Negative pressure wound therapy: A review of efficacy in pressure ulcers

KEY WORDS
- Negative pressure wound therapy
- Pressure ulcer
- Topical negative pressure
- Vacuum-assisted closure

Pressure ulcers place a significant burden on both patients and the healthcare system and it has been suggested that the use of negative pressure wound therapy (NPWT) in the treatment of pressure ulcers may lead to faster healing. However, the role of NPWT in the management of chronic wounds has become a controversial issue, following a Cochrane review that concluded there was no valid or reliable evidence to suggest NPWT aided chronic wound healing (Ubbink et al, 2008). The aim of this article is to discuss the evidence assessed in the Cochrane review, as well as to consider other types of evidence available and more recent studies. Current evidence does not allow a firm conclusion regarding the efficacy of NPWT for the management of pressure ulcers, but is suggestive of improvements in ulcer size and wound bed quality.

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Negative pressure wound therapy (NPWT) was introduced in the 1990s and has been used in the treatment of a variety of acute and chronic wounds. Several different systems are available, but all operate on the same principles: a foam, or sometimes gauze, is placed in the wound and covered with an adhesive film, a seal is created and a suction device connected (Gregor et al, 2008).

The negative pressure exerted on the wound aids healing in several ways. First, blood flow changes adjacent to the wound are thought to improve the delivery of oxygen and nutrients, as well as aid the removal of waste products (Orgill et al, 2009). An increase in the volume of granulation tissue in the wound bed has also been reported following NPWT, which provides the essential matrix for epithelial cell migration and, ultimately, healing (Morris et al, 2007).

Mechanical forces within the wound have been proposed as the catalyst behind reducing the wound size, as well as stimulating cellular proliferation on the microscopic level (Orgill and Bayer, 2011). Wound exudate contains cytokines, proteinases, and oxygen-free-radials – all of which may inhibit healing in the chronic wound – and removal of these through NPWT may also improve healing (Morris et al, 2007).

Pressure ulcers place a significant burden on patients and the healthcare system, with the inpatient prevalence of pressure ulcers estimated to be 18.1% across Europe (Vanderwee et al, 2007). Pressure ulcers occur as a result of pressure and shear, often overlying bony prominences, causing the breakdown of skin and/or underlying tissues (Bouten et al, 2003). Pressure ulcers frequently become chronic wounds, often due to patient comorbidities that impede healing, such as malnutrition, diabetes, and anaemia (Gupta et al, 2004).

It has been suggested that the use of NPWT in the management of pressure ulcers may lead to faster healing compared with alternative dressings, such as alginates and hydrocolloids (Smith, 2004), which appears to be supported by some clinical experience (Wanner et al, 2003). There is also evidence to suggest that using NPWT may also confer cost savings due to the decreased frequency of dressing changes required and the reduction in the time clinicians spend treating them (Mody et al, 2008).

CONTROVERSIAL ROLE OF NPWT

The role of NPWT in the management of chronic wounds has become a controversial issue, following the publication of a Cochrane

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review (Ubbink et al, 2008) that concluded there was no reliable evidence to demonstrate that NPWT aids chronic wound healing. This review only included randomised controlled trials (RCTs) and did not take into account other levels of evidence, such as case series.

The aim of the present review is to discuss the evidence analysed by Ubbink et al (2008) regarding the use of NPWT in pressure ulcers, and to investigate other relevant evidence that was not included in their review. Areas of controversy surrounding NPWT in pressure ulcers are discussed throughout.

RANDOMISED CONTROLLED TRIALS

Two RCTs were identified by Ubbink et al (2008), who reviewed the use of NPWT on pressure ulcers. First, Ford et al (2002) recruited 28 participants with a total of 41 pressure ulcers (all Grade IV) of more than 4 weeks' duration. Participants were randomised to receive NPWT or the Healthpoint System (HP), which uses one of three gel dressings selected on the basis of the stage of wound healing.

Exclusion criteria included potentially important participants who would represent patients with chronic diseases, including chronic pulmonary or cardiac disease, and limits the real-life applicability of findings. Those assessing the wounds at 3 and 6 weeks were blinded as to the treatment group, however, it is questionable whether truly blind trials of NPWT are possible since the wound bed takes on a characteristic appearance and thus gives the identity of the treatment group away.

Ford et al's (2002) findings included a larger decrease in wound volume and absolute dimensions in the NPWT group and a larger decrease in the number of white cells present in tissue biopsies in the NPWT group, compared with the HP group, suggesting an improvement in the wound environment. Participants receiving NPWT were found to have a greater number of capillaries, suggestive of the stimulation of granulation tissue.

While these findings seem to support NPWT as the more effective treatment, the between-group differences were not statistically significant, despite the careful methodology, so perhaps the small trial sample limited the strength of the findings.

The second study identified was conducted by Wanner et al (2003) who recruited 22 participants with Grade III–IV pressure ulcers. Similar to Ford et al's (2002) study, the researchers chose to measure total wound volume directly and not merely by calculation. However, in contrast to Ford et al's study, where NPWT dressings were changed every 2 days, Wanner et al (2003) stipulated that dressing changes would take place at 2–7-day intervals, which left this variable less well controlled.

Participants were randomised to receive either NPWT or "standard treatment", which was wet gauze, changed three times a day. This comparison has been questioned as wet gauze may be considered a suboptimal dressing for the management of pressure ulcers (Morris et al, 2007) and not representative of common practice. Start- and end-points for this study were well defined, from initial surgical debridement to a reduction in wound volume of 50%. Results showed no between-group difference in time taken to reach the end-point, but mean wound volume in the NPWT group was larger, and had a greater size range at baseline than for controls.

As a secondary conclusion, it is noted that changing dressings three times a day – as required with wet gauze – causes significantly more discomfort for the patient than NPWT, which is changed every 2 days. This is an important consideration in holistic patient care (Wanner et al, 2003).

Grading inconsistencies

While these two trials report inclusion of similar ulcers (Grade III–IV) neither article states which grading system was used for these definitions, although it seems likely that these were defined using the widely accepted European Pressure Ulcer Advisory Panel (EPUAP) grading system (EPUAP and NPUAP, 2009). Ulcers are graded in this system from I (non-blanching erythema) to IV (muscle or bone exposure). A range of pressure ulcer

grading systems are available and clear definitions of the system used are essential to compare studies (Dealey and Lindholm, 2006).

ADDITIONAL EVIDENCE FOR NPWT

Evidence not evaluated by Ubbink et al (2008) was available at the time of review, but was excluded due to the chosen review methodology. Müllner et al (1997) evaluated the efficacy of NPWT in several wound types, including one group of patients with pressure ulcers. This small group comprised 17 participants who had developed pressure ulcers following orthopaedic trauma. The pressure ulcers had been present for an average of 2 weeks, and varied in size from 12–72 cm^2, with the sacral bone exposed in 66% of ulcers. No information was provided regarding how the pressure ulcers were assessed in terms of size, depth, exudate levels, or infection, making it difficult to compare Müllner et al's (1997) results with those of other studies.

There was no control group in the Müllner et al (1997) study and the authors defined response to treatment as an 80% reduction in wound size or when the wound bed was covered with granulation tissue. By this definition, 71% (12/17) of the pressure ulcers responded to NPWT. The time taken to achieve full healing ranged from 12 to 46 days, but, due to the lack of a control group, the conclusions that can be drawn are limited.

In a case series comprising seven patients with pressure ulcers and spinal cord injuries, Coggrave et al (2002) concluded that NPWT could be useful in the management of pressure ulcers, but response to treatment varied, with percentage volume reduction over the course of therapy ranging from 33%–96%. In addition, this study highlighted some practical concerns with NPWT, including growth of granulation tissue into the foam dressing, causing bleeding on removal and difficulties in forming an effective seal in certain anatomical areas.

In a subsequent study of 10 participants with Grade IV pressure ulcers treated with NPWT, the authors concluded that NPWT was effective in reducing the size of pressure ulcers (Isago et al, 2003). In this study ulcer area was determined by using the calculation of width × length ÷ 2, which does not take into account the variability in ulcer shape and depth.

The difficulty in controlling variables was highlighted by Isago et al (2003) who planned to apply 125 mmHg of negative pressure to all wounds. However, 30% of patients reported pain at this setting, so the range used was 50–125 mmHg. An overall lack of methodological detail makes assessment difficult (e.g. NPWT treatment periods varied from 4–7 weeks), but all participants saw an improvement in their pressure ulcers during the study period.

VARIATION IN ASSESSING ULCER SIZE

In the studies described here, each used a different method to assess ulcers and response to treatment. The flawed calculation of area used by Isago et al (2003) has been described. Methods used for measuring the volume of pressure ulcers varied between the studies, from making a cast of the wound using plaster (Ford et al, 2002) or alginate material (Coggrave et al, 2002), to covering the wound surface with a film dressing and injecting measured amounts of saline into the space (Wanner et al, 2003). Computer software is also available that analyses photographs to determine wound surface area and depth in some studies (Ho et al, 2010). Thus, there is a need for a validated and widely available tool to determine ulcer area and depth to ensure comparability.

NPWT RESEARCH, POST-2008

In an RCT comparing the efficacy of NPWT with wet gauze for wound closure, Mody et al (2008) looked at wounds of varying aetiology, but performed a subset analysis of pressure ulcer results. It was found that pressure ulcers healed in a shorter time with NPWT (10 ± 7 days) than wet gauze (27.4 ± 10.6 days; P=0.05). However, as only 10 pressure ulcers were studied, this represents a small sample from which to draw conclusions.

Again, difficulties in adequately controlling the application of negative pressure were

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reported by Mody et al (2008) due to participant intolerance of higher levels of negative pressure. Individual clinicians were allowed to determine whether continuous or intermittent NPWT was used.

NPWT in Mody et al's (2008) study was also delivered via a device connected to wall suction as commercially available units were too expensive for the hospital in India. The wall suction device was situated at the patient's bedside, usually wall mounted. It is normally used with a yankauer sucker to clear airways, but, in this case, was used as a substitute for a NPWT pump.

While this was a pragmatic solution, this system may not be as well-controlled as other devices. Other methods used to deliver NPWT include surgical suction drains (Müllner et al, 1997), in which the negative pressure generated cannot be measured.

Perhaps the first widely available NPWT device, VAC® Therapy (KCI Medical), is the best known, however, even the nomenclature of this can be a cause of potential confusion as the term 'VAC' is often used to mean vacuum-assisted closure and does not refer to the branded device.

Recognising the difficulties in undertaking an effective RCT to assess NPWT in chronic wounds, Witkowski et al (2009) set out to perform a non-controlled investigative study. The primary aims were to assess the acceptability of NPWT to both clinicians and patients, and to observe wound outcomes. Acceptability is a valid outcome to observe because if the system was difficult to work with, this may result in ineffective application and if patients find the treatment uncomfortable, compliance may be reduced.

Witkowski et al (2009) found that NPWT was mostly acceptable to patients and clinicians, although one patient with a pressure ulcer requested the treatment be discontinued. The reason for this was not given. Pressure ulcer surface areas reduced during the study period and the quality of tissue in the wound bed improved, although the length of treatment was relatively short (2–14 days) so sustainability of these improvements could not be assessed.

A larger trial comprising 86 participants with Grade III–IV pressure ulcers in patients with spinal cord injuries was undertaken by Ho et al (2010). This was a controlled trial with one group receiving standard care, the other NPWT treatment in addition to standard care. Participants were not randomised, but selected for NPWT as clinicians deemed appropriate. Although this introduces selection bias, it replicates a more realistic clinical scenario. Standard treatment was also varied, with a wide range of treatments used, including antimicrobials, foams, hydrocolloids, and alginates, which, again, provides a more realistic control compared with trials in which only wet gauze was used.

Patients were followed up over a period of 28 days and results showed no difference in wound size between the two groups. The main limitation of this study was that, while wound surface area was assessed in an accurate manner using specialised computer software to analyse photographs, there was no measurement of wound depth, so changes in wound volume were not detected.

A different approach to the assessment of efficacy was taken by Nakayama (2010). NPWT was applied to Grade IV pressure ulcers, which were recalcitrant to previous treatments and had a mean duration of 240 days (range 28–2154 days). The chronicity of the wounds included would suggest that any changes were likely to be the result of NPWT, but other factors cannot be ruled out, for example, the presence of an occlusive dressing or, indeed, a placebo effect.

A cohort of 32 older participants (mean age, 82.4 years) with multiple comorbidites were recruited as there were no exclusion criteria to limit study of this type of patient. This study included participants for who NPWT may be a nonsurgical wound management option due to their being unfit for anaesthesia. Furthermore, patients of such advanced age are often excluded from studies. Five patients died during the study period, but all other wounds achieved complete healing, either by secondary intention or surgical procedure, once granulation tissue covered the wound bed (mean time, 46.4 days).

"Effective research into pressure ulcers and their treatment is not a straightforward undertaking within the setting of randomised control trials."

The extensive follow-up time (mean time, 640 days) made this study unique. Only four patients had subsequent wound breakdown during follow-up.

CONCLUSION

Effective research into pressure ulcer management is not a straightforward undertaking. Patient populations can be an extremely heterogeneous, often presenting with multiple comorbidities and wounds that vary greatly in size, characteristics, and duration.

Measuring wounds, and defining appropriate endpoints, also pose challenges. Follow-up to complete healing may require long periods of time.

Other outcomes also need to be considered, including patient comfort, quality of life, and management of ulcer symptoms, such as pain, malodour, and exudate.

Control treatments with which to compare NPWT are also difficult to determine as pressure ulcers may be managed using many different treatments meaning there is no "standard treatment" with which to compare.

The number of RCTs in this area of care is limited, and have been conducted in small samples, making it difficult to generalise the results. Case series and uncontrolled trials may not generate gold-standard evidence, but they may represent a more pragmatic approach to studying pressure ulcers and chronic wounds. Thus, evidence from case series and uncontrolled trials should be considered when determining the strength of evidence for the use of NPWT.

Available evidence does not allow for a firm conclusion to be reached regarding the efficacy of NPWT in pressure ulcers. However, there are indications that pressure ulcers improve in terms of size and wound bed quality following NPWT and in chronic wounds this should be considered a positive outcome. WUK

STATEMENT

The author carried out this research at the Department of Wound Healing and Tissue Repair, Cardiff University, Cardiff, UK.

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