DIABETIC FOOT & ANKLE

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CLINICAL RESEARCH ARTICLE

# Vacuum-assisted closure versus conventional dressings in the management of diabetic foot ulcers: a prospective case–control study

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***Objective***: To compare the effectiveness of vacuum-assisted closure (VAC) versus conventional dressings in the healing of diabetic foot ulcerations (DFUs) in terms of healing rate (time to prepare the wound for closure either spontaneously or by surgery), safety, and patient satisfaction.

***Methods***: Randomized case–control study enrolling 56 patients, divided into two groups. Group A (patients treated with VAC) and Group B (patients treated with conventional dressings), with an equal number of patients in each group. DFUs were treated until wound closure, either spontaneously, surgically, or until completion of the 8-week period.

***Results***: Granulation tissue appeared in 26 (92.85%) patients by the end of Week 2 in Group A, while it appeared in 15 (53.57%) patients by that time in Group B. 100% granulation was achieved in 21 (77.78%) patients by the end of Week 5 in Group A as compared to only 10 (40%) patients by that time in Group B. Patients in Group A had fewer number of positive blood cultures, secondary amputations and were satisfied with treatment as compared to Group B.

***Conclusion***: VAC appears to be more effective, safe, and patient satisfactory compared to conventional dressings for the treatment of DFUs.

Keywords: *diabetic foot ulcer*; *infections*; *conventional dressings*; *vacuum-assisted closure*; *wound closure*

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Foot complications are a major cause of hospitalization in patients with diabetes mellitus (DM), which consumes a high number of hospital days because of multiple surgical procedures and prolonged length of stay (1). Patients with DM have up to a 25% lifetime risk of developing a foot ulcer (2), which precedes amputation in up to 85% of cases (3). A mainstay of diabetic foot ulcer (DFU) therapy is debridement of all necrotic, callus, and fibrous tissue (4, 5), with a primary goal to obtain wound closure. The management of the DFU is largely determined by its severity (grade), vascularity of the limb, and the presence of infection (6–8).

The optimal topical therapy for DFU remains ill-defined. Saline-moistened gauze has been the standard method; however, it has been difficult to continuously maintain a moist wound environment with these dressings. Subsequently, various hydrocolloid wound gels, growth factors, enzymatic debridement compounds, hyperbaric oxygen therapy, cultured skin substitutes, and other wound therapies have been advocated. All of these therapies are associated with significant expense and are being utilized in some situations without sufficient scientific evidence in favor of their efficacy (9).

Negative pressure wound therapy (NPWT) is a newer non-invasive adjunctive therapy system that uses controlled negative pressure, using vacuum-assisted closure (VAC) device, to help promote wound healing by removing fluid from open wounds, preparing the wound bed for closure, reducing edema, and promoting formation and perfusion of granulation tissue. NPWT can be used to treat Charcot neuroarthropathy wounds produced as a result of neuropathy and deformity, following debridement of infection or amputation, and in reconstructive soft tissue and osseous procedures (10). The use of

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sub-atmospheric pressure devices, available commercially as VAC devices, has been shown to be an effective way to accelerate healing of various wounds (11–14).

The data available on the role of NPWT for the management of DFU is limited. Therefore, we conducted a study to compare the effectiveness of VAC with conventional dressings in the healing of DFU, in terms of: 1) healing rate (time to prepare the wound for closure either spontaneously or by surgery), 2) safety, and 3) patient satisfaction.

## Methods and materials

This study was conducted in the departments of plastic surgery and endocrinology at a tertiary care hospital in North India. It was a randomized case–control study to compare the effectiveness of VAC with conventional dressings in the healing of DFU. The study population included patients with DM aged 20–70 years, with stage 2 or 3 DFU (as defined by Wagner's classification (15), randomized either to Group A (patients treated with VAC) or Group B (patients treated with conventional dressings), with an equal number of patients in each group ($n = 28$). Patients aged $< 20$ or $> 70$ years, pregnant or nursing mothers, patients with foot ulcers other than diabetes, osteomyelitis of the underlying bone, peripheral vascular disease, comorbidities involving respiratory, cardiovascular or other systems of the body, were not included. Similarly, people on medications, such as corticosteroids, immunosuppressive agents or chemotherapy, were also not included. A detailed history, clinical examination and relevant investigations were performed in all patients. An institutional ethical committee approved the study.

Before starting the treatment, patients were made to understand in their local language and informed consent was obtained before randomizing into the two groups. Group A composed of patients with an even hospital medical record number and Group B composed of patients with an odd hospital number. Wounds of all the patients included in the study underwent sharp surgical debridement initially and during subsequent dressing change to remove necrotic tissue and slough. After debridement in the emergency operation theatre, a foam-based dressing was applied over the wounds of the study group patients under all aseptic conditions. The dressing was covered with an adhesive drape to create an airtight seal. An evacuation tube embedded in the foam was connected to a vacuum and sub-atmospheric (negative) pressure was applied within a range of 80–125 mmHg on a continuous basis for 72 hours. The control group received once daily saline soaked gauze dressing. Oral analgesics were administered to all of the patients at the time of changing the dressing. After every 3 days, cultures were taken from the base of the ulcer to assess for the bacterial flora. Blood cultures were also taken regularly from both groups. Standard antibiotic regimens were administered to all patients, which consisted of broad-spectrum antibiotics initially and later guided by the culture sensitivity reports. Ulcers were treated until the wound was closed spontaneously, surgically or until completion of the 8-week period, whichever was earlier. Blood glucose levels were monitored strictly during treatment and controlled by appropriate doses of insulin. After wound closure, patients were followed on a regular basis. Patients who were discharged from the hospital after wound closure were followed weekly, then bi-weekly, followed by monthly and then every 2 months.

Treatment outcome and patient satisfaction was assessed in terms of time taken for wound closure, the number of antibiotics used and the need for amputation. Treatment success was defined as wound closure within a period of 8 weeks and failure, as inability of wound closure within 8 weeks. Patient satisfaction was considered to be excellent, if wound closure occurred before 8 weeks and needed only one antibiotic during treatment; very good, if the wound closed before 8 weeks and needed two antibiotics; good, if the wound closed during Week 8 or if amputation was needed of one or more digits and; unsatisfactory, if the wound did not close within the treatment period or if the patient had either major or foot amputation.

Data were entered in SPSS 14 and analyzed. Categorical variables were analyzed by using the Pearson's Chi-square/Fishers exact test. Two groups were compared using Student's $t$-test. Results were expressed as $n$ (%). $p$-Values of $< 0.05$ were considered to be statistically significant.

## Results

A total of 56 patients with DM and grade 2–3 DFU were randomly assigned to either VAC or conventional dressing as per the pre-defined protocol with the end points of healing rate and patient satisfaction. Patients, either in VAC or conventional group, were matched for age, gender and duration of DM. The age of patients was between 47 and 64 years in Group A with a mean age of 53.79 years and between 48 and 62 years in Group B with a mean age of 54.57 years. Men constituted 35.71% and women around 64.28% in each group. All of the patients needed insulin for control of their DM and were initially managed with multiple subcutaneous insulin injections and followed by two doses of premixed insulin (30/70), once their glycemic control was achieved.

By Week 4, wound discharge disappeared in 44.4% of cases versus none in the control group. Wound discharge disappeared in two (7.4%) patients in Group A and seven (28%) in Group B in Week 8. Granulation tissue appeared in 26 (92.85%) patients by the end of Week 2 in Group A in contrast to 15 (53.57%) patients by that time in Group B. 100% granulation was achieved in 21 (77.8%)



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patients by the end of Week 5 in Group A as compared to only 10 (40%) patients by that time in Group B. Granulation tissue was defined in terms of gross appearance of ulcer (based on time to 76–100% formation in wound bed (Table 1).

The predominant organism cultured from the wounds in group A patients was *Pseudomonas aeruginosa* in 11 (39.3%) and *Acinetobacter baumannii* in four (14.3%) and that from the wounds in Group B was *P. aeruginosa* in 13 (46.4%) and *Klebsiella* in four (14.3%). Blood cultures were positive in 10 (35.7%) patients in Group A as compared to 14 (50%) patients in Group B. The predominant organisms from the blood cultures in Group A patients were *P. aeruginosa, Staphylococcus aureus,* and *Klebsiella pneumoniae* in four (40%), four (40%), and two (20%), respectively. In Group B patients, the predominant organisms from the blood cultures were *S. aureus* in four (28.6%) patients, *Escherichia coli* in four (28.6%), followed by *Pseudomonas* in two (14.3%), *Klebsiella* in two (14.3%) and *methicillin-resistant S. aureus* in two (14.3%). In most of the patients in Group A, the blood cultures were reported sterile in Week 1 after the application of VAC, as compared to Week 2 in Group B, after the initiation of treatment.

*Table 1.* Safety and efficacy of VAC over conventional dressings in the treatment of diabetic foot ulcers

| Patient characteristics | Cases | Controls | *p |
|---|---|---|---|
| Age (mean ± SD years) | 53.79 ± 5.45 | 54.57 ± 4.78 | 0.569 |
| 100% granulation (*N*) | 27 | 25 | 0.049 |
| Week 4 (%) | 18 (66.7%) | 7 (28%) | |
| Week 5 | 3 (11.1%) | 3 (12%) | |
| Week 6 | 2 (7.4%) | 2 (8%) | |
| Week 7 | 0 | 3 (12%) | |
| Week 8 | 0 | 2 (8%) | |
| Never during treatment | 4 (14.8%) | 8 (32%) | |
| Disappearance of wound discharge | | | 0.0001 |
| Week 2 | 2 (7.4%) | 0 (0.0%) | |
| Week 3 | 4 (14.8%) | 0 | |
| Week 4 | 12 (44.4%) | 0 | |
| Week 5 | 3 (11.1%) | 4 (16%) | |
| Week 6 | 1 (3.7%) | 5 (20%) | |
| Week 7 | 3 (11%) | 9 (36%) | |
| Week 8 | 2 (7.4%) | 7 (28%) | |
| Blood culture positivity | 10 (35.7%) | 14 (50%) | 0.187 |
| Change in wound size† | | | |
| Decrease | 22 (78.6%) | 15 (53.6%) | |
| No change | 5 (17.9%) | 10 (35.7%) | |
| Increase | 1 (3.6%) | 3 (10.7) | |
| Need for amputation | 1 (3.6%) | 3 (10.7) | 0.299 |
| Spontaneous wound closure | 3 (13.6%) | 1 (6.67%) | 0.503 |
| Endpoint reached | | | 0.048 |
| Yes | 22 (78.6%) | 15 (53.6%) | |
| No | 6 (21.4%) | 13 (46.4%) | |
| Patient satisfaction | | | |
| Excellent | 22 (78.6%) | 3 (10.7%) | 0.00 |
| Very good | 0 | 3 (10.7%) | 0.00 |
| Good | 0 | 9 (32.1%) | 0.00 |
| Not satisfied | | | 0.00 |

*Chi-square test; †measured as length (cm) × width (cm).

Wound size decreased in 22 (78.6%) patients in Group A as compared to 15 (53.6%) patients in Group B. The majority of wounds in Group A (81.8%) got closed in 5 weeks as compared to only 60% in Group B in 8 weeks. One patient required amputation in Group A as compared to three in Group B. The majority of wounds were closed by a split-thickness skin graft in both groups. Treatment was successful in 78.6% of patients in Group A and 53.6% of patients in Group B. Patient satisfaction was excellent in the majority of patients in Group A compared to those in Group B (Table 1).

## Discussion

NPWT has been advocated as a novel method in the healing of DFU by stimulating the chronic wound environment in such a way that it reduces bacterial burden and chronic interstitial wound fluid, increases vascularity and cytokine expression and to an extent mechanically exploiting the viscoelasticity of periwound tissues (16). VAC is generally well tolerated and, with few contraindications or complications, is fast becoming a mainstay of current wound care. Hence, we planned to use NPWT for the treatment and fast healing of DFU. Our study composed of 56 patients who were randomly divided into two even groups. The demographic profile was statistically studied and found comparable with no significant difference between the two groups ($p = 0.569$). The mean age was comparable to the previous multicenter randomized controlled trial, enrolling 342 patients, who had a mean age of 58 years (17).

Application of negative pressure over the wound bed allows the arterioles to dilate, increasing the effectiveness of local circulation, promoting angiogenesis, which assists in the proliferation of granulation tissue (18). We observed that the patients on VAC therapy had the early appearance of granulation tissue as compared to the patients treated by moist saline gauze dressings. Complete (100%) granulation was achieved earlier and in a higher proportion of patients in Group A as compared to Group B. Similar observations were made in a series of animal studies using a sub-atmospheric pressure technique for wound healing (18). Armstrong and Lavery observed that the use of negative pressure therapy resulted in an increased rate of granulation tissue formation and a higher proportion of healed wounds compared to saline gauze dressings (16). We observed that the rate of disappearance of wound discharge was faster in Group A

as compared to Group B, which was statistically significant ($p < 0.0001$), similar to observations made previously (19). The patients who underwent amputation were excluded from this analysis.

Colonization of a wound, corresponding to a level of $>10^5$ colonies of bacteria per gram of tissue, has been recognized as a detrimental factor in the process of wound healing. VAC therapy enhances bacterial clearance, which may account for the wound healing effects. Blood culture positivity was less with patients in Group A compared to Group B. However, blood culture negativity was documented earlier in Group A patients as compared to Group B patients. The majority of wounds in the VAC group (78.6%) decreased in size as compared to that in the conventional group (53.6%). McCallon et al. observed an average decrease of 28.4% ($\pm$24.3) in wound size in the VAC group as compared to 9.5% ($\pm$16.9) average increase in wound size in the control group (treated by saline-moistened gauze dressings) (20). Mark et al. had also observed that the wound volume and depth decreased significantly in VAC dressings as compared to moist gauze dressings (21). We observed the safety of VAC over saline-moistened gauze dressings, in terms of fewer numbers of secondary amputations in Group A as compared to Group B. While assessing the safety of VAC, Blume et al. also reported fewer number of secondary amputations in VAC treated patients as compared to those treated by gauze dressings (17). In our study, the endpoint taken was a completely granulated wound or a wound ready for skin grafting or spontaneous healing by secondary intention.

Both of the groups received similar treatment for the closure of the wound, the most common mode of wound closure being a split-thickness skin graft. In 86.4% of patients, wounds were closed by a split-thickness skin graft in Group A as compared to 93.33% of patients in Group B. The rest of the patient's wounds were closed spontaneously. Our observations are consistent with those of Prabhdeep et al. who also reported a split-thickness skin graft as the most common mode of wound closure (19). In Group A patients, overall lower doses of insulin were required to control hyperglycemia compared to Group B. Success rate in terms of complete granulation and readiness for closure by split-thickness skin grafting or secondary intention was more in Group A compared to Group B and the need for amputation was more in Group B. Armstrong et al. observed that NPWT delivered by VAC device was safe and effective treatment for complex diabetic foot wounds and could lead to a higher proportion of healed wounds, faster healing rates and potentially fewer re-amputations than standard care (16).

Patient satisfaction in terms of time taken for wound closure, number of antibiotics used, treatment related complications and outcome was better in Group A compared to Group B and overall resource utilization was more in Group B. Apelqvist J et al. also found a beneficial effect in terms of direct economic cost and resource utilization in patients treated with VAC compared to standard moist wound therapy (22).

In conclusion, NPWT appears to be more effective, safe and patient-satisfactory compared to conventional dressings in the treatment of foot ulcers in people with DM.

## Conflict of interest and funding

The authors have no conflict of interest. The authors have not received any funding or benefits from industry to conduct this study.

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