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Original Research Article

Effectiveness of negative pressure wound therapy in the management of chronic diabetic ulcers: a prospective study

Dhruv Sharma, Biplav Singh*, K. S. Jaswal, Vishal Thakur, Vibhor Nanda, Rishi Nabh

Department of General Surgery, Indira Gandhi Medical College and Hospital, Shimla, Himachal Pradesh, India

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***Correspondence:**
Dr. Biplav Singh,
E-mail: biplavsingh.1@gmail.com

ABSTRACT

Background: Chronic ulcers in patients with diabetes are complex and treatment is often difficult. At the moment, negative pressure wound therapy (NPWT) is widely used for the treatment of several types of wounds. Nevertheless, the clinical evidence to support the application of this dressing in chronic diabetic ulcers is scarce. The aim of this study was to evaluate the efficacy of NPWT to treat chronic diabetic ulcers.
Methods: Prospective time bound comparative study. Diabetic patients aged 18 years or older with an ulcer were assigned to treatment with NPWT. Primary efficacy end point was time in reaching complete ulcer closure. A size of sample of 15 patients was used. NPWT was prepared with a polyurethane foam dressing, a Silicone catheter, a transparent adhesive drape and continuous negative pressure of 125 mm Hg. The wound was treated for cycles of 5 days and evaluated at every dressing change. Descriptive and analytical statistics were used.
Results: There were 15 patients, with a mean age of 54.4 years (73.3% men). The average time to complete ulcer closure was (41.2 [8.5] days).
Conclusions: NPWT is an effective modality of treatment of chronic diabetic ulcers with early appearance of granulation tissue and faster rates of overall complete wound closure.

Keywords: Chronic, Diabetic, NPWT, Negative pressure wound therapy, Wound

INTRODUCTION

Over 150 million people worldwide affiliated by diabetes mellitus live in the developing countries. The lifetime risk for ulcers in people with diabetes has been estimated to be 15%.[1] The incidence of diabetic infections is similar to that of diabetes in various ethnic groups and most frequently affect elderly patients. There are no significant differences between the sexes. Foot ulcer occur in 15% of all diabetic patients and up to 3% will have lower limb amputations during their life time. The overall risk of amputation is increased by 15 folds in diabetics than non-diabetic population.[3] A multi factorial etiopathogenesis consisting of decreased arterial pressure, neuropathy, abnormal foot mechanics, and increased susceptibility to infections is commonly involved.

India is considered the "diabetic capital of the world" 22, alone currently counts over 35 million people harboring diabetes. This is estimated to touch 73.5 million by 2025. In 2010, India (31.7 million) topped the world with the highest number of people with diabetes mellitus followed by China (20.8 million) with the United States (17.7 million) in second and third place respectively. It is predicted that by 2030 diabetes mellitus may afflict up to 79.4 million individuals in India, while China (42.3 million) and the United States (30.3 million) will also see significant increases in those affected by the disease.

The management of diabetic ulcers are poorly defined in contrast to other complications such as nephropathy, hyperlipidaemia and retinopathy and requires a multidisciplinary team approach. This strategy has been shown to reduce both the incidence of major leg amputation (by 40% or more), and the duration of in-patient admissions for the treatment of diabetic ulceration.[2]

Prevention is the first step towards solving diabetic foot problems. An ankle is lost to diabetes somewhere in the world every 30 seconds and up to 85% of all amputations in diabetes should be preventable. Diabetes is now the most common cause of Charcot neuro-arthropathy in Western countries, another condition that should be generally preventable.[4]

Wounds and their management are fundamental to the practice of surgery. Dressings are applications for wounds, burns, ulcers and other skin lesions to provide the ideal environment for wound healing. Standard wound management consists of initial surgical debridement, a rapid and effective technique to remove devitalised tissue. Then either wet to moist gauze dressing or occlusive dressings, which needs to be changed frequently to cover the wound. These dressings are relatively inexpensive, readily available and easy to apply. However there are some disadvantages, non-selective debridement with dressing removal, possible wound desiccation, pain, and the need for frequent dressing changes. Other approaches include topical enzymes, bio-surgical therapy and topical antimicrobial agents.

It was in 1995, Vacuum Assisted Closure Therapy or VAC the revolutionary wound closure system - was developed and launched by KCI USA San Antonio, Tx, USA founded in 1976 by Dr. Jim Leininger - an emergency room physician. In the past few years, negative pressure wound dressing therapy (NPWT) or VAC has emerged as a treatment of these complex wounds. 9,11-13 The clinical perception, case series, small cohort and weekly powered randomized controlled trials constitute a substantial number of publications but with an overall low amount of evidence.

Negative pressure wound therapy (NPWT) is a relatively new technology with applications in a variety of difficult to manage acute and chronic wounds. It is known by many pseudonyms - NPWD (negative pressure wound dressing), TNP (topical negative pressure), SPD (sub-atmospheric pressure dressing), VST (Vacuum Sealing Technique), SSS (Sealed Surface wound suction). NPWT is a non-invasive technique by which negative pressure is delivered uniformly to a wound. It involves the application of open cell foam to a suitable wound, adding a seal of adhesive drape and then the application of sub atmospheric pressure to the wound in a controlled way. The system allows the arteriole to dilate, so increasing the effectiveness of local circulation, which assists in the proliferation of granulation tissue. The technique removes excessive fluid from the area, so reducing edema. The therapy is both simple and easy to use. It is a system that should be considered when other more conventional methods of wound management have failed. NPWT provides sub atmospheric pressure medical grade polyurethane, polyvinyl alcohol or collagen base foam dressing that is fitted at the bedside to the appropriate size for each wound. The dressing is covered with an adhesive drape to create an airtight seal. An evacuation tube embedded in the foam is connected to a fluid collection canister contained within a portable computer controlled vacuum machine. The machine creates sub atmospheric (negative) pressure at the wound interface surface. The NPWT can provide either continuous or intermittent negative pressure within a range of pressure options (-25 mmHg to -200 mmHg) to provide optimal fluid level, tissue tension, and capillary flow to enhance vascular perfusion. Depending on the type of wound, the negative pressure initially may be applied in a continuous mode for 48 hours to remove larger amounts of fluid and subsequently, an intermittent mode may be used to provide a more aggressive stimulus for promoting granulation.

Very limited data is available on the effectiveness of NPWT in the treatment of chronic diabetic ulcers and this study aims to establish its role in regards to time to appearance of granulation tissue, time to complete granulation of wound and time to complete ulcer closure.

METHODS

Study population

Patients admitted in the Department of General Surgery, IGMC, Shimla between July, 2015 and June, 2016 with chronic diabetic ulcers. Inclusion criteria were chronic non-healing wounds in a diabetic patient. Exclusion criteria included ulcers associated with malignancy, collagen vascular diseases, extensive osteomyelitis or charcots arthropathy, pregnancy, and medications like corticosteroids, immunosuppressive, chemotherapy.

Study design and conduct

The study was a prospective time bound study conducted over a period of 1 year (July 2015 to June 2016). All patients were admitted under the department of General Surgery, IGMC. History, relevant investigations and local examination of wound was done in all patients. This was followed by thorough initial wound irrigation and debridement of the diabetic foot in all patients. NPWT dressing was then applied to the patients. The NPWT dressing was changed every 5 days and repeated debridement's done as and when required. Wound characteristics were recorded at every dressing change. Patients were treated until complete ulcer closure by either direct closure/secondary closure/SSG/Flap. The NPWT system included a sterile non-adherent nanocrystalline silver gauze, gauze foam, transparent polyurethane adhesive dressing, paper tape, silicon drain with connecting tube, 500 ml canister with absorbent polymer, and negative pressure generating unit. Negative pressures of between -125 mmHg and -150 mmHg was maintained for all patients.

Follow up and efficacy assessment

Patients were examined at every dressing change until wound closure. The primary efficacy end point was complete wound closure rate. Complete wound closure was defined as skin closure (100% reepithelization of wound) without drainage or dressing requirements. Secondary end points included time to appearance of granulation tissue, reduction of ulcer size, overall duration of hospital stay.

Sample size

A total of 15 patients were included.

Figure 1: Negative pressure wound therapy applied to a diabetic wound.

RESULTS

Thirty subjects were selected. The average global age was 54.4 years (37-74 year-old). Eleven patients (73.3%) were male. Nine subjects (70%) were smokers, five subjects (33.3%) presented with deranged lipid profile, and three subjects (20%) presented high blood pressure controlled with only one drug.

The average HbA1C level was 9.48 (SD = 2.2). Most common organism isolated on wound cultures was *E. coli* (8 patients, 53.3%).

There were no statistically significant differences between the biodemographic variables and the clinical variables of the study population.

All subjects attained complete ulcer closure and 2 cases (13.3%) required split skin grafting for wound closure while 4 patients (26.6%) attained wound closure by secondary healing. There were no losses or interruptions of treatment in study subjects. The average time of complete wound healing was 41.2 (SD = 8.5) days.

None of the subjects presented with bleeding, while there was one subject that presented pain. There were no re-amputations, asepsis or mortality in this series.

Figure 2: Wound at presentation to hospital.

Figure 3: Wound after initial debridement and following 1st cycle NPWT.

Figure 4: Wound after 3rd cycle of NPWT.

Figure 4: Wound after 5th cycle of NPWT.

Figure 5: Completely healed wound at 3 months follow up.

Table 1: Clinical and bio - demographical characteristics of study population (n = 15).

Demographical characteristics		
Age	Mean = 54.4 years	SD = 8.97
Sex	Male = 11 subjects	73.3%
	Female = 4 subjects	26.6%
Smokers	9 subjects	60.0%
Arterial Hypertension	3subjects	20.0%
Glycated Hb (HbA_{1c})	Mean = 9.48	SD = 2.2
Dyslipidemia	5 subjects	33.3%
Time to appearance of granulation tissue	Mean = 15.1 days	SD = 5.4
Time to appearance of 100% granulation tissue	Mean = 25.1 days	SD = 8.4
Time to complete wound closure (days)	Mean = 41.2 days	SD = 8.5
Skin Closure by Split Skin Graft	2 subjects	13.3%
Secondary Healing	4 subjects	26.6%
Direct closure	9 subjects	60.0%
Complications	Pain = 1	6.6%
	Bleeding = none, Infection = none, allergy = none	0%

DISCUSSION

The present study measures as a result variable the time in reaching complete wound closure in chronic diabetic ulcers with the use of negative pressure wound therapy. This study shows that first appearance of granulation, time to appearance of 100% granulation tissue and time to complete ulcer healing, all were attained rapidly in the study population (15.1, 25.1, 41.2 days with SD of 5.4, 8.4, 8.5).

Time to complete ulcer healing by conventional dressings according to multiple RCTs and prospective studies range between 59 to 133 days.[7-9]

NPWT is an effective treatment modality in chronic diabetic ulcers as shown in our study with reduction in duration of complete ulcer healing by at least 25%.

This study is in agreement with multiple other studies that state that NPWT is superior to conventional dressings for the management of Chronic diabetic foot ulcers.[10,14-16]

The explanation of the success of the use of the NPWT is found in the work of Argenta and Morykwas, that postulated that this new treatment technique removes excess interstitial liquid, increases angiogenesis, decreases bacterial colonization, and increases the formation of granulated tissues as a response to the stimulus of the mechanical forces created by the negative pressure transmitted through the sponge. It is an already proven theory that the excess of liquid is not removed adequately from the wound after an operation act like physical and chemical impediments to the closure of the wound.[6]

Mechanism of action of NPWT

Macrodeformation

Macrodeformation refers to induced wound shrinkage caused by collapse of the pores and centripetal forces exerted onto the wound surface by the foam.[13,14] Polyurethane ether foams exposed to 125 mm Hg suction can decrease the foam volume by approximately 80% and result in a substantial decrease in wound surface area.

Microdeformation

Microdeformation refers to the physical changes that occur on the micron-to-millimeter scale.[14] In NPWT, cells are subjected to shear and hydrostatic pressure from extracellular fluid, stretch and compression from their surrounding matrix, and the ubiquitous pull of gravity. Microdeformation, in essence, is the morphologic result of these integrated mechanics. Cell shape has been demonstrated to be a determinant of cellular function. Therefore, changes in cellular functions can be initiated by these dynamic physical inputs.

Fluid removal

Depending on the underlying pathology, chronic wounds and edema are often concomitant, as is the case with diabetic ulcers.[15] Excess fluid buildup is commonly accepted as a contravening factor in healing, partly owing to the compressive effect it can exert on local cells and tissues. The evacuation of fluid reduces microvascular compression, increasing perfusion and allowing faster wound healing. Toxins from the wound, bacteria, and exudate can also be removed with the fluids. NPWT also induces a gradual increase in lymphatic density at wound edges, thereby improving drainage.

Alteration of the wound environment

The PU drape is semi occlusive thereby restricting evaporative water losses while remaining impermeable to proteins and microorganisms thereby maintaining a favourable and moist wound. In comparison with conventional therapies, the reduced number of required dressing changes in NPWT also can add to patient comfort.

Modulation of inflammation

During the inflammation phase, NPWT removes infiltrating leukocytes while simultaneously inducing inflammation.[15] These findings are supported by the evidence of increased wound exudate cellularity (particularly leukocytes and erythrocytes) and increased gene expression of leukocyte chemoattractants, such as IL-8 and CXCL5, in wounds treated with NPWT.

Cellular responses

NPWT generates a complex mechanical environment at the wound surface. The associated cell stretch caused by NPWT induce cell proliferation, thereby promoting wound healing. There is cellular spherization of unhealthy cells followed by apoptosis

Angiogenesis

Negative Pressure Wound Therapy induces wound site local hypoxia and stimulation of Vascular Endothelial Growth Factor with subsequent angiogenesis.[18] It is not surprising that NPWT demonstrates increased microvessel density during chronic wound treatment. NPWT stimulates wound-site angiogenesis through a number of mechanisms: mechanical stimulation (microdeformation), removal of factors inhibiting angiogenesis, and upregulating proangiogenic factors. Blood vessel dilation is also observed.

Granulation tissue formation

The result of endothelial cell and fibroblast ingrowth at the wound surface, that is, granulation tissue, which also includes the ancillary ECM and migratory macrophages, represents a specialized stroma designated for repair. In the proliferation phase, effects of NPWT include robust tissue granulation, cell proliferation, and blood vessel sprouting.[19]

Alterations in bioburden

The effect of NPWT in this regard remains controversial with some studies suggesting a decrease in local bioburden while others that state no significant difference.[21,23,24] The effect of NPWT on bacterial load remains an area to further explore, particularly in terms of the variety of responses that may be elicited by different strains. This study has some limitations in the form of a smaller sample size and lack of a control group and that it was a prospective study, which decreases the level of evidence. So further randomized controlled trials are needed to confirm the results of this study.

CONCLUSION

This study shows that vacuum assisted closure is an effective method of treatment and more effective than conventional dressings in the management of chronic diabetic ulcers.

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