Comparison of Vacuum Assisted Closure Therapy and Nano-Silver Coated Dressing on Wound Healing in Patients with Diabetic Foot Wound: A Randomized Prospective Trial

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Received: 22 October 2023
Revised: 2 November 2023
Accepted: 6 November 2023
Published: 31 January 2024

The Egyptian Journal of Surgery 2024, 43:271–279

Background
Diabetic foot ulcers constitute one of the most important complications of diabetes mellitus. If not treated promptly, progression of infection and sepsis may necessitate a limb amputation.
Aim
To assess wound healing and to assess the time for wound healing of diabetic foot ulcers using vacuum-assisted closure (VAC) in comparison with nano-silver coated dressing.
Patients and methods
This was a simple randomized cohort prospective trial included two groups of postoperative diabetic foot patients, in which we had a comparison between VAC and nano-silver dressing in order to investigate which procedures had the least time of follow up weeks for full granulation of wound.
Results
VAC significantly reduces the time to complete wound healing by enhancement the formation of granulation tissue.
Conclusion
The time to complete wound healing was significantly better in the VAC therapy group as compared with nano-silver dressing.

Keywords:
diabetic foot ulcers, nano-silver dressing, NPWT, VAC, wound healing

Egyptian J Surgery 43:271–279

1110-1121

Introduction

A considerable proportion of patients with diabetes mellitus develop diabetic foot ulcer (DFUs). The incidence of DFU ranges from 1% in the West to as high as 11% in African populations DFUs comprise the most common cause of nontraumatic amputation preceding as high as 85% of the cases. Mortality rate among DFU patients is almost twice than in diabetics without DFU. It was found that the cost of care in patients with DFUs was over five times higher in the 1st year than in diabetics without foot ulcers. This is mainly due to the long duration of hospital stay needed in DFU patients [1].

DFUs constitute one of the most important complications of diabetes mellitus, with a staggering 25% lifetime risk. If not treated promptly, progression of infection and sepsis may necessitate a limb amputation. Studies from Western population have shown significant implication of vacuum-assisted closure (VAC) therapy in various wounds including DFUs [2].

The main approaches applied so far for DFU management are ulcer debridement, infection control, and off-loading and basic and advanced wound contact dressings. However, there is little quality evidence to support the use of any single dressing product over another in promoting a moist wound bed for the DFU [3].

The standard of care for DFUs involves debridement, local wound care, infection control, and off-loading of pressure. Various treatments advocated in recent years include advanced wound dressings, growth factors, hyperbaric oxygen therapy, cultured skin substitutes, and other wound therapies. Negative pressure wound therapy (NPWT) is a newer, noninvasive adjunctive therapy system. A VAC device to control subatmospheric pressure helps 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 [4].

Nano-silver has been used in a different field as a class of antibacterial materials. It plays an important role in the treatment of diabetic foot. Nanotechnology is used to make nano-silver dressings. In addition to serving the corresponding role of traditional dressings, nano-silver dressings have specific antibacterial effects, and the antibacterial effect is efficient, wide spectrum, difficult to form drug resistance, safe, reliable, etc. [5].

Aim

To assess wound healing (defined as 100% granulation or wound fit for split skin grafting) and to assess the time for wound healing of DFUs using VAC in comparison with nano-silver–coated dressing.

Patients and methods

Study population

This is a simple randomized cohort prospective trial that was conducted on 40 patients included between June 1, 2022 and June 1, 2023 at two hospitals, Ain Shams University and NIDE (National Institute of Diabetes and Endocrinology) throughout 6 months.

The ethical committee of Ain Shams University approved the study. Oral and written consent were obtained from all participants.

The study included patients with diabetes mellitus, nonischemic diabetic foot with =or > 0.8, and patients with DFU, infection or neuropathic ulcer. The study excluded patients with ischemic DFU (ankle brachial index >0.8), severe diabetic foot infection that make the limb nonsalvageable, patients with active cancer condition receiving radiation therapy or chemotherapy, patients with chronic kidney disease, and patients with chronic liver disease.

Study procedures

The included 40 diabetic foot patients divided into two groups, 20 patients in the VAC group and 20 patients in the nano-silver dressing group. All included diabetic foot patients were hospitalized and underwent surgical debridement or minor amputations (distal to ankle amputation). They received daily ordinary dressing with saline and gauze for 7 days followed by VAC and nano-silver dressing had been applied according to simple randomization.

VAC therapy was applied on the first group. The wound was thoroughly irrigated with normal saline, adequate hemostasis was achieved and periwound skin was made dry. Sterile foam was applied on the wound with surrounding 1–2 cm of healthy skin. A fenestrated evacuation tube was fixed in the foam, which is connected to a vacuum pump. The wound was then sealed with an adhesive drape that should be covered the foam and tubing and at least 3–5 cm of surrounding healthy tissue to ensure a watertight/airtight seal. The negative pressure mode was set on interrupted mode

Table 1 Demographic data, *P* value above 0.05: nonsignificant; *P* value les than 0.05: significant; *P* value less than 0.01: highly significant

	VAC *N*=20	Nano-silver *N*=20	Test value	*P*	Significance
Age					
Mean±SD	63.30±8.36	61.35±7.56	0.774	0.444	NS
Range	52–78	51–78			
Sex, n (%)					
Female	14 (70.0)	12 (60.0)	0.440*	0.507	NS
Male	6 (30.0)	8 (40.0)			
Morbidity, n (%)					
DM					
No	0 (0.0)	0 (0.0)	–	–	–
Yes	20 (100.0)	20 (100.0)			
HTN, n (%)					
No	16 (80.0)	15 (75.0)	0.143*	0.705	NS
Yes	4 (20.0)	5 (25.0)			
Smoking, n (%)					
No	15 (75.0)	16 (80.0)	0.143*	0.705	NS
Yes	5 (25.0)	4 (20.0)			
Renal insufficiency, n (%)					
No	17 (85.0)	18 (90.0)	0.229*	0.633	NS
Yes	3 (15.0)	2 (10.0)			

*Non significant, as there are no differences between the two compared groups. NS, not significant; VAC, vacuum-assisted closure.

around 125 mm Hg and a cycle of 5 min on and 2 min off phase. The dressing was changed on third day.

Nano-silver dressing was applied on the second group. The wound was thoroughly irrigated with normal saline, adequate hemostasis was achieved and peri-wound skin was made dry. Then nano-silver dressing was applied on the wound as the silver matrix surface (gray surface) facing the wound and extending to the peri-wound skin with a secondary dressing covering. The dressing was changed on third day.

Follow up of patients was done clinically every 2 weeks to assess wound depth, wound surface area (length × width), wound infection according to Wound Ischemia Foot Infection (WIFI) classification and assessment of granulation tissue.

Results

This is a simple randomized cohort prospective trial that was conducted on 40 patients divided equally into two groups. In VAC group, there were six males (30%) and 14 females (70%). The age range of patients was 52–78 years, with a mean age of 63.3. In nano-silver group, there were eight males (40%) and 12 females (60%). The age range of patients was 51–78 years, with a mean age of 61.35. There was no statistically significant difference between variables of demographic data (Table 1).

The patients were classified by WIFI classification. Fifty percent of patients of VAC group were classified to stage 2 while 40% of patients of nano-silver group were classified as stage 1. There was no statistically significant difference between the studied groups regarding WIFI classification, Table 2.

The patients were investigated to assess hemoglobin level, total leucocyte counts, hemoglobin A1C, renal function, and serum albumin. There was no statistically difference between the studied groups (Table 3).

All patients were received foot surgical interventions. At the VAC group, six patients (30%) underwent toes amputation, five patients (25%) underwent trans-metatarsal amputation, and rest of patients underwent foot debridement. While in nano-silver group, nine patients (45%) underwent toes amputation, four patients (20%) underwent trans-metatarsal, and rest of patients underwent foot debridement. There was no statistically significant difference between the studied groups regarding surgical interventions (Table 4).

Follow up of cases study based on clinical assessment of the wound depth and surface area (in centimeters) every 2 weeks.

At the VAC group, it was 0.21–0.35 cm in depth and range of 16–112 cm (median of 71 cm) for surface area before VAC therapy, to become then 0 cm for depth and range of 16–63 cm (median of 48 cm) for surface area after six weeks with completely granulated wound (Figs. 1 and 2).

Table 2 WIFI classification, *P* value above 0.05: nonsignificant; *P* value less than 0.05: significant; *P* value above 0.01: highly significant

WIFI classification	VAC *N*=20	Nano=-silver *N*=20	Test value*	*P*	Significance
Wound grade, n (%)					
Grade 0	3 (15.0)	4 (20.0)			
Grade 1	9 (45.0)	10 (50.0)	2.195	0.533	NS
Grade 2	6 (30.0)	6 (30.0)			
Grade 3	2 (10.0)	0 (0.0)			
Ischemia grade					
Grade 0	20 (100.0)	20 (100.0)	–	–	–
Foot infection grade					
Grade 0	0 (0.0)	1 (5.0)			
Grade 1	7 (35.0)	7 (35.0)			
Grade 2	11 (55.0)	9 (45.0)	1.400	0.706	NS
Grade 3	2 (10.0)	3 (15.0)			
WIFI stage					
Stage 1	4 (20.0)	8 (40.0)			
Stage 2	10 (50.0)	5 (25.0)			
Stage 3	3 (15.0)	5 (25.0)	3.700	0.296	NS
Stage 4	3 (15.0)	2 (10.0)			

*Non significant, as there are no differences between the two compared groups. NS, not significant; VAC, vacuum-assisted closure; WIFI, Wound Ischemia Foot Infection.

Table 3 Initial laboratory investigations, *P* value above 0.05: nonsignificant; *P* value below 0.05: significant; *P* value below 0.01: highly significant

Initial laboratory investigations	VAC *N*= 20	Nano-silver *N*= 20	Test value*	*P*	Significance
Hb					
Mean±SD	11.87±0.95	12.10±0.82	−0.800	0.429	NS
Range	10.4–14	10.5–13.5			
TLC					
Mean±SD	9.85±2.50	10.76±2.26	−1.214	0.232	NS
Range	6.8–14.5	7.9–15.1			
HbA1c					
Mean±SD	8.53±1.68	8.05±1.78	0.869	0.390	NS
Range	5.3–11.1	5.3–10.6			
S. creat					
Mean±SD	0.98±0.43	0.99±0.36	−0.121	0.904	NS
Range	0.6–2.1	0.6–1.9			
S. albumin					
Mean±SD	4.28±0.75	4.03±0.71	1.086	0.285	NS
Range	3.3–5.6	3–5.2			

*Non significant, as there are no differences between the two compared groups. NS, not significant; VAC, vacuum-assisted closure.

Table 4 Surgical intervention, *P* value below 0.05: nonsignificant; *P* value above 0.05: significant; *P* value above 0.01: highly significant

Surgical intervention	VAC *N*= 20	Nano-silver *N*= 20	Test value*	*P*	Significance
Toes amputation	6 (30.0%)	9 (45.0%)	0.960	0.327	NS
Sole debridement	11 (55.0%)	13 (65.0%)	0.417	0.519	NS
Dorsum debridement	7 (35.0%)	7 (35.0%)	0.000	1.000	NS
Heel debridement	4 (20.0%)	3 (15.0%)	0.173	0.677	NS
Trans-metatarsal amputation	5 (25.0%)	4 (20.0%)	0.143	0.705	NS
Medial aspect of foot debridement	1 (5.0%)	1 (5.0%)	0.000	1.000	NS

*Non significant, as there are no differences between the two compared groups. NS, not significant; VAC, vacuum-assisted closure.

While in the nano-silver group, it was 0.15–0.36 cm in depth and range of 12–120 cm (median 74 cm) for surface area before applied the nano-silver dressing, to become then 0 cm and 17.5–87 cm (median of 76 cm) for surface area after 10 weeks with completely granulated wound (Figs. 3 and 4).

There was statistically significant difference between type of dressing and duration of wound healing (Table 5).

There is a potential difference between the two groups as regard wound complete granulation, VAC group required four to six weeks to reach full granulation tissue in comparison to six to ten weeks in nano-silver group (Fig. 5).

So, VAC dressing is faster to achieve complete wound granulation than nano-silver dressing. There was no statistically significant difference found between the two studied groups regarding surgical reintervention, minor amputation, major amputation and limb salvage (Table 6).

Discussion

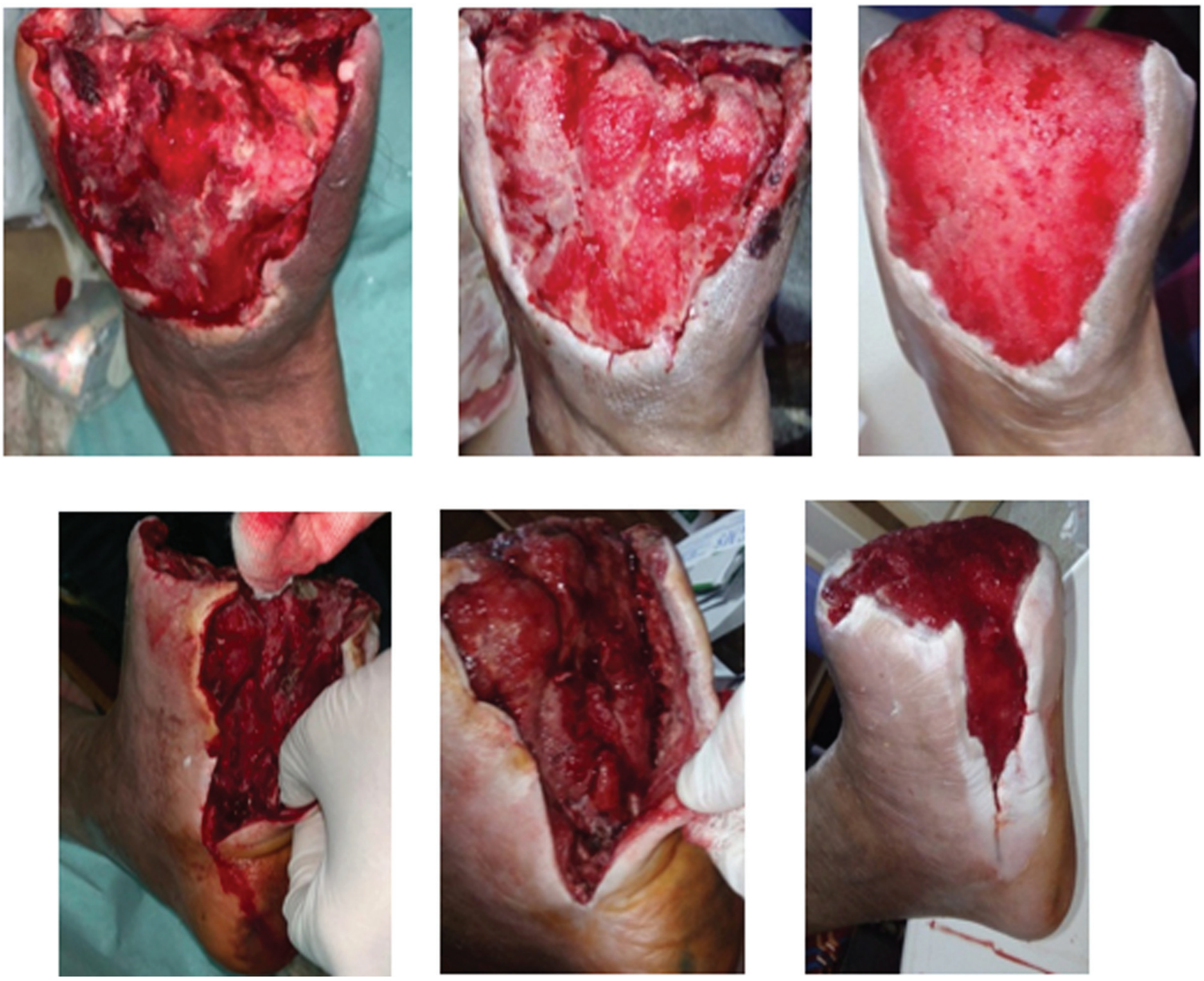
To our knowledge, this is the first study to compare between VAC and nano-silver dressings in DFUs.

Our results revealed that there was no statistically significant difference found between two groups regarding demographic data.

Regarding the current study, comparison between VAC and nano-silver dressing groups results, follow-up done in 2, 4, 6, 8 and 10 weeks; we found that the results in the VAC group were high statistically different from the nano-silver dressing group concerning ulcer depth, percentage of surface area reduction and complete granulation tissue.

Armstrong and Lavery conducted their study on 162 patients divided into two groups into a 16-week, the

Figure 1



Post transmetarsal amputation, dorsum and sole debridement (4 weeks on vacuum-assisted closure).

Figure 2

Post sole, heel and medial aspect of foot debridement (6 weeks on vacuum-assisted closure).

first group of 77 patients were treated by VAC therapy while the second group of 85 patients were treated by conventional dressing. Their results showed that the median time to achieve 76–100% granulation was almost twice as faster using NPWT than conventional dressing (median time of 42 days *vs.* 84 days) [6].

McCallon and colleagues in their study conducted on 10 patients were compared between VAC therapy and

Figure 3

Posttransmetarsal amputation and sole debridement (8 weeks on nano-silver dressing).

Figure 4

Post second toe amputation and sole debridement (10 weeks on nano-silver dressing).

Table 5 Follow up, *P* value above 0.05: nonsignificant; *P* value below 0.05: significant; *P* value below 0.01: highly significant

Follow up	VAC *N*=20	Nano-silver *N*=20	Test value	*P*	Significance
Initial clinical data					
Depth					
Median (IQR)	0.28 (0.26–0.31)	0.27 (0.24–0.31)	–0.925†	0.355	NS
Range	0.21–0.35	0.15–0.36			
Surface area					
Median (IQR)	71 (41–84)	74 (30–96)	–0.162†	0.871	NS
Range	16–112	12–120			
After 2 weeks					
Depth					
Median (IQR)	29.4 (23.93–38.61)	12.5 (9.9–14.84)	–4.912†	0.000	HS
Range	16.67–61.9	5.88–35.71			
Surface area					
Median (IQR)	10.56 (8.92–12.5)	2.89 (1.89–4.09)	–5.277†	0.000	HS
Range	7.14–16.67	0.67–8.33			
Complete granulation					
No	20 (100.0%)	20 (100.0%)	–	–	–
Yes	0 (0.0%)	0 (0.0%)			

(*Continued*)

Table 5 (*Continued*)

Follow up	VAC *N*=20	Nano-silver *N*=20	Test value	*P*	Significance
After 4 weeks					
Depth					
Median (IQR)	100 (63.1–100)	25.84 (22.22–28)	−5.506†	0.000	HS
Range	53.57–100	15.38–42.86			
Surface area					
Median (IQR)	22.54 (21.25–30.91)	5.78 (4.54–12.92)	−5.047†	0.000	HS
Range	18.75–56.25	2.08–28.57			
Complete granulation					
No	7 (35.0%)	20 (100.0%)	19.259*	0.000	HS
Yes	13 (65.0%)	0 (0.0%)			
After 6 weeks					
Depth					
Median (IQR)	100 (100–100)	43.88 (40–55.24)	−3.379†	0.001	HS
Range	100–100	30.43–100			
Surface area					
Median (IQR)	31.94 (28.57–50)	16.67 (11.81–29.17)	−2.662†	0.008	HS
Range	21.25–58.33	6.25–44.44			
Complete granulation					
No	0 (0.0%)	17 (85.0%)	16.065*	0.000	HS
Yes	7 (100.0%)	3 (15.0%)			
After 8 weeks					
Depth					
Median (IQR)	–	100 (57.14–100)			
Range	–	47.62–100			
Surface area					
Median (IQR)	–	22.22 (14.44–25)			
Range	–	8.33–58.33			
Complete granulation					
No	–	7 (41.2%)	–	–	–
Yes	–	10 (58.8%)			
After 10 weeks					
Depth					
Median (IQR)	–	100 (100–100)			
Range	–	100–100			
Surface area					
Median (IQR)	–	18.87 (14.45–27.29)			
Range	–	9.38–100			
Complete granulation					
No	–	0 (0.0%)	–	–	–
Yes	–	7 (100.0%)			

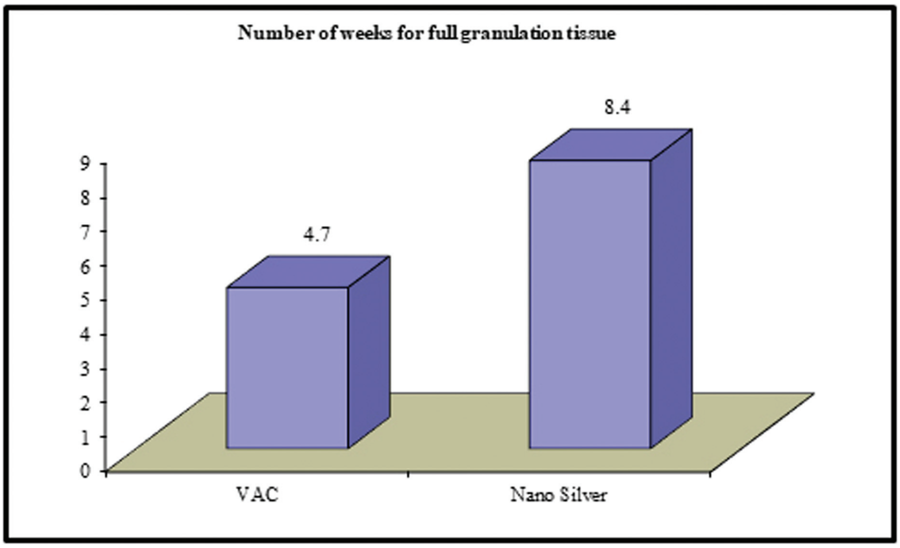
*Highly significant, as the VAC group shows more rapid prognosis and healing than the Nano silver dressing group. IQR, interquartile range; NS, not significant; VAC, vacuum-assisted closure; WIFI, Wound Ischemia Foot Infection.

saline moistened gauze in the treatment of postoperative DFUs. Their results showed satisfactory healing in the VAC compared with saline gauze (22.8 days, 42.8 days; respectively) [7].

According to the previous two studies, they showed that NPWT took less time of wound healing which is in agreement with our study.

In our study the end point of the complete wound healing is 100% granulation tissue or the wound ready for skin graft. But in some studies the end point of wound healing defined as spontaneous complete closure, that is, 100% re-epithelization. The disadvantage of having complete closure as an end point is that this may not be achieved in all wounds, as the wound size differs considerably between patients; in none of the these studies did all patients reached spontaneous closure. Further waiting for a wound to fully epithelize requires prolonged follow up or hospital stay which adds on to the cost of treatment.

Figure 5



Numbers of weeks for full granulation tissue. VAC, vacuum-assisted closure.

Table 6 Comparison between VAC and nano-silver group regarding number of weeks for full granulation tissue, number of trips to OR, minor amputation, major amputation, and limb salvage, *P* value above 0.05: nonsignificant; *P* value below 0.05: significant; *P* value below 0.01: highly significant

	VAC *N*=20	Nano-silver *N*=20	Test value	*P*	Significance
Number of weeks for full granulation tissue					
Mean±SD	4.70±0.98	8.40±1.39	–9.726*	0.000	NS
Range	4–6	6–10			
Number of trips to OR					
1	18 (90.0%)	16 (80.0%)			
2	2 (10.0%)	2 (10.0%)	2.118*	0.347	NS
3	0 (0.0%)	2 (10.0%)			
Minor amputation					
No	20 (100.0%)	20 (100.0%)			
Yes	0 (0.0%)	0 (0.0%)	–	–	–
Major amputation					
No	20 (100.0%)	19 (95.0%)	1.026*	0.311	NS
Yes	0 (0.0%)	1 (5.0%)			
Limb salavage					
No	0 (0.0%)	0 (0.0%)	–	–	–
Yes	20 (100.0%)	20 (100.0%)			

*Non significant, as there are no differences between the two compared groups. NS, not significant; VAC, vacuum-assisted closure.

The results of the present study found that the median rate of granulation tissue formation was found to be statistically significant.

Faster healing in NPWT is attributed to macro-deformation, wound environment stabilization and decrease in edema, micro-deformation leading to increased cellular proliferation and angiogenesis, and decreased bacterial load, all of which lead to enhanced granulation cover [8].

Increased levels of fibroblast growth factor, transforming growth factor β, fibroblast proliferation, α smooth muscle actin, interleukin 8, and vascular endothelial growth factor are implicated in the enhancement of granulation tissue formation in NPWT [9].

Although few studies have shown NPWT to reduce the need of re amputations, there is no explainable direct correlation of re amputations with NPWT.

The FDA Safety Communication Report has warned about the potential adverse effects of NPWT including wound maceration, wound infection, bleeding, and retention of dressings [10]. Our present study shows less side effects in the VAC group.

Huang *et al.* [11] stated that the use of nano-silver dressings in various surgical infections and DFUs has shown good results.

Lafontaine and colleagues compared in a placebo-controlled study between silver and nonsilver dressings on 63 and 55 patients with DFUs, respectively. Their results showed no difference in the proportion of ulcers healed by 12 weeks in the silver versus control group (69% *vs*. 75%) [12].

Regarding to our study, the time needed to reach full granulation tissue was (mean 4.70 weeks in VAC group and 8.40 weeks in the nano-silver dressing group) which is highly significant.

Accordingly, we conclude that nano-silver wound healing results are as good as VAC wound healing results but needs longer time.

Conclusion

The standardized management and application of NPWT improves wound exudate drainage, enhance blood perfusion and promote wound healing.

The present simple randomized cohort prospective trial reports that VAC therapy is effective and safe in the postoperative wound management in diabetic foot patients.

It significantly reduces the time needed for complete wound healing by speeding up granulation tissue formation without affecting the limb salvage.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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