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ORIGINAL ARTICLE

Negative pressure wound therapy with saline instillation: 131 patient case series

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Abstract

Negative pressure wound therapy combined with timed, cyclical instillation (NPWTi) of topical wound solutions has been recently presented as a new adjunctive modality for treating wounds with signs of infection. Normal saline, antiseptics and antimicrobials all have been proposed in scientific and clinical studies as potentially effective when used with NPWTi for treating heavily infected wounds. This is a prospective clinical study of 131 patients with 131 wounds treated with NPWTi using saline between January 2012 and December 2012 in two orthopaedic centres and one surgical wound healing centre in France. Saline was exclusively used. Results were favourable: in 98% of the cases, the wounds could be closed after debridement and following the use of NPWTi. Mean duration of NPWTi was 12·19 days. This does not preclude the need for treating the biofilm appropriately with more active antibacterial products when biofilm has been documented.

Introduction

Negative pressure wound therapy (NPWT) as delivered by V.A.C.® Therapy (KCI USA, Inc., San Antonio, TX), was introduced by Argenta and Morykwas (1, 2) in 1997. This advancement has been considered one of the most innovative technologies to simplify the coverage of highly complex wounds, such as post-traumatic wounds and chronic wounds (e.g. diabetic foot ulcers [DFUs]). Armstrong and Lavery (3) and Blume *et al.* (4) also carried out randomised controlled trials, demonstrating successful use of NPWT for diabetic foot wounds and DFUs, respectively. NPWT can be applied to most types of acute and chronic wounds. Mechanisms of action for NPWT include drawing wound edges together, removing infectious materials, reducing oedema, promoting perfusion and creating tissue microdeformations, leading to cell stretching and subsequent cellular activity important for wound healing (5–11). The most visible clinical effect is wound reduction linked to subsequent granulation tissue formation. However, some wounds remain difficult to treat. For these reasons, a technically improved NPWT system with instillation was designed, V.A.C. VeraFlo™ Therapy (NPWTi; KCI USA Inc.), with volumetric distribution and removal of topical solutions that could be used as adjunctive treatment for infected wounds, wounds at high risk of infection and/or wounds that have not responded to conventional NPWT. The instillation principle involves irrigating and soaking the wound, followed by removal of the fluid via application of

Key Messages

- negative pressure wound therapy with instillation (NPWTi) has been recently presented as a new adjunctive modality for treating wounds with signs of infection
- the purpose of this study was to evaluate the outcomes of 131 complex wounds (e.g. open fracture, infected haematoma, pressure ulcer and non-healing postoperative dehiscence wounds) in 131 patients who were treated with NPWTi using saline in three different centres in France
- in 98% of the cases, the wounds could be closed after debridement and the use of NPWTi

negative pressure at timed, regular intervals, while the foam dressing remains in place.

Three centres in France (Montpellier, Orléans and Strasbourg) collaborated to collect data on a series of 131 wounds of various aetiologies, including orthopaedic infected wounds, complex traumas, DFUs, postoperative sepsis and necrotising fasciitis that were treated with NPWTi using saline. The purpose of this study was to evaluate the outcomes of complex wounds treated with the new NPWTi technology.

Materials and methods

Between January 2012 and December 2012, a total of 131 patients were prospectively treated with NPWTi using V.A.C. VeraFlo Therapy by three teams in three different facilities: (i) Wound Healing Unit at Montpellier University Hospital, (ii) Department of Orthopaedic and Traumatologic Surgery at Orléans Hospital and (iii) Department of Orthopaedic and Traumatologic Surgery at Strasbourg University Hospital.

Patients aged 18 years or older with an infected wound or wound at risk of infection were eligible to receive NPWTi (V.A.C. VeraFlo Therapy). Patients who were already being treated with conventional NPWT were also eligible to receive NPWTi. All patients consented to participate in this study. A total of 46 patients (35·1%) received conventional NPWT prior to NPWTi. NPWTi was applied as the primary therapy to the remaining 85 patients (64·9%) after radical surgical bone and soft tissue debridement.

Postoperatively, all patients were treated with systemic antibiotics according to bacteriological biopsies performed during the surgical debridement. Duration of the antibiotic treatment was determined under the supervision of the infectiology department and in accordance with the type of germ and level of involvement of bone and deep structures.

The decision to apply or discontinue NPWTi was made by consensual agreement of all involved team members at each facility. All patients and wounds were assessed at each dressing change during which time a decision was made to convert to conventional NPWT or close the wound. In cases of exposed hardware or bone, NPWTi was continued until sufficient granulation coverage was achieved. In cases of persistent thick exudate or lack of wound improvement, additional debridement was performed, and NPWTi was reinitiated.

The NPWTi system consisted of a reticulated open-cell foam (V.A.C. VeraFlo™ Dressing; KCI USA, Inc.) that was placed into the wound and sealed with a semi-occlusive dressing, and was used in the vast majority of cases. In a few cases, a white polyvinyl foam (V.A.C.® WhiteFoam Dressing; KCI USA, Inc.) was applied to the wound in order to reduce the pain at dressing change.

An integrated set of suction and solution delivery tubing (V.A.C. VeraT.R.A.C.™ Pad; KCI USA, Inc.) was secured over a hole cut in the dressing, thereby allowing contact with the foam. The distal end of the suction tubing was attached to the canister within the negative pressure unit and the distal end of the solution delivery tubing was attached to the saline bag fastened to the unit arm. The NPWTi unit instilled normal saline for 20 or 30 seconds, depending on patient and wound conditions. The mean time of instillation was 20 seconds. The appropriate volume to be instilled was set manually and was then automated to deliver the same volume throughout the length of therapy. Soak time was set to 10 minutes.

Length of negative pressure was set between 4 and 12 hours, depending on the wound condition and the discomfort of the patient (fewer cycles at night). Mean number of instillation cycles used per 24 hours was 4 (range: 2–6). Subatmospheric continuous pressure of −125 mmHg was applied to all wounds. No topical antiseptic or antibiotics were instilled. Frequency of dressing changes was initiated at the recommended 48 hours and could be extended with increased personal experience. On an average, the entire dressing, including the foam and tubing, was changed every 3 days.

Results

A total of 131 patients were treated with V.A.C. VeraFlo Therapy; of these 41·9% patients were female and 58·1% patients were male. On an average, the patients were aged 59·2 years (range: 21–101 years). Comorbidities (e.g. diabetes, arteriopathy, renal failure and blood hypertension) were present in a high percentage of the studied population (Table 1).

Wound aetiologies are listed below.

1. Open fracture ($n = 46$; 35%)
2. Infected haematoma (leg, thorax, abdomen and perineal area) ($n = 31$; 24%)
3. Pressure ulcer (perineal area and heel) ($n = 27$; 21%)
4. Non-healing postoperative dehiscence ($n = 25$; 19%)
5. Diabetic foot ulcer ($n = 17$; 13%)
6. Necrotising fasciitis ($n = 13$; 10%)
7. Limited exposure to osteosynthetic hardware ($n = 7$; 5%)
8. Leg ulcer ($n = 3$; 2%)

In 46 of 131 (35%) cases, the patients had already been receiving conventional NPWT, which had been unsuccessful in promoting productive granulation tissue formation (Table 2) owing to comorbidities, residual infection and poor debridement. NPWTi was initiated for a mean period of 12·19 days (Table 3). In 48·8% of the cases, conventional NPWT was reinitiated after this period of NPWTi until secondary closure occurred or a surgical closing technique was indicated (Table 4). Wound closure was achieved in 128 of 131 wounds.

Closure was performed surgically via skin graft, flap or primary suture in 74 (57·76%), 22 (17·33%) and 32 (24·83%) patients, respectively (Table 5). There was no incidence of wound recurrence or dehiscence at the operated site. Incomplete wound closure was observed in 3 of 131 cases (2·2%) – one due to limb ischaemia and two due to death unrelated to the therapy.

Investigators from all three test sites observed a common positive effect of the saline instillation after a few days with respect to increased granulation tissue formation and reduced wound volume. The newly formed granulation tissue after NPWTi was more beefy red and moist. Granulation tissue production was enhanced compared to conventional NPWT, in terms of filling the dead space more rapidly and completely. Undermined cavities and exposed bones were also more

Table 1 Comorbidities

Comorbidities	$N = 131$
Diabetes	31 (23·6%)
Arteriopathy	26 (19%)
Chronic renal failure	20 (15%)
Hypertension	11 (8%)
Obesity	8 (6%)
Drug addiction	7 (5%)
Neurological deficiency	6 (4%)
Malnutrition	4 (3%)
Septicaemia	5 (3%)
Alcoholism	2 (1·5%)

Table 2 Percentage of patients receiving conventional NPWT before NPWTi

	% of Patients
Centre 1 (Orléans)	42
Centre 2 (Montpellier)	37
Centre 3 (Strasbourg)	35
Mean	35

NPWT, negative pressure wound therapy; NPWTi, NPWT with instillation.

Table 3 Number of NPWTi days

	Days
Centre 1 (Orléans)	12·57
Centre 2 (Montpellier)	10·6
Centre 3 (Strasbourg)	13·42
Mean	12·19

NPWTi, negative pressure wound therapy with instillation.

rapidly covered during NPWTi. The effects of instillation were likely more striking owing to systematic surgical debridement prior to initiating NPWTi and at each dressing change as appropriate.

Discussion

Anecdotal results in this series are encouraging and suggest that NPWTi using saline during a limited time period may play a positive role in closure of complex wounds. Surgical closure was achieved and maintained after an average of 12·19 days of NPWTi in 128 of 131 wounds. A positive healing progression was achieved in 98% of the cases. This technique, combined with systematic surgical debridement, jump-started previously stalled granulation tissue formation in some of the at-risk wounds that had failed to progress with conventional NPWT.

Goals for instillation therapy were to condition the wound for closure after surgical bone and/or tissue debridement or to boost the local reaction of the wound after a period of unproductive conventional NPWT. Minimising the length of the instillation period to achieve these short-term goals helped to limit the cost of the therapy.

Nurses considered this newest NPWTi system used during the study period to be more reliable and easier to manage

Table 4 Percentage of patients receiving conventional NPWT after NPWTi

	% of Patients
Centre 1 (Orléans)	51
Centre 2 (Montpellier)	72
Centre 3 (Strasbourg)	23
Mean	48·8

NPWT, negative pressure wound therapy; NPWTi, NPWT with instillation.

Table 5 Percentage of patients for each closure method

	Skin graft (%)	Flap (%)	Primary suture (%)
Centre 1 (Orléans)	70	1	29
Centre 2 (Montpellier)	59	31	10
Centre 3 (Strasbourg)	44·30	20	35·50
Mean	57·76	17·33	24·83

compared with previous commercialised NPWTi systems. Solution delivery, instillation time and negative pressure cycles are all automated with the new NPWTi system.

While the exact mechanisms that contribute to increased volume of granulation tissue formation observed with adjunctive NPWTi are unclear, investigators have proposed that addition of an instilled fluid lowers wound fluid viscosity, which in turn facilitates more efficient removal of exudate and infectious material into the canister (12). Regular irrigation with instilled solutions naturally assists in wound bed preparation, by cleaning wounds and removing infectious material, which may prompt enhanced granulation tissue formation (13,14).

Successful use of NPWTi was initially described by Fleischmann *et al.* (15) in 1993 in non-infected open fractures, and subsequently in 27 infections of bone and soft tissues, chronic osteomyelitis or chronic wounds (16). Following 7 days of intermittent instillation of antiseptic or antibiotic solutions combined with a vacuum source, immediate or delayed wound closure was achieved in all 27 wounds. During an average follow-up of 4·2 months, there was one recurrence of infection in a patient with chronic osteomyelitis.

Much of the earlier literature regarding negative pressure with instillation refers to the use of antiseptics and/or antibiotics intermittently instilled into the foam. In 2004, Wolvos reported his initial clinical results with the first commercially available NPWTi device in a pilot series of five patients. In all cases, instillation of a topical anaesthetic appeared to effectively minimise wound pain occasionally associated with NPWT (17). The use of instillation in complicated orthopaedic cases was reinforced by observational studies conducted by several authors (18,19). Lehner *et al.* reported in a series of 32 patients with an infected orthopaedic implant that 86·4% of patients with an acute infection and 80% of patients with a chronic infection retained their implant at 4–6 months follow-up after treatment with polyhexanide instillation and NPWT (18).

In a retrospective case–control cohort study comparing negative pressure instillation therapy (with antiseptic solution) versus gentamicin polymethylmethacrylate beads and

long-term intravenous antibiotic treatment of wounds with osteomyelitis, the rate of recurrence of infection was 3 of 30 for the negative pressure instillation group versus 55 of 93 for the control group (19). In 2012, Gabriel (13) reviewed the different clinical indications of instillation in infected wounds and concluded that most wounds appear to benefit from at least 1–2 days of instillation/irrigation, and use of NPWTi may lead to fewer trips to the operating room for washouts. Leung *et al.* (20) studied saline-based instillation therapy in a porcine model and found that NPWTi with normal saline may lead to wound filled with higher quality granulation tissue composed of increased collagen, compared to the use of NPWT alone.

Authors have recommended the use of NPWTi over conventional NPWT in wounds with high levels of exudate and slough content, as well as acute traumatic wounds or wounds acutely debrided owing to infected soft tissue (21). Successful use of the combination therapy has also been reported in cases of large areas of post-debrided exposed bone and cases of critical bacterial colonisation levels as an alternative to antibiotic-impregnated beads, when appropriate (12). NPWTi should be immediately discontinued if any condition of gross infection, sepsis, recurrent infection or untreated osteomyelitis is revealed.

In our series of 131 clinical wound cases, critical colonisation or infection was identified either by presence of clinical signs (pus, lymphangitis, oedema and swelling) or by exposure of a minimal zone of osteosynthetic material. Systemic antibiotics were administered as appropriate. However, investigators chose to instil normal saline over all wounds, because of lack of controlled clinical evidence in the literature demonstrating superiority of instilled topical antiseptics compared with saline in similarly infected wounds treated with NPWTi. While several series have described successful use of NPWTi with instillation of antiseptic or antimicrobial solutions (12,19,21,22), we are unaware of any clinical studies that have compared NPWTi outcomes with instilled saline versus antiseptics or antimicrobials.

In a recent porcine *in vitro* study model (23), investigators analysed the reaction of a mature *Pseudomonas aeruginosa* PAO1 biofilm to NPWTi with six different instilled solutions: saline, povidone iodine (PV-1), chlorhexidine gluconate, polyhexamethylene biguanide (PHMB), polydiallyldimethylammonium chloride (PolyDADMAC) or a novel antimicrobial solution. Results indicated that the novel antimicrobial solution, PHMB, polyDADMAC and PV-1 solutions significantly reduced bacterial load of the gram-negative biofilm compared with saline.

However, in our cases, biofilms were not identified or confirmed by a specific bacteriological examination. Also, hardware exposure was limited to a screw exposure or minimal zone of osteosynthetic material. Logistical difficulties in identifying the presence and type of biofilms during routine surgical practice prevented the investigators from exploring use of biofilm-specific antimicrobial or antiseptic solutions in this study. In our experience, after proper cleansing and debridement, regularly instilled saline was sufficient enough to allow granulation tissue to cover the exposed area and shift the wound healing trajectory from risk of infection and delayed healing. A need for adding antiseptic to the instillation solution was not demonstrated, even in the presence of mildly exposed osteosynthetic material. However, adding antiseptics to the instillation solution should certainly be useful when appropriate. The need for topical antiseptic instillation may appear, for example, when biofilm is bacteriologically documented or when a zone of exposed material (osteosynthetic/prosthetic) is visible in the wound. However, additional studies are needed to further address the interest of instilled antiseptics.

This study has all of the limitations of an uncontrolled, non-randomised study. The nature of the study was largely observational, and findings cannot be generalised to larger populations. However, these positive preliminary results in a relatively large patient population warrant further research regarding the efficacy of cyclical irrigation of saline water during NPWT. Well-designed controlled studies are needed to substantiate the clinical and cost-effectiveness of NPWTi and saline instillation in at-risk wounds.

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