which a honey could be diluted and still inhibit bacterial growth.³ In vitro studies have shown that active honey is bactericidal against strains of antibiotic-resistant bacteria isolated from infected wounds such as MRSA, vancomycin-resistant enterococci and *Burkholderia cepacia* to the list of susceptible bacteria.⁴

Honey naturally contains small amounts of enzymes. The predominant enzymes in honey are diastase (amylase), invertase (alpha-glucosidase) and glucose oxidase.⁵ Honey has been proven to have significant antibacterial properties and is a useful constituent in wound and burn care.⁶ The antibacterial properties arise from the presence of glucose oxidase, which converts glucose to gluconolactone, which in turn yields gluconic acid and hydrogen peroxide.⁷ Invertase has been considered responsible for most of the chemical changes that take place during the conversion of nectar to honey. Invertase is generally present in small amounts and is inactivated by heating.⁸

Glucose oxidase is another enzyme in honey that originates from bees. Like invertase and diastase, it plays a part in the formation of honey in the hive- it oxidises glucose in the unripened honey.⁹

Malodour is a common feature of chronic wounds. It is attributed to the presence of anaerobic bacterial species such as *Bacteroides* spp., *Peptostreptococci* and *Prevotella* spp.¹⁰

The malodorous substances produced by bacteria are short-chain fatty acids, ammonia, amines and sulphur compounds. These are formed by the metabolism of amino acids from decomposed serum and tissue proteins. Honey provides a copious quantity of glucose, a substrate

metabolised by bacteria in preference to amino acids. Also, honey at a concentration of 1% has been reported to stimulate monocytes in cell culture to release the cytokines TNF-1, IL-1 and IL-6, which are intermediates in the immune response.¹¹ In addition to the reported stimulation of leucocytes, honey has the potential to augment further the immune response by supplying glucose.¹² Unlike other wound dressings, honey creates a moist environment by drawing out lymph fluid from the wound tissues through its strong osmotic action.¹³ Another possible explanation for the observed rapid debridement is activation of the proteases by hydrogen peroxide liberated by honey. The matrix metalloproteases of connective tissue normally present in a catalytically inactive conformation maybe activated by the hydrogen peroxide.¹⁴

The stimulation of cell growth seen with honey is probably also responsible for 'kick-starting' the healing process in chronic wounds that have remained non-healing for long periods.¹⁵ Honey has a broad spectrum of activity against bacteria and fungi.

A variety of bacteria capable of causing wound infection have now been tested under laboratory conditions for their susceptibility to honey.¹⁶ Gram-positive bacteria are often involved in wound infection. *Staphylococcus aureus*- the most common cause of wound infection has been shown to be inhibited by relatively low concentrations of honey, as have antibiotic resistant strains, such as Methicillin-Resistant *Staphylococcus Aureus* (MRSA), vancomycin-sensitive and vancomycin-resistant *Enterococci* and coagulase-negative *Staphylococci*.¹⁷

A recent study showed that the growth of 15 cultures of *Streptococcus* species isolated from wounds were inhibited by honey.¹⁸ Gram-negative bacteria commonly implicated in wound infection *Pseudomonas aeruginosa*, *Stenotrophomonas* species and *Acinetobacter baumannii* have been shown to be susceptible to honey in vitro.¹⁹ Cells exposed to honey accumulated at the end of the cell cycle with fully-formed cross walls, but did not separate into daughter cells. Without completing cell division, bacteria cannot establish a colony. Multiple changes in cellular proteins have also been observed in *S. aureus*.²⁰ Analysis of changes in *Escherichia coli* following exposure to honey demonstrated multiple effects on the expression of genes.²¹ Following report that links the presence of biofilms in a wound to chronicity, interest in the control of biofilms has increased. Unsurprisingly, research indicates that higher concentrations of honey are required to disrupt established biofilms than to prevent biofilm formation and they also indicate that planktonic bacteria are more susceptible to honey than are biofilms.²²

The adherence of bacteria to a wound is an important step in establishing initiation of infection and biofilm formation. Study into the effects of honey on planktonic and biofilm-embedded bacteria suggested that honey has a bactericidal effect against the wound pathogens grown in the laboratory as biofilms.²³ Biofilms of *S. aureus* and *P. aeruginosa* exposed to honey were inhibited in vitro. Methylglyoxal has been implicated in the inhibition of

biofilms. Biofilms of Methicillin-Sensitive Staphylococcus Aureus (MSSA), MRSA and VRE can be prevented from forming and established biofilms can be inhibited in vitro with varying concentrations honey.²⁴

Efem (1988) reported that clinical observations on the healing with honey of 59 cases of wounds and skin ulcers that was not healing 4-5 months with conventional treatment. He also reported that 20 cases of Fournier's gangrene were treated by daily application of honey with no surgery and 21 similar cases treated by surgical removal of infected tissue and systemic antibiotics. Treatment with honey wound becoming sterile within a week and does not require plastic surgery.²⁵

The study of Dunford and Hanano (2004) was reported by Lay Karen in her article on honey in wound care. The study revealed the acceptability of honey dressing in patients with non-healing leg ulcers particularly in terms of pain reduction, odour control and general patient satisfaction. 40 patients were recruited, 20 reported a decrease in pain levels. Overall, patient satisfaction with honey dressing was high. 20 out of 21 patients also reported decrease in odour due to use of honey.²⁶

Khan Fasal from North West Wales found that honey offers a number of benefits as reported by Magget K in her article (2007). The researcher suggests that honey seems to be especially indicated when wounds become infected or fail to close or heal.²⁷

Yapucu Gunes (2007) University of Turkey conducted a study to compare the effect of a honey dressing versus an ethoxy-diaminoacridine plus nitrofurazone dressing in patients with pressure ulcers. After 5 weeks, scores showed that healing among subjects using a honey dressing was approximately 4 times the rate of healing in the comparison group. The use of a honey dressing was found effective and practical.²⁸

Subrahmanyam (1991) reported that a randomised controlled trial in which honey was compared with silver sulfadiazine for efficacy as a dressing for burns. With silver sulfadiazine, the most widely used agent to prevent infections in burns, 17% of the patient had infections in the burns, whereas with honey 91% of wounds were sterile within 7 days.

Honey also gave a lower incidence of raised scars and contractures.²⁹

A prospective comparative study was conducted between honey dressing and povidone-iodine dressing for Wagner type II diabetic foot ulcers at International Islamic University Malaysia to compare the effect of honey with controlled dressing group (povidone iodine followed by normal saline). Surgical debridement and appropriate antibiotics were prescribed in all patients. It was concluded that honey dressing is a safe alternative dressing for Wagner grade II diabetic foot ulcers.³⁰

A comparative study was conducted at Medical Research Institute of New Zealand (MRINZ) on honey in the treatment of burns to determine the efficacy of honey in burn wound management. It was a systematic review with meta-analysis of randomised controlled trial, which

compared the efficacy of honey with a comparator dressing. Eight studies with 624 subjects were included in the meta-analysis. The outcome of the research study showed significantly greater efficacy for honey compared with alternative dressing treatments for superficial or partial thickness of burns.³¹

A comparative study was conducted to assess the effect of medical grade honey with conventional treatments on the healing rates of wound healing by secondary intention at Aintree University Hospitals, Liverpool, UK. The sample size was 105 patients involved in a single centre open label randomised controlled trial in which patients received either a conventional wound dressing or honey. These results support the proposition that there are significant clinical benefits from using honey in wound care.³²

A study was conducted on honey as a topical treatment for wounds at clinical trials research unit, University of Auckland, New Zealand, to determine whether honey increases the rate of healing in acute wounds (burns, lacerations and other traumatic wounds) and chronic wounds (venous ulcers, arterial ulcers, diabetic ulcers, pressure ulcers and infected surgical wounds). In chronic wounds, two trials evaluated the effect of honey in venous leg ulcers and one trial in pressure ulcers, two trials recruited people with mixed groups of chronic or acute wounds. Thus, it was concluded that Honey improve healing times in mild-to-moderate superficial and partial thickness burns compared with some conventional dressings.³³

A randomised comparative study was conducted on honey and sugar at Beit CURE International Hospital, Blantyre, South East Africa. With an objective to investigate whether there is a difference between the efficacy of honey and sugar as wound dressings. This study concludes that honey appears to be more effective than sugar in reducing bacterial contamination and promoting wound healing and slightly less painful than sugar during dressing changes and motion.

Non-randomised prospective study was conducted on impact of Manuka honey dressings on the surface pH of chronic wounds at Research Centre, Faculty of Nursing and Midwifery, Royal College of Surgeons Ireland (RCSI), Dublin, Ireland. The use of Manuka honey dressings was associated with a statistically significant decrease in wound pH and a reduction in wound size.³⁴

A study was conducted at Woodfield Retirement Village, Haberfield, New South Wales, Australia, on use of honey for the treatment of pressure ulcers. A trial on honey alginate on two elderly males was done in a nursing home who were suffering from pressure ulcers (one on the ankle and one on the sacral region) to evaluate its effectiveness to the current wound management practices in nursing homes. The use of honey resulted in a rapid and complete healing of both wounds. In addition, the antibacterial activity of honey had a deodorising effect on the wounds and its anti-inflammatory actions helped to reduce the level of pain. Similar healing results are also being observed in other patients with pressure-induced ulcers and as a result honey is now being used as the 'standard' treatment for chronic wounds.

A study was conducted on systematic review of honey uses and its potential value within oncology care at School of Nursing, Social Work and Midwifery, University of Manchester, Manchester, UK. To synthesise the evidence regarding honey's role in healthcare and to identify whether this evidence applies more specifically to cancer care. From the study, it was concluded that honey found to be a suitable alternative for wound healing, burns and various skin conditions and to potentially have a role within cancer care. In the cancer setting, honey maybe used for radiation-induced mucositis, radiotherapy-induced skin reactions, hand and foot skin reactions in chemotherapy patients and for oral cavity and external surgical wounds.

An in vitro study was conducted in Academic Department of Biomedical Sciences, Faculty of Health Sciences, University of Stellenbosch, South Africa, to establish whether honey and silver-impregnated dressings used by wound-healing practitioners are cytotoxic in vitro to human skin keratinocytes and dermal fibroblasts. Human keratinocyte and fibroblast tissue cultures were established in vitro. From the study, it is concluded that the honey-based product showed excellent cytocompatibility with tissue cell cultures compared with the silver dressing, which demonstrated consistent culture and cell toxicity.

A prospective, randomised, double-blind controlled trial study was conducted to compare honey and IntraSite Gel as wound healing agents. The outcome measures were healing times of shallow wounds and abrasions; side-effects; patient satisfaction with treatment; the cost-effectiveness. From the above, it was concluded that the average cost of treatment per patient was Rs. 0.49 with honey and Rs. 12.03 with IntraSite Gel. Also, there was no evidence of a real difference between honey and IntraSite Gel as healing agents, but honey is a safe, satisfying and effective healing agent. Natural honey is extremely cost effective.

A triple-blinded randomised prospective clinical trial-Women with caesarean section were randomly designated as drug (37 cases) and placebo (38 cases) groups. The drug group received local honey gel 25%, while the placebo group received similar free-honey gel on abdominal caesarean incision twice a day for 14 days. REEDA scale (redness, oedema, ecchymosis, discharge and approximation of wound edges) was used to assess wound healing. Redness, oedema and haematoma in the drug group were significantly lower on the 7th and 14th days. Conclusion was that honey was effective in healing the caesarean section incision. Using topical honey is suggested as a natural product with rare side effects in order to reduce the complications of caesarean wound.

MATERIALS AND METHODS

Study Design- Open label study.

Study Setting- Study is conducted in medical college, Trivandrum, which is a tertiary care centre. Patients are selected from orthopaedic and general surgical wards.

Aim of Study- To study the advantage of honey dressing over conventional saline dressing in the management of chronic ulcer.

Objective- To prove that the duration with which a chronic non-healing ulcer will become bacteriologically sterile and develop healthy granulation tissue is less with honey dressing compared to conventional saline dressing.

Study Period- One year extending from July 2014 to June 2015.

Study Population- Patients admitted in General Surgery and Orthopaedics Ward, MCH, Trivandrum, with chronic non-healing ulcers during this period. Saline dressing is given for the patients admitted in the first 6 months of study. Honey dressing is given for the next 6 months of study.

Sample Size- Patients who meet the inclusion criteria was selected during the study period. For the first 6 months of study, saline dressing was given. For the next 6 months of study, honey dressing was given.

Inclusion Criteria

All patients of age group 13-80 years included in this study are classified according to the grade of ulcer by Wagner classification and EPUAP classification for pressure sores.

1. All grades included except those in which gangrene has already occurred.
2. Diabetic ulcer.
3. Traumatic ulcer.
4. Venous ulcer.
5. Ulcer due to povidone.

Exclusion Criteria

1. Fistulas to organs or cavities.
2. Discharging sinus from bone.
3. Malignancy.
4. Exposed blood vessels.
5. Tuberculous ulcer.

Study Procedure- The study was conducted after obtaining clearance from the research and ethical committee. The author has obtained informed written consent from the patients after explaining to them about the procedure and purpose of study.

On admission, pus culture and sensitivity was taken for both groups.

Arterial Doppler study to assess the vascularity of the limb was done in both groups.

X-ray of the affected region was taken to rule out osteomyelitis.

If abundant slough was present, debridement of wound was done in both groups.

One group of patients were given conventional saline dressing, i.e. cleaning the ulcer with saline, debridement if abundant slough was present, covering the wound skin with sterile surgical pads after cleaning the surrounding skin with povidone-iodine. Alternate day cleaning and dressing was done. Oral or parenteral antibiotics were also given.

Other group was given honey dressing. Wound was cleaned with saline. Debridement done if abundant slough

was present. Honey poured over the ulcer to fill three quarter of the depth. Gauze was placed over the ulcer, then dry sterile surgical pad was applied after cleaning the surrounding area with povidone-iodine. Antibiotics were also given orally or parenterally and alternate day dressing was given.

Materials Used for Study

- Honey (government supply bottled honey)- Honey used in this study is sterilised by heating at 65 degree Celsius for 5 minutes. It is obtained from College of Agriculture, Vellayani.
- Sterile surgical gauze.
- Sterile surgical pad.
- Normal saline.

Assessment of Outcome- Done at the end of 1st week.

Factors assessed-

1. Pus culture and sensitivity- For presence or absence of organism.
2. Nature of discharge- Whether purulent or serous.
3. Appearance of healthy granulation tissue.

The factors used in comparison of saline dressing and honey dressing include-

- Pus culture before and after dressing.
- Outcome plan- Whether patient was discharged, amputated or grafted. Grafting was done in patients with healthy granulation tissue and minimal serous discharge. In those patients whose wound culture was sterile, but not fit for grafting were discharged for dressing in local hospital and asked to review later. Amputation was done in those patients who had spreading infection with a nonviable limb.
- Duration of hospital stay.
- Whether there is any difference of outcome in different distribution of grades of ulcer.
- Whether there is any difference of outcome in patients with vascular compromise, which is found out by Doppler ultrasound.
- Whether there is any difference of outcome in patients with diabetes mellitus.

Statistical Analysis- Clinical data obtained from the study was analysed using SPSS software. Mean, median and mode was calculated for categorical data. The tests of significance used include Student's t-test and Chi-square test. Level of significance is p value <0.05.



Figure 1. Grade 2 Diabetic Ulcer Leg Healed with 3 Weeks of Honey Dressing



Figure 2. Venous Ulcer Granulated After 2 Weeks of Honey Dressing (SSG was Done Later)

OBSERVATION AND ANALYSIS

This study was conducted in male and female surgical wards of T.D. Medical College, Alappuzha, among patients admitted with chronic non-healing ulcer. The patients who were admitted in first 6 months of study were treated using conventional saline dressing and in the second six months honey dressing was used. The different tests used for statistical analysis of the data include Student's t-test and Chi-square test. Both epidemiological as well as clinical data was studied.

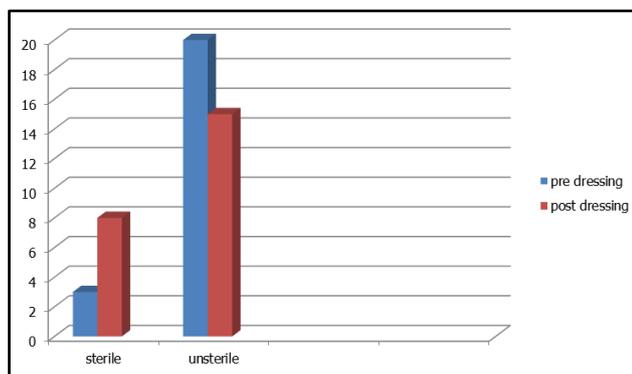
Age Distribution- According to inclusion criteria, patients between age of 13-80 were included in study. People included in the study were categorised under 4 groups with regard to age, i.e. those who are- <40 years, 40-49 years, 50-59 years and >60 years.

Majority of the patients that is 94% of patients are between the age group 40-59. In none of these groups, the difference in number of patients between honey dressing and saline dressing were statistically significant (p value >0.05).

Mean age of patient included under honey dressing was 60.29 with a standard deviation of 6.7 and median being 61. Mean age of patient dressed with normal saline is 59.34 with a standard deviation of 7.27. Difference in means of the two groups was proven not to be statistically significant by Student's t-test (t value=0.479, p value=0.316).

Analysis of Culture Sterility- Pre and Post Honey Dressing-

- Swab was taken from ulcer site and was sent for culture and sensitivity to our microbiology lab, both before dressing and 7 days after dressing.
- It was observed that honey dressing turned 92% of cultures sterile. Chi-square value was calculated as 35.9 and p value 0.0001. Hence, the effect of honey dressing on turning unsterile cultures sterile was proved to be highly significant.
- Normal saline could not turn much dressing unsterile significantly. Chi-square test value is 2.98 and 'p' value >0.05 (0.08).



Graph 1. Analysis of Culture Sterility- Pre and Post Honey Dressing

Analysis of Outcome of Honey Dressing- 63% of patients who were dressed with honey could be grafted during their hospital stay, whereas only 17% of normal saline dressing group could be grafted. This difference was proven to be statistically significant with a p value of 0.004 (Chi-square=10.77), thus confirming that honey dressing helps in early grafting of the patient and hence superior to conventional saline dressing.

Analysis with Regard to Duration of Hospital Stay- Average duration of hospital stay in those dressed using normal saline was found to be 31.3 with standard deviation 6.5 and median being 30 and mean duration in those dressed with honey was found to be 25.77 with standard deviation 5.27, median being 26. Difference in average duration of hospital stay in both groups was proven to be highly statistically significant with a p value of 0.000934 (t value=3.29).

Duration of hospital stay was further divided into-

- 7-13 days,
- 14-21 days,
- 22-28 days,
- 29-35 days,
- >35 days.

Among these groups, 21 of total 50 (42%) belonged to 22-28 days group. Another observation was that only 1 among the honey dressing group stayed for more than 35 days, whereas 7 among the normal saline group stayed in hospital for more than 35 days. This difference in both groups was studied using Chi-square test and was found to be statistically significant with a p value of 0.018 (Chi-square value=11.8).

Comparison of Saline and Honey Dressing with Regard to Grades of Ulcer- Majority of the patients belonged to grade 2 and 3 ulcer in both study groups. This difference in distribution of grades of ulcer in both groups were proven to be statistically insignificant with a p value >0.05 (Chi-square=2.29, p value=0.512).

This confirms that better outcome in honey dressing like less mean duration of hospital stay and possibility of early grafting is not affected by the grade of ulcer. Thus,

superiority of honey dressing over conventional saline dressing is proved irrespective of grade of ulcer.

Doppler Findings in Study Population- For each patient enrolled in the study, a Doppler ultrasound was also performed from our Radiodiagnosis Department to look for presence of vascular compromise in these patients.

Doppler Findings in Saline Dressing Group- Out of the total 23 patients, 11 had a normal Doppler study, whereas 12 patients had evidence of vascular compromise.

Doppler Findings in Honey Dressing Group- 17 among the 27 patients had normal Doppler scan, whereas 10 had evidence of vascular compromise according to Doppler. 52% of saline dressing group and 37% of honey dressing group had evidence of vascular compromise in Doppler study. When tested using Chi-square test, it was found that the difference in number of vascular compromised patients in both study groups was not statistically significant with a p value >0.05 (Chi-square=1.15; p value=0.28).

Distribution of Diabetes Mellitus in Study Population- Among 50 patients included in the study, 20 patients were diabetic. 47.8% of patients in whom saline dressing was used and 59.2% of patients in whom honey dressing was used were nondiabetic. This difference in distribution of number of diabetic patients were proved not significant with p value >0.05.

REFERENCES

- [1] Shah JB. The history of wound care. Journal American College of Certified Wound Specialists 2011;3(3):65-66.
- [2] Molan PC. Honey as a topical antibacterial agent for treatment of infected wounds. World Wide Wounds 2001;49(7-8):96.
- [3] Templeton S. A review of the use of honey in wounds. ACCNS J Community Nurses 2002;7(1):13-14.
- [4] Cooper R. A review of the evidence for the use of topical antimicrobial agents in wound care. World Wide Wounds 2004;58:46-48.
- [5] Gethin GT, Cowman S, Conroy RM, et al. The impact of Manuka honey dressings on the surface of chronic wounds. Int Wound J 2008;5(2):185-194.
- [6] Crane E. A Book of honey. Charles Scribner's Sons. New York: Journal of Apicultural Research 1980;27(4):244.
- [7] Babacan S, Rand AG. Characterization of honey amylase. Journal of Food Science 2007;72(1):50-55.
- [8] Giri KV. The chemical composition and enzyme content of Indian honey. Madras Agricultural Journal 1938;26(2):68-72.
- [9] White JW, Subers MH, Schepartz AI. The identification of inhibine, the antibacterial factor in honey, as hydrogen peroxide and its origin in a honey glucose-oxidase system. Biochim Biophys Acta 1963;73:57-70.

- [10] Babacan S, Pivarnik LF, Rand AG. Honey amylase activity and food starch degradation. *Journal of Food Science* 2002;67(5):1625-1630.
- [11] Babacan S, Rand AG. Purification of amylase from honey. *Journal of Food Science* 2005;70(6):1625-1630.
- [12] Allen KL, Molan PC, Reid GM. A survey of the antibacterial activity of some New Zealand honeys. *J Pharm Pharmacol* 1991;43(12):817-822.
- [13] Agren MS, Eaglstein WH, Ferguson MW, et al. Causes and effects of the chronic inflammation in venous leg ulcers. *Acta Derm Venereol (Stockh)* 2000;210:3-17.
- [14] Ahmed AK, Hoekstra MJ, Hage JJ, et al. Honey-medicated dressing: transformation of an ancient remedy into modern therapy. *Ann Plast Surg* 2003;50(2):147-148.
- [15] Bromfield R. Honey for decubitus ulcers. *JAMA* 1973;224(6):905.
- [16] Kwakman PH, te Velde AA, de Boer L, et al. How honey kills bacteria. *FASEB J* 2010;24(7):2576-2582.
- [17] Kwakman P, te Velde AA, de Boer L, et al. Two major medicinal honeys have different mechanisms of bactericidal activity. *PLoS One* 2011;6(3):e17709.
- [18] Leong AG, Herst PM, Harper JL. Indigenous New Zealand honeys exhibit multiple anti-inflammatory activities. *Innate Immun* 2012;18(3):459-466.
- [19] Lin SM, Molan PC, Cursons RT. The controlled in vitro susceptibility of gastrointestinal pathogens to the antibacterial effect of Manuka honey. *Eur J Clin Microbiol Infect Dis* 2011;30(4):569-574.
- [20] Maddocks SE, Lopez MS, Rowlands RS, et al. Manuka honey inhibits the development of streptococcus pyogenes biofilms and causes reduced expression of two fibronectin binding proteins. *Microbiology* 2012;158(Pt 3):781-790.
- [21] Majtan J, Majtanova L, Bohova J, et al. Honeydew honey as a potent antibacterial agent in eradication of multidrug-resistant *Stenotrophomonas maltophilia* isolates from cancer patients. *Phytother Res* 2011;25(4):584-587.
- [22] Merckoll P, Jonassen T, Vad ME, et al. Bacteria, biofilm and honey: a study of the effects of honey on planktonic and biofilm embedded chronic wound bacteria. *Scand J Infect Dis* 2009;41(5):341-347.
- [23] Molan PC. The antibacterial activity of honey. The nature of the antibacterial activity. *Bee World* 1992;73(1):5-28.
- [24] Molan PC. The role of honey in the management of wounds. *J Wound Care* 1999;8(8):415-418.
- [25] Efem SE. Clinical observations on the wound healing properties of honey. *Br J Surg* 1988;75(7):679-681.
- [26] Lay-Flurrie K. Honey in wound care, effects, clinical application and patient benefit. *Br J Surg* 2008;17(11):S30-S36.
- [27] Megget K. Honey speeds and wound healing. *International Journal of Clinical Practice* 2007;19(31):57-61.
- [28] Yapucu Güneş U, Eşer I. Effectiveness of a honey dressing for healing pressure ulcers. *J Wound Ostomy Continence Nurs* 2007;34(2):184-190.
- [29] Subrahmanyam M. Topical application of honey in treatment of burns. *British Journal of Nursing* 1991;78(4):497-498.
- [30] Shukrimi A, Sulaiman AR, Halim AY, et al. A comparative study between honey and povidone iodine as dressing solution for Wagner type II diabetic foot ulcers. *Med J Malaysia* 2008;63(1):44-46.
- [31] Wijesinghe M, Weatherall M, Perrin K, et al. Honey in the treatment of burns: a systematic review and meta-analysis of its efficacy. *N Z Med J* 2009;122(1295):47-60.
- [32] Robson V, Dodd S, Thomas S. Standardized antibacterial honey (Medihoney) with standard therapy in wound care: randomized clinical trial. *J Adv Nurs* 2009;65(3):565-575.
- [33] Mphande AN, Killowe C, Phalira S, et al. Effects of honey and sugar dressings on wound healing. *J Wound Care* 2007;(7):317-319.
- [34] van der Weyden EA. Treatment of a venous leg ulcer with a honey alginate dressing. *Br J Community Nurs* 2005;Suppl:S21-S27.