Comparative study between vacuum-assisted closure therapy and tetra-silver nitrate in the management of diabetic foot ulcer

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Received: 20 July 2023
Revised: 4 August 2023
Accepted: 8 August 2023
Published: 7 December 2023

The Egyptian Journal of Surgery 2023, 42:827–834

Background
Diabetes-related foot ulcers are becoming more common. The percentage range is 15 to 25%. Several procedures and dressing agents have been investigated. In the vacuum-assisted closure technique, sub-atmospheric pressure is employed to accelerate the healing process.

Aim and objectives
In this study, the healing rates of diabetic foot ulcers (DFUs) treated with tetra-silver nitrate dressing were compared with those treated with negative pressure wound care.

Patients and methods
More than 30 patients were randomly allocated to one of two study groups by the Vascular Surgery department at Aswan University Medical School. Group A received a vacuum-assisted closure (VAC) dressing for a total of 30 patients, while group B received tetra-silver nitrate.

Result
After 6 weeks, there was a statistically significant difference in wound-healing rates between the two groups.

Conclusion
Patients who got VAC developed granulation tissue faster than those who received tetra-silver nitrate. VAC treatment is safe and effective in diabetic foot ulcers. Granulation tissue formation accelerates healing and reduces the risk of problems such as infection or amputation.

Keywords:
diabetic foot ulcers, granulation, negative pressure wound therapy, silver nitrate, vacuum-assisted closure

Egyptian J Surgery 42:827–834

1110-1121

Introduction

Diabetic foot ulcers (DFUs) are more common and serious in diabetics because of peripheral neuropathy, atherosclerotic peripheral artery disease, and mechanical defects in the foot's bone architecture [1].

DFUs are the most common reason for hospitalization in the United States. In the United States, diabetes mellitus (DM) is the leading cause of nontraumatic lower extremity amputations. Every year, 5% of diabetics develop foot ulcers, with 1% requiring amputation [2].

Diabetes patients with foot ulcers are 85% more likely to require a leg amputation. DFUs are best treated by removing all necrotic, callus, and fibrous tissue from the affected area. The degree of the injury, the vascularity of the limb, and the presence of infection all influence how a DFU is treated [3].

One promising therapeutic therapy for DFUs is liquid silver nitrate. Higher graft bed quality results in better graft uptake and faster wound-healing [4].

The sophisticated drainage system with vacuum-aided closure (VAC) seeks to maintain a constant negative pressure environment. VAC promotes angiogenesis as well as granulation tissue production, blood flow, and infection prevention. One of its many medicinal applications is the treatment of acute, chronic, and specialized wounds. However, before using VAC, one must evaluate potential side effects and safety considerations [5].

Topical negative pressure (TNP) therapy is often used to treat acute wounds in vascular patients due to its numerous stated benefits. According to various scientific studies, less evidence has been produced to support its benefits [6].

 DOI: 10.4103/ejs.ejs_156_23

DM foot with ischemic causes require revascularization (either open vascular surgery or endovascular procedures) in addition to proper medical treatment. When VAC therapy is combined with debridement and the right bacterial treatment, more limbs can be preserved [7].

It has been established that applying pressure to a wound area that is less than air pressure aids in its recovery [8].

Patients and methods

Sample size

The sample size was estimated using the OPENEPI software version 3 (www. OpenEpi.com) to be 30 with 15 in each group and a range of 20 days in the time necessary for complete granulation cover [9].

Study design

In a case-control study, 30 DFU patients were separated into two groups.

Place of study

The Vascular Surgery Program at Aswan University School of Medicine conducted this prospective study.

Study patient

DM patients with foot ulcers.

Inclusion criteria

(1) All patients with DFU of greater than 2 weeks duration.
(2) Size of ulcer greater than3 cm.
(3) Well controlled DM (HbA1C = 6-8.3%).
(4) Age 25-65 years.
(5) Both sexes.

Exclusion criteria

(1) Anemic patients (hemoglobin <10 g/dl).
(2) Patients with history of steroid intake.
(3) Patients with chronic renal failure (assessed on history and s/creatinine greater than 1.5 mg/dl).
(4) Patients with history of immunosuppressive therapy.
(5) Ulcers involving bone as well.
(6) Untreated underlying osteomyelitis.
(7) Exposed arteries or veins.
(8) Malignancy within wounds.
(9) Dry gangrene.
(10) Wounds resulting from electrical, chemical, or radiation burns.
(11) Those with collagen vascular disease.

Randomization

(1) Before beginning therapy, all patients who met the study's eligibility criteria were randomly allocated to one of two groups by a computer program.
(2) Group A (15 patients): was planned for VAC dressing.
(3) Group B (15 patients): was planned for treatment with tetra-silver nitrate.

Follow-up

(1) DFUs were followed weekly for 6 weeks. To evaluate wound follow-up, the following clinical criteria were used:
(2) Reduction in the wound size
(3) The time needed for healthy granulation tissue formation in days
(4) Number of surgical debridement sessions
(5) Local wound complications (cellulitis– secondary amputation).
(6) Skin grafting was required for permanent wound closure when wounds exhibited evidence of incomplete healing but had strong granulation tissue after some time had passed.
(7) 10 patients were followed up on until they had complete wound-healing (defined as 100% granulation and wound ready for split skin grafting). The rate at which wounds healed was the most important criterion of success. Secondary outcomes included the presence of bleeding, pain, and infection, as well as visual scoring of granulation tissue formation.
(8) For grade 11, only pink, healthy granulation tissue was considered. The absence of granulation was assigned a value of 1. Scores ranged from 2 to 3 for wounds with granulation tissue covering 25% to 74% of the region. A score of four indicates that at least 75% of the wound has been covered with granulation tissue.
(9) 12 h VAS pain assessments were obtained twice a week, and the weekly mean value was used for analysis. The amount of blood loss was determined by counting the number of times the wound dressing was changed (excluding the change after 48 h). The number of dressing changes required due to blood soakage was counted and evaluated on a weekly basis. Wound culture sensitivity was given out once a week to detect infection. There was also secondary debridement and small amputations.

Ethical consideration

Following the local ethics committee's review and acceptance of the study protocol, all participants signed written informed consents.

Methods

(1) 1 Each patient received a thorough clinical evaluation, as well as any necessary diagnostics and wound debridement. The ulcers' depth and extent were also measured. After initial debridement and photography, VAC therapy was initiated, but not before the wound was measured. The wound was wrapped in two layers of polyethylene, and the surrounding region was labeled with a permanent marker. The bandage that had been in touch with the wound was removed.
(2) Two- During repeated VAC dressing changes, pictures and measurements of the wound's dimensions were taken using the double polyethylene sheet approach. Before any surgical intervention, the wound's final appearance was examined once after VAC therapy.
(3) Third, using a synthetic hydrocolloid sheet, a vacuum suction equipment, and a transparent semipermeable adhesive membrane sheet to apply wet topical therapies under negative pressure necessitates skill.
(4) VAC dressings combine sponge dressing and vacuum-assisted wound closure to help seal wounds. Everyone in Group A received one of the six therapies listed below:
(5) The wound was thoroughly debrided and devitalized tissue removed.
(6) A sticky, semipermeable, and translucent membrane was used to cover the foam and the surrounding natural skin. This allowed the wound to be effectively closed.
(7) Distal end of the drain tube was connected to a device, which provided a negative pressure of −125 mmHg, applied to the wound, intermittently (5 min 'on', 2 min 'off').
(8) This was achieved by wall suction apparatus, computerized devices or mobile suction drain devices.
(9) Once vacuum was applied, the sponge collapsed into the wound bed, thus giving the surface concave appearance.

The wound fluid was absorbed by the sponge and suctioned out of the wound bed on the tenth.

According to studies, using negative pressure for an average of two days produces the best results. After enough granulation tissue had formed, the dressing was removed, and skin grafting was utilized to permanently close the incision.

Group B cleansed and dried the wound with distilled water and sterile gauze before applying 2 ml of silver nitrate solution using a syringe. The incision was then bandaged in gauze soaked in a silver nitrate solution, and dressings were changed twice daily for the next 14 days. The ulcer's growth was monitored every week. On day 1, we obtained a culture from the incision and monitored for any local or systemic adverse effects until day 14.

The bandages were removed from the NPWT group after two days, and the wounds were evaluated. To compare injuries, the following criteria were employed. Researchers calculated the rate of granulation tissue development as a percentage of the ulcer' DFUs are classified and compared s surface area after examining the ulcer's present dimensions and surface area. Both groups received split-thickness skin grafts. The patients were evaluated and managed according to Wagner's grade with surgical options ranging from debridement, incision, and drainage to below-knee amputation.

Wagner's classification of diabetic foot ulcers

Wagner's Classification	
Grade 0	Skin intact but bony deformities lead to "foot at risk"
Grade 1	Superficial ulcer
Grade 2	Deeper, full thickness extension
Grade 3	Deep abscess formation or osteomyelitis
Grade 4	Partial Gangrene of forefoot
Grade 5	Extensive Gangrene

Following surgery, each group received the same course of systemic antibiotics. We reevaluated the wounds on the fifth postoperative day and computed the total number of hospital days and the percentage of skin transplant as a function of the total surface area of the ulcer.

Tetra-silver nitrate and negative pressure wound therapy (NPWT) were used to treat DM foot wounds. Wound severity and complication rates were assessed before and after therapy, and patients on tetra-silver nitrate and VAC were both well observed.

Statistical analysis

IBM SPSS 20.0 was used for statistical analysis and data interpretation. IBM Corp. is headquartered in Armonk, New York. The quantitative and percentage terminology was used to describe qualitative data. The Kolmogorov-Smirnov test was used to determine the

normality of the sample distribution. To summarize quantitative data, minimum and maximum values, the mean, standard deviation, median, and interquartile range (IQR) were all employed. A 5% threshold of significance was assigned to the collected data.

The used tests were:

(1) χ^2test: For categorical variables, to compare between different groups.
(2) Student *t*-test: For normally distributed quantitative variables, to compare between two studied groups.

Results

Table 1

According to the data in the table below, there were no early differences between the research groups Table 2.

The wound assessment results did not differ statistically significantly across groups Table 3.

The data in the table show that wound-healing differed significantly between groups after six weeks Table 4.

In terms of follow-up rates, there was no statistically significant difference between the groups Table 5.

The table below demonstrates that neither group had significantly higher rates of issues than the other Table 6.

In Wagner's classification, there was no statistically significant difference between the groups.

Discussion

DFUs, a common complication of DM, have become more widespread in the last ten years. DFU will occur in 15% of DM people. Although precise prevalence figures for DFU are difficult to obtain, estimates place the occurrence of this complication between 4 and 27%. Diabetes-related foot ulcers frequently result in lower limb amputations Bardill and colleagues [10].

Ischemia, abnormal angiogenesis, and reduced immunity all contribute to DFUs. There are various effective strategies for dealing with DFUs. VAC is one such breakthrough that has changed the favored way of treating DM wounds. According to multiple studies, VAC accelerated DFU healing when compared with standard dressing. Between 50 and 75% of lower limb

Table 1 Comparison between studied cases according to baseline data

	Group A (*n*=15)	Group B (*n*=15)	Test of Significance	*P*
Age (years)				
Range.	33–70	40–61	*t*=1.154	0.258
Mean±SD.	53.47±11.01	49.53±7.28		
Sex	No. (%)	No. (%)		
Female	9 (60.0)	10 (66.7)	χ^2=0.144	0.705
Male	6 (40.0)	5 (33.3)		

χ^2, Chi square test; SD, Standard deviation; t, student *t*-test. *P*: *P* value for comparing between studied groups. *: Statistically significant at *P* less than or equal to 0.05.

Table 2 Comparison between studied cases according to wound examination data

	Group A (*n*=15)	Group B (*n*=15)	Test of Significance	*P*
Duration (days)				
Range.	53–105	53–113	*t*=0.247	0.807
Mean±SD.	73.67±18.73	75.4±19.67		
Largest dimension				
Range.	5.2–10.8	5.8–10.1	*t*=0.414	0.682
Mean±SD.	8±1.47	7.79±1.36		
Site	**No. (%)**	**No. (%)**		
Front	7 (46.7)	7 (46.7)		
Med. sole	3 (20.0)	3 (20.0)	χ^2=4.286	0.232
Lat. sole	2 (13.3)	5 (33.3)		
Heel	3 (20.0)	0		

χ^2, Chi square test; SD, Standard deviation; t, student *t*-test. *P*: *P* value for comparing between studied groups. *: Statistically significant at *P* less than or equal to 0.05.

Table 3 Comparison between studied cases according to wound reduction after 6 weeks

	Group A (*n*=15)	Group B (*n*=15)	Test of Significance	*P*
Size (cm)				
Range.	1.3–3.2	2.3–4.2	*t*=3.100	0.004*
Mean±SD.	2.34±0.61	3±0.55		
Percentage of size reduction (%)				
Range.	63.9–78.4	54.9–69.4	*t*=5.375	<0.001*
Mean±SD.	70.85±4.96	61.23±4.85		

SD, Standard deviation; t, student *t*-test. *P*: *P* value for comparing between studied groups. *: Statistically significant at *P* less than or equal to 0.05.

Table 4 Comparison between studied cases according to Follow-Up

	Group A (*n*=15)	Group B (*n*=15)	Test of Significance	*P*
Healthy granulation tissue formation (days)				
Range.	4–12	6–14	*t*=1.548	0.133
Mean±SD.	6.47±1.88	7.73±2.55		
Number of debridement sessions				
Range.	1–3	1–4	*t*=1.266	0.216
Mean±SD.	1.6±0.83	2.07±1.16		

χ^2, Chi square test; SD, Standard deviation; t, student *t*-test. *P*: *P* value for comparing between studied groups. *: Statistically significant at *P* less than or equal to 0.05.

Table 5 Comparison between studied cases according to complication

	Group A (*n*=15) No (%)	Group B (*n*=15) No (%)	χ^2	*P*
Wound infection	1 (6.7)	3 (20.0)	1.154	0.283
2nd amputation	0	0	0.0	1.0

χ^2, Chi square test; SD, Standard deviation; t, student *t*-test. *P*: *P* value for comparing between studied groups. *: Statistically significant at *P* less than or equal to 0.05.

amputations may be caused by 12 DFU. Every 30 s, someone loses a limb to DFU somewhere in the world. One of the more modern noninvasive adjunctive therapies, NPWT, uses VAC devices to remove fluid from open wounds, prepare the wound bed for closure, reduce edema, and increase the creation and perfusion of granulation tissue. NPWT can be used to treat Charcot neuroarthropathy wounds as well as reconstructive soft tissue and osseous operations. Neuropathy and deformity induce Charcot neuroarthropathy wounds. VAC devices that apply sub-atmospheric pressure can be utilized to accelerate the healing of a variety of wounds Arora and colleagues [11]. VAC therapy accelerates wound granulation and reduces bacterial colonization. Numerous studies have demonstrated the complex consequences of applying a regulated vacuum force at the wound dressing interface. Changes in protease profiles, expression of growth factors and cytokines, cellular activity, control of interstitial fluid flow and exudates, reduction of oedema, improvement of wound-healing properties, and acceleration of granulation tissue formation occur at both the microscopic and macroscopic levels Agarwal and colleagues [12].

One promising therapeutic therapy for DFUs is liquid silver nitrate. Higher graft bed quality results in better graft uptake and faster wound-healing Yang and colleagues [13].

The purpose of this study was to compare the success rates of DFUs treated with negative pressure wound

Table 6 Comparison between studied cases according to Wagner's classification

	Group A (*n*=15) No (%)	Group B (*n*=15) No (%)	χ^2	*P*
Grade I	1 (6.7)	0 (0.0)		
Grade II	6 (40.0)	7 (46.7)		
Grade III	5 (33.3)	4 (26.7)	χ^2= 1.388	0.846
Grade IV	2 (13.3)	3 (20.0)		
Grade V	1 (6.7)	1 (6.7)		

χ^2, Chi square test; SD, Standard deviation; t, student *t*-test. *P*: *P* value for comparing between studied groups. *: Statistically significant at *P* less than or equal to 0.05.

care to those treated with tetra-silver nitrate wound dressings in a control group.

In this study, age (measured in years) and gender did not differ substantially between groups.

According to James and colleagues, patients in both groups had similar ages, sexes, mean BMIs, blood counts (hemoglobin, albumin, and HbA1c), and glucose control levels.

The average age of Mooghal and colleagues study was 53.339.01 years, with a range of 25-65 years. The median age of patients in groups A and B was 53.139.09 years. The majority of the 49 (8167%) patients were between the ages of 46 and 65. The overall number of patients included 19 (31.67%) women and 41 (68.33%) men.

There were no statistically significant differences between the groups in terms of the number of days, the maximum size, or the location of the wound being studied in this study.

In ulcer locations, Essa and colleagues [14] discovered a similar absence of statistically significant alterations. Only seven of the forty ulcers in group A were larger, with 33 measuring less than 7.6 cm^2 and less than 2 cm^3. In group B, 35 of the 40 ulcers had a volume of less than 2 cubic centimeters and a surface area of less than 7.3 mm^2. There were no discernible variations in ulcer size between the two groups.

According to Mooghal and colleagues, the average ulcer duration in group A was 4.671.18 weeks and 4.531.14 weeks in group B. The ulcers in groups A and B measured 5.301.21 mm, 5.131.20 cm, and 5.221.20 cm, respectively. The mean BMI was 28.582.60 kg/m^2, with group A having a mean BMI of 28.702.69 and group B having a mean BMI of 28.472.53.

Our findings demonstrated a statistically significant difference in wound improvement across groups after 6 weeks.

Mooghal and colleagues [3] reported a statistically significant difference in mean healing time between the two groups for patients with 5 cm ulcers, noting that group A's mean healing time was 12.192.56 days and group B's mean healing time was 18.442.77 days ($P = 0.0001$). The ulcers in Group A healed in 11.931.64 days, but the ulcers in Group B healed in 16.083.29 days ($P = 0.0012$). Investigating the association between BMI and the average time required to recover from an accident.

Essa and colleagues [14] discovered a statistically significant difference in the number of patients with entirely healed ulcers at weeks 8, 10, and 12. Their findings corroborated ours.

According to James and colleagues [9], VAC therapy significantly reduced recovery time (21 days vs. 34 days). The median healing period for DFUs with a diameter of less than 10 cm in the study group was 17.5 days and 30 days in the control group. The median reduction in ulcer size in the treatment group was 3.5 cm^2, compared with 10.34 cm^2 in the control group. When comparing DFUs greater than 10 cm (7.73 cm^2 vs. 3 cm^2) with those less than 10 cm (25 cm^2 compared 6.854 cm^2), we find a statistically significant reduction in ulcer area associated with smaller DFUs. This is because the size of an ulcer influences how long it takes to heal.

In an Indian study, DFUs treated with NPWT had a 16.14 cm^2 smaller mean ulcer area than DFUs treated with traditional dressing.

In the current study, the time it took for healthy granulation tissue to grow and the number of debridement sessions required did not differ significantly across groups.

James and colleagues [9] reported a statistically significant difference in the average timeframes required to achieve granulation cover of greater than 75% (visual score 4) (23.33 vs. 32.15 days). The median granulation rate (cm^2/day) did not differ statistically across groups (2.4 and 1.7). In the stratified analysis for DFUs 10 cm, however, no such connection was identified. The first week's median visual analog scale (VAS) score for discomfort was 8.5 in both groups. The median scores (3 in the study group and 4 in the control group) differed statistically significantly after week 3.

Armstrong and Lavery discovered that the median time to full closure for the VAC therapy group was 56 days, while the traditional saline dressing group took 77 days. The median time for granulation with NPWT was 42 days, compared with 84 days using standard dressing.

According to Singh and colleagues study, wounds in the VAC therapy group healed in 41.2 days on average, compared with 58.9 days in the conventional therapy group. The NPWT group required only 15.1 days, but

the normal dressing group required 21.5 days for 100% of the granulation tissue to emerge.

An Indian study of 60 DFU patients reported similar results; wound-healing was complete in 17.2 days in the VAC therapy group versus 34.9 days in the control group.

In comparison to the NPWT group, the traditional dressing group required 32.3 days on average to achieve 90% granulation.

A study conducted in Los Angeles, California by McCallon and colleagues [15] compared VAC to regular saline dressing for DM foot wounds and discovered that the VAC group recovered enough, as defined by 100% granulation tissue, after 22.8 (17.4) days. The VAC group's wound surface area dropped by 28.4% (24.3) over the evaluation period, while the control group's increased by 9.5% (16.9).

According to Aslam and colleagues [16], patients treated with VAC healed in less than half the time required by patients treated with conventional dressings.

In a case-control study published on May 25, 56 patients with DM with DFU grades 2 and 3 were randomly assigned to either VAC or traditional dressing. Patients in Group A had a median age of 53.79 years (range: 47–64 years), while patients in Group B had a median age of 54.57 years (range: 48–62 years). Women made up 64.28 percent of the population in the samples, while men made up 35.71%. By week 4, 44% of patients had wound discharge comparable with the control group. By the eighth week, two (7.4%) of group A patients and seven (28%) of group B patients were still unable to leave the hospital due to their wounds. By the end of Week 2, 26 (92.85%) patients in group A and 15 (53.57%) patients in group B had granulation tissue. Only 10 patients (or 40%) in group B had attained 100% granulation at the end of week 5, compared with 21 patients (or 77.8%) in group A. Only 15 (53.6%) of group B patients had their wound size reduced, compared with 22 (78.6%) of group A patients. After 5 weeks, group A had a closure rate of 81.8%, while group B had a rate of 60%. Amputations were required for three patients in group B versus one patient in group A.

Mous and colleagues [17] discovered that vacuum-assisted closure therapy is superior to standard dressings in the treatment of infected wounds due to a faster reduction in wound surface area and the production of red granulation tissue within the wound.

The authors of the meta-analysis, Zhang and colleagues [18], picked eight publications to investigate. Several studies came to the same conclusion. In total, 600 DFU patients participated in the eight investigations. It was discovered that when NPWT was utilized instead of routine wound care, more ulcers healed. Secondary amputations, ulcer size, wound-healing length, and the size of newly formed ulcers all decreased dramatically.

According to the findings of Eginton and colleagues [19], VAC therapy reduced the wound depth and volume of 6 DFUs by 49 and 59%, respectively. This was a significant improvement over wet gauze dressings, resulting in a 7.7% decrease in wound depth and a 0.1% decrease in wound volume. However, the wound did not heal any faster than it had before VAC therapy. The considerable shrinkage of the wound was attributed to the three-dimensional force applied across the wound by VAC.

Blume and colleagues [20] conducted a randomized controlled experiment with 342 patients from all over the world. After 112 days, we realized that the problem had been correctly rectified. VAC cured more foot ulcers (73 of 169; 43.2%) than advanced moist wound therapy (AMWT; 48 of 166; 28.9%) during the 112-day active treatment period. In comparison to the AMWT group (85/166), the VAC group (105/169) showed a larger proportion of patients with completely healed ulcers.

At random, 30 people were given either a saline dressing (n=54) or vacuum-aided closure treatment (VAC). The VAC group recovered in 183.4 days, but the control group took 383.8 days.

Statistics revealed that there were no statistically significant differences in the incidence of difficulties between research groups.

James and colleagues [9] discovered no statistically significant difference in the number of patients requiring debridement and subsequent minor amputations between the two groups.

According to Essa and colleagues experiments, none of the intervention groups showed any negative impacts. No one who used the nanoparticles (SilvrSTAT Gel) felt nauseated or irritable.

Given that VAC patients developed granulation tissue before tetra-silver nitrate patients, VAC therapy is both efficient and safe in DFUs. Granulation tissue formation accelerates healing and reduces the risk of problems such as infection or amputation.

Conclusion

Finally, individuals given VAC generated granulation tissue faster than those given tetra-silver nitrate. VAC treatment is safe and effective in DFUs. Granulation tissue formation accelerates healing and reduces the risk of problems such as infection or amputation.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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