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REVIEW ARTICLE

The evidence-based principles of negative pressure wound therapy (NPWT) dressing applications; A review of the literature

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Abstract
Wound healing can be an uncomfortable and painful process that may at times lead to infection, hospitalisation and even death of the patient. Throughout the years, attempts have been made to make this process more manageable for patients, as well as clinicians. In 1993, negative pressure was first described with the intention of wound healing and by 1997 was being utilised in the clinical setting. The purpose of this literature review is to identify the available evidence for the use of negative pressure wound therapy (NPWT) and the extent of its applications. A literature search of the online resources was undertaken in July 2013 for articles published from 1993 till that date and out of 212 articles and studies, 77 were found to match our inclusion criteria. NPWT has been described as the preferred method of wound management (including in degloving injuries, infected sternotomy wounds, soft tissue injuries, open fractures of lower extremities, and diabetic foot ulcers) due to its ability to reduce healing time, help in prevention of infection and being cost-effective.

Keywords: Negative-pressure wound therapy; Wound closure technique; Evidence-based practice

Introduction
Negative Pressure Wound Therapy (NPWT), also known as Vacuum Assisted closure (VAC), Vacuum Therapy (VT), Topical Negative Pressure Therapy (TNPT) or Vacuum Sealing (VS) is a non invasive, active wound management system, which uses negative pressure in order to enhance the healing process.[1-4] When the wound bed is exposed to sub-atmospheric pressure, the fluid from the extravascular space is removed, helping to reduce both the risk of wound infection and enhancing the formation of granulation tissue.

The way in which this technique is applied is based along several determined steps. In order to achieve NPWT, an open cell structured sponge is cut to fit the size of the wound adequately and placed inside

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the wound cavity. The target is for the foam to be in contact with the wound bed and edges to ensure an equal negative pressure distribution to every part of the wound. This also should reduce the possibility of localised high negative pressure to any one area, which might lead to tissue necrosis. This foam should next be covered by a transparent adhesive layer which extends on, and adhering, to the skin surrounding the wound. Next, this seal should be broken at a single point where a drain is placed to allow direct contact to the underlying foam. The plastic membrane nature of the seal prevents the entrance of air and creates a partial vacuum atmosphere. The distal end of the drain is connected to a vacuum source (NPWT Unit), which allows the drainage of the fluid away from the wound; this in turn promotes wound healing.[3-5]

Figure 1. Wound cleaning prior to NPWT dressing application

Figure 2. Sponge is cut to the size, to cover the whole wound

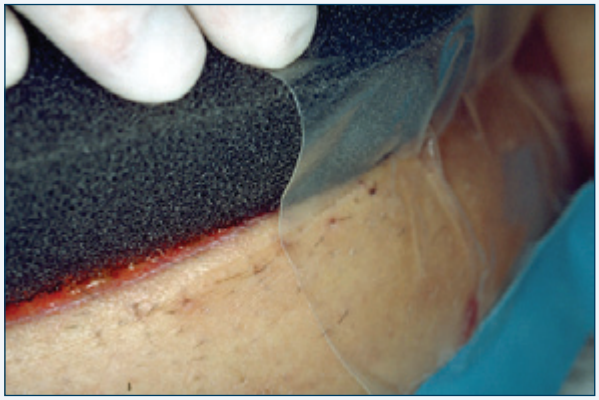

Figure 3. The adhesive film is applied to create an airtight seal

Figure 4. NPWT dressing, prior to application of negative pressure

Figure 5. NPWT dressing with negative pressure

Different steps of applying a NPWT dressing are demonstrated below (Figures 1 to 5):

Materials and methodology

The articles for this review were located primarily on the electronic data bases AMED, ASSIA (CSA Illumina), CINAHL (EBSCO), Conference Proceedings Citation Index: Science (ISI), EMBASE, Medline, PREMEDLINE In-Process & Non-Indexed Citations (OvidSP), PsycINFO (OvidSP), PubMed, Science Citation Index (ISI), Social Sciences Citation Index (ISI) on Web of Knowledge and Cochrane Library (Wiley) and ZETOC.

The following key words were used for citing the appropriate articles: topical negative pressure therapy; vacuum assisted closure; vacuum sealing; vacuum therapy; wound closure.

The following inclusion criteria were used to select relevant studies: A) Using sub-atmospheric pressure for wound healing in humans, B) Contained information about the applicability of NPWT in various implications, C) Articles using NPWT on animal studies for human applications, D) Case studies which used vacuum assisted closure, E) Relevant articles written in languages other than English.

Excluded Articles: A) Did not include negative pressure wound therapy B) Unpublished articles regarding NPWT applications.

The literature search of the online resources was undertaken in July 2013 for articles published from 1993 till that date. Out of 212 articles and studies that were reviewed, 77 were found relevant and suited the inclusion criteria. The relevant information from these articles is summarized below.

The development of negative pressure wound therapy:

The use of negative pressure with the intention to improve wound healing, was first described in 1993 by Fleishmann *et al.*[6] Fifteen patients with open fractures had a successful recovery after their wounds were exposed to sub-atmospheric pressure. The authors described this method of wound management as an efficient way to promote proliferation of granulation tissue and an effective way to achieve a clean wound bed. There was no evidence of bone infection in any of the cases. Fleishmann and his colleagues also used this novel technique of wound management, to treat lower limb compartment syndrome[7] and in patients with various types of acute and chronic infections.[8]

In the compartment syndrome group, a study cohort of 25 patients was treated by vacuum therapy for lower limb compartment syndrome, with an average duration of 12.7 days and 2.1 dressing changes per patient.[7] The majority of these wounds were closed by delayed suturing; with the remaining wounds were closed by skin grafts after a partial closure, by suturing. No significant complication was reported in this study.

In Fleischmann's study that looked at infected cases, treated with negative pressure, 313 patients were included with an average duration of therapy of 16.7 days, with an average of 3.1 dressing changes.[8] About two thirds of the wounds involved acute infections that were generally closed by secondary suturing. The remainder were allowed to epithelialise, or required skin grafting or flap transfer. In this study 6 (1.9%) patients died, and results showed a 4% (12/313) recurrence of infection rate.

Initially, negative pressure within the wound was created by the use of wall suction apparatus or surgical vacuum bottles. The main limitations in both these methods was found to be in the delivery, control and maintenance of the desired levels of negative pressure. Banwell *et al.* analysed these drawbacks and suggested several ways to overcome these problems.[9]

Soon after this study, a system promoting vacuum assisted closure was introduced to the United States market, specifically designed to avoid the problems described by Banwell. This system solved the previously mentioned problems by using a microprocessor-controlled vacuum unit. With the aid of this device, standardised levels of continuous or intermittent negative pressure, from 25 to 200 mmHg could be provided.[10]

In 1997 Muller *et al.*, reported further success in the application of vacuum therapy after treating 300 patients with infected wounds in Germany.[11] Another prospective study, again by Muller *et al.*, reported on

the use of vacuum therapy in 45 patients with soft tissue injuries, including sacral pressure ulcers, acute traumatic soft tissue wounds and infected soft tissue defects associated with lower limb fractures. After an initial wound debridement, in 84% of cases, the use of VAC decreased the healing time, size of the wound and significantly reduced the rate of wound infection.[12] Another study, by Kovacs *et al.* in 1998, showed NPWT was proven to be of benefit when treating chronic radiation ulcers.[5]

In 1997, Morykwas *et al.*[2] performed a series of animal experiments, in order to identify the optimal negative suction pressure needed to achieve the best wound healing. Deep circular lesions on the back of pigs were dressed with open-cell polyurethane-ether foam. By using a laser Doppler technique, the blood flow of subcutaneous tissue and muscles surrounding the wound were measured. Negative pressure was applied in two forms; continuous and intermittent. The results revealed that there is a four times increase in the blood flow when using NPWT with a negative pressure of 125 mmHg compared to the baseline technique of simple wound closure. However, blood flow appeared to be inhibited when the negative pressure exceeded 400 mmHg. From the observations of this study, a sub-atmospheric pressure of 125 mmHg was used for further studies.[2] In addition to blood flow measurements, they also monitored the rate of granulation tissue production, by using the same method. In order to compare the growth of bacteria in NPWT, large numbers of microorganisms were introduced to punch biopsy wounds; after four days of NPWT there was a remarkable reduction in the number of bacteria. It was also discovered that there was a 21% increase in the flap survival rate when compared with controlled values, which is hypothesised to be due to removal of interstitial fluid. The aetiology for this is being a reduction of localised oedema, increased blood flow and a reduction in bacterial counts. Further investigations by Fabian *et al.*[13] and Morykwas *et al.*[14] showed that using vacuum therapy enhances angiogenesis and matrix molecule synthesis. The authors suggested that by removing the oedema, which encompasses cellular debris, osmotically active molecules and biochemical mediators released following injury, interruption in the blood flow can be prevented.

Using a rabbit ear model Fabian *et al.*[13] demonstrated the effects of negative wound pressure on production of granulation tissue as well as epithelialisation. There is further evidence, using partial thickness burns in pigs that the use of NPWT results in prevention of progressive tissue damage at the site of initial injury. The effect can be depicted within 12 hours following injury and a treatment time of 6 hours is adequate to demonstrate the beneficial effects.[14]

It is interesting to note that when negative pressure is applied continually, it appeared to be less effective than cycled treatment. The basis for this observation is not clear but, according to Philbeck *et al.*,[15] there might be two reasons that can explain this. One theory suggests that the cyclic treatment leads to the maintenance of the rhythmic perfusion of the tissue as the process of capillary autoregulation is not activated. The other theory indicates that during mitosis, there is a stage of rest for the cell. When pressure is applied intermittently, there is enough time for the cell to rest and prepare for the next stage but when the pressure is applied continuously cells might ignore the stimulus. There is still some controversy between the authors whether an initial 48 hour period of continuous negative pressure should be used to initiate a rapid cleansing effect at the start of therapy.[16,17]

Clinical use of NPWT

In 1997, inspired by animal studies, Argenta *et al.* used NPWT clinically for the treatment of 300 wounds with various aetiologies. These wounds were treated until they were either completely healed, could be covered with a split-thickness skin graft, or were suitable for surgical reconstruction with a rotation flap. The vast majority of cases (296/300 = 98.7%) had a satisfactory response to Vacuum Assisted Closure. Consequently, the authors agreed that NPWT can make a significant difference when dealing with chronic, resistant wounds.[1]

There have been many papers published regarding the different applications of NPWT for varying forms of wound and wound healing. Amongst the most significant are extensive degloving injuries,[18,19] infected sternotomy wounds,[17,20-23] soft tissue injuries prior to surgical closure,[24] open fractures of lower extremities,[25] diabetic foot ulcers,[26-30] and grafting or reconstructive surgery techniques.[31]

Table I. Examples of wounds being managed with NPWT

Examples of wounds being managed with NPWT:[48]

- Pressure sores
- Burn wounds
- Chronic open wounds
- Acute and subacute wounds, including traumatic
- Flaps
- Meshed grafts
- Compromised skin grafts
- Venous ulcers
- Dehisced incisions
- Diabetic ulcers

Table II. Indications/aims and contraindications for NPWT

Indications or aims of use of NPWT[49]

- Remove exudate and reduce periwound oedema
- Increase local microvascular blood flow
- Promote formation of granulation tissue
- Reduce complexity/size of the wound
- Optimise the wound bed prior to and following surgery
- Reduce complexity of surgical wound closing procedures

Contraindications and precautions for NPWT:

- Anticoagulated patients
- Eschar
- Irradiated blood vessels within wound
- Fistulas
- Untreated osteomyelitis
- Malignancy
- Directly on big vessels (e.g. femoral artery)

One of the most important applications of NPWT is in the treatment of donor sites that are difficult to manage using other methods. For instance, when using conventional techniques in patients with radial forearm free flap reconstructions, at least one third develop tendon complications according to Greer *et al.*[32-34] Greer suggested that these individuals would benefit from the use of vacuum therapy as a donor site dressing.

In a four year retrospective review conducted in 1997 by Smith *et al.*, the use of NPWT for management of the open abdomen was described in 93 cases; it was concluded that vacuum assisted closure is a favourable choice to manage the open abdominal wound, at least in a temporary setting.[35]

A further application of NPWT is in the treatment of burns; studies conducted by Schneider *et al.*[36] and Pfau *et al.*[37] concluded that the use of NPWT in combination with split thickness skin graft for burn management, especially in irregular surfaces, such as the axilla, hand and perineum. With help of the sub-atmospheric pressure the graft is securely held onto the wound bed, therefore the accumulation of tissue fluid is prevented thus keeping the graft stable.

Vacuum assisted closure has also been used for treatment of full thickness loss of the scalp due to burns, or following excision of widespread Carcinomata. This is proven in Molnar *et al.*'s study that focuses on the outcome of four patients who benefited from this treatment.[38] Primary scalp wound closure was not possible with the use of a flap; punctate bleeding was obtained by removing the outer tables of the skull, followed by NPWT application to promote the formation of granulation tissue. About two weeks later a skin graft was applied as definitive wound closure.

There are several articles about the use of NPWT in patients with infected sternal wounds. The study carried out by Damiani *et al.* in 2011, chiefly looked at the length of hospital stay. They demonstrated that negative pressure on infected sternal wounds decreased the hospital admittance by 7.18 days.[22,23]

In a randomised controlled trial published by Karatepe and his colleagues in 2011, the findings of vacuum assisted closure for patients with diabetic feet were published. In this study, they compared the effect on the quality of life, and the wound healing time, in patients undergoing NPWT and compared to those treated with standard conventional wound care. The results were greatly in favour of using vacuum assisted

closure management as it significantly reduced the wound healing time in particular.[26]

A further study looking at the use of negative pressure wound therapy in complex pleural empyema in eight patients.[39] NPWT with a negative pressure of 125 mmHg ensured local control of the pathology, as well as control of sepsis with cleaning of the thoracic cavity, resulting in rapid healing.

In addition to the above, there are also many case studies reporting the success of applying vacuum therapy for a wide range of non-healing or chronic wounds. Amongst the most successful are pressure sores,[16] anterior tracheal necrosis after total thyroidectomy,[40] below knee amputation wounds,[41] leg ulcers and longstanding wounds[42-46] as well as wound secondary to brown Recluse Spider bites.[47]

Discussion

In this review we have summarised the various applications of vacuum assisted closure dressings by looking at the published evidence. The application of NPWT dressing has improved the wound healing process, compared to conventional therapies.

This section deals with some commonly asked questions about NPWT dressing. Among the most significant questions are: A) whether there is adequate evidence for applying NPWT dressing to eligible patients B) factors that should be considered prior to applying vacuum assisted closure; and C) can cost play a role in limiting the use of NPWT.

In 2011 a review published by Mouës *et al*.[50] over 400 peer-reviewed articles related to the use of Topical Negative Pressure therapy (animal, human, and in vitro studies) were considered. The vast majority of these articles concluded that there is improvement in blood flow, promotion of angiogenesis, induction of cell proliferation as well as accelerated reduction in wound surface area. However, the mechanisms of oedema reduction and bacterial clearance have not been proven in basic research.[50] After reviewing 78 NPWT related articles the clinical observations appeared similar to Mouës *et al*.

By looking at the number of articles regarding NPWT, it is noticeable that there have been a significant number of publications that considered the efficacy of vacuum assisted closure compared to the usual way of wound treatment. However, it should not be overlooked that some trails are hard to interpret due to apparent bias and the fact that different types of wounds were treated each time.[5]

In order to achieve the most out of NPWT, it must be applied correctly. In order to do so, several factors should be considered. A correct patient selection prior to the treatment plays a very important role. The chosen patient should be able to withstand NPWT for about 22 hours a day as well as being nutritionally stable.[5] Furthermore, the patients need to have at least 2cm of intact peri-wound tissue to maintain the airtight seal.[51] Obtaining an airtight seal can be problematic at times, especially if the lesion is near the anus or vagina or anywhere where the surrounding skin is moist. Applying a hydrocolloid dressing such as Duoderm can often aid obtaining an optimal seal.[42]

To achieve the best outcome, it is important to know how to regulate and adjust the negative pressure for different types of wounds. In some occasions the negative pressure should be increased to maintain its efficacy, particularly in large volume wounds with excessive drainage. The vacuum pressure should be down regulated especially when the patient is in pain, in the case of excessive bleeding or compromised circulation, as well as in patients who develop bruising within the wound bed.[52] There may be benefits to starting negative pressure therapy as early as possible. Delaying therapy may allow the wound to deteriorate before being treated effectively.[49] NPWT has also been reported to reduce wound pain, improving the patient's experience along their wound treatment journey.

The cost issue of NPWT has been an ongoing debate since its introduction. Many articles have been published which evaluate and compare the cost of NPWT with the conventional treatment used in different countries. According to a literature review regarding the cost effectiveness of negative pressure wound therapy (NPWT) by Othman, published in 2012,[53] there is enough evidence that NPWT could be a useful source of cutting costs of chronic wound management for the national health system (NHS) in the UK. Braakenburg *et al*.[54] in the Netherlands concluded in a randomised controlled trial, that NPWT

dressing did not show a significant improvement in wound healing, but it highly increased patient comfort. In addition to that the time involvement and costs of nursing staff were remarkably lower with the use of NPWT on wounds.

Further papers comment on the cost of the varying amounts of equipment which may limit rural use of NPWT, although again note that the nursing, time and hospitalisation costs are reduced particularly in diabetic and chronic lower limb wounds.[48] This economic pay-off is supplemented with a quicker wound resolution time, although the author of the health economic portion of this report, Trueman, does note a distinct lack of literature in regard to cost analysis. One paper which does compare the specific costs involved between NPWT and moist wound therapy, did find a reduced resource utilisation and lower overall cost of care in post amputation diabetics.[55]

Conclusion

Vacuum assisted closure therapy has been around for no longer than 20 years and has facilitated the wound healing process to a large extent. This wound healing system has proven beneficial in a wide range of applications, predominantly in the management of chronic, open wounds as well as in acute and sub-acute wounds. Likewise, benefits have been seen in cases involving meshed skin grafts, diabetic ulcers and pressure sores. By reducing healing time and being cost-effective, NPWT dressing has made wound healing a more comfortable, and cheaper, process, as well as improving the quality of life and morbidity of the patients requiring therapy.

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