The high costs and inaccessibility of skin substitute therapies: an emerging alternative for hard-to-heal leg ulcer treatments in a post-pandemic environment

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Rising rates of diabetes, obesity and vascular disease, in addition to rapidly ageing populations, have increased the prevalence of hard-to-heal wounds to epidemic proportions, creating a vital need for efficient wound management therapies. Lost efficiency and economic productivity due to time off work, lost wages and psychosocial suffering of patients impose a financial and social drain on our society. It is estimated that nearly 10% of our population will develop a hard-to-heal wound during their lifetime, with a wound-related mortality rate of 2.5%.[1] Among hard-to-heal wounds, in particular leg ulcers (predominately diabetic and venous), a significant clinical and medical challenge is currently faced by our society. Diabetic foot ulcers (DFUs) are one of the most common complications of poorly controlled diabetes. More than 50% of DFUs will become infected, increasing the risk of hospitalisation, amputation and death. Venous leg ulcers (VLUs) account for >70% of all lower extremity wounds in the adult population[2] and approximately 90% of all vascular ulcers.[3] Risk factors for VLUs include increased age and body mass index (BMI), hypertension, low physical activity, deep vein thrombosis and a family history of VLUs.[4] VLUs are common in ageing populations, occurring in an estimated 1–3% of adults worldwide.[5]

Lower leg ulcers are associated with long healing times and high recurrence rates (78% incidence of recurrence) within three years of initial healing.[6] Due to this chronicity and high rate of recurrence, DFUs and VLUs are costly for both the patient and the healthcare system. Rice et al. analysed the payer cost burden of Medicare-covered patients with a VLU (aged 65 years and older) as well as private insurance-covered patients with a VLU (aged 18–65 years) in the US, utilising two insurance claims databases.[7] The estimated US payer cost-burden, including medical costs and missed work days, was reported to be $14.9 billion. Another published study showed that the average annual expenditure of diabetic foot care was $8659 per patient, with the total medical cost for the management of diabetic foot disease in the US ranging from $9–13 billion.[8,9]

Skin substitutes have increasingly been added to the management armamentarium in wound clinics for the treatment of hard-to-heal DFUs and VLUs. However, higher costs associated with skin substitutes preclude treatment of the uninsured, and often the insured patient populations. In an analysis of efficacy rates using skin substitutes and 2018 Centers for Medicare & Medicaid Services (CMS) cost data, it has been reported that the average cost for skin substitute treatment of a single DFU ranged from $2001 to $14,507 (outpatient) and from $1207 to $8791 (office setting).[10] In the same analysis, the estimated number of wounds healed out of 100 DFUs per $1000 expenditure/patient ranged from 3.9–26.5 (outpatient) and 4.3–36.4 (office setting).

Post-pandemic challenges

During the ongoing COVID-19 global pandemic, access to some DFU and VLU treatments has become restricted, for both the insured and uninsured patient populations. Clinic visits have been significantly reduced, often preventing these high-risk patients from receiving the requisite weekly applications of skin substitutes. The reduction of in-clinic visits has directly impacted the insured patient population, resulting in high unmet deductibles and increasingly high co-payments. The pandemic has also affected access to healthcare providers, specifically home health nurses, which has further limited the ability to deliver conventional therapies for the treatment of DFUs and VLUs, which

require frequent dressing changes. Disruptions in the supply chain have created a shortage of treatment supplies, generating increased costs for both conventional and advanced wound care dressing therapy. The COVID-19 pandemic and changes associated with increased insurance-related costs, reduced clinic visits, unavailable home healthcare and supply chain availability issues, have resulted in neglected wounds and increased complications, including increasing numbers of amputations.

Addressing the post-pandemic need

While skin substitute therapy is currently used as a treatment for patients with non-healing DFUs and VLUs, its overall efficacy remains under investigation. The COVID-19 pandemic has created a need for clinicians to consider a paradigm shift to ensure adequate management and care of our patients. The optimal treatment strategy in the post-pandemic environment will facilitate wound healing, be accessible to and comfortable for all patients, minimise insurance and out-of-pocket costs, provide ease of use and mitigate the need for multiple dressing changes.

Emerging alternative

A promising dressing option for post-pandemic patients with hard-to-heal DFUs and VLUs is based on a novel methacrylate-based transforming powder dressing (TPD). Made of the same polymers used to produce contact lenses and controlled-release eye medications, TPD transforms in situ to a shape-retentive wound matrix when it comes into contact with moisture. After exposure to hydration, TPD conforms to the wound's shape and solidifies into a scab-like cover that flakes off as the wound heals. Upon hydration, the methacrylate polymers in TPD form hydrogels. They have a tendency to swell but do not dissolve in water and can safely perform their required functions without being absorbed into the bloodstream of the host. Consequently, there are limited side-effects and a dressing can remain in place for an extended period of time, with changes only as needed. TPD can be left on the wound for up to 30 days, is easily transportable and shelf-stable for four years. More powder may be added from time to time for more exudative wounds without requiring a primary dressing change, and simple secondary dressings may be used to cover TPD in areas of high exudation or friction.

TPD, when applied to a wound, can retain up to a 68% moisture level (equivalent to skin) while its capillary channels wick excess exudate from the wound surface with a high moisture vapour transpiration rate. TPD conforms to the wound margin, covers and protects the wound and allows oxygen transport, at the same time shielding the wound from bacteria, creating an ideal environment for proper wound healing. Its extended wear time and visible margins enable wound inspection without disruption of wound healing due to frequent dressing changes, thus minimising potential exposure to contamination. Decreased dressing changes also enhance patient comfort and further reduce overall healthcare resource use. From a patient, payer and provider perspective, the TPD extended wear time of up to 30 days, overall decrease in dressing changes compared with other treatment modalities, reduction in resource use and significantly lower direct costs, compared with skin substitutes, all combine to make TPD a promising alternative treatment for patients with hard-to-heal DFUs and VLUs in the post-pandemic environment.

Early evidence

Retrospective evaluations of use of TPD in patients with hard-to-heal DFUs and VLUs highlight the potential of TPD to serve as a viable alternative treatment strategy. While these retrospective evaluations are limited in sample size and have no control groups, their data are being described to provide an overview of some of the early evidence associated with TPD treatment.

A retrospective, multicentre case series involving 17 patients was conducted by Galiano et al. to assess the efficacy of TPD treatment of stage 2–3 DFUs with Wagner Grade 2 or 3 (data on file). Patients who had previously failed standard of care treatment for DFUs met the inclusion criteria. Patients without stage 2–3 DFUs were excluded from this study. Wounds were cleansed using saline and TPD was applied before being covered with the appropriate secondary dressing. The wounds were evaluated at weekly intervals and TPD was reapplied with dressing change as needed. Days to healing, number of dressing changes and days between dressing changes were recorded. Treatment with TPD dressing continued until the physician determined that the condition of the diabetic ulcer no longer warranted its use. Historical data on 17 patients (mean age 58 years) were assessed and evaluated. Each patient had DFUs of different stages and duration that failed previous wound management therapies, ranging from simple dressing changes to multiple amputations. Of the patients, 13 (77%) had severe stage 3 DFUs and four (23%) had moderate stage 2 DFUs. The majority of the DFUs were hard-to-heal, with a mean wound duration of 33 months (range: 4 days–18 years). TPD dressings were changed on a weekly to monthly schedule, based on the clinician's judgement and the needs of the individual patient. The mean number of dressing changes was 5.9 and the mean time to heal was 45.7 days. All patients experienced accelerated wound closure and avoidance of amputations.

In a published case series, seven patients with VLUs were treated with TPD during an initial evaluation of the dressing's utility in wound management. All patients had failed previous wound healing attempts using various advanced dressings, bioengineered skin or split-thickness skin grafts. All patients also had varying levels of non-adherence to the systemic plan of care, including inconsistency with compression garments/dressings, management of optimal glucose levels and routine

consistent dressing changes. Duration of wounds ranged from 3–27 years. All patients reported pain as an inhibiting factor to adherence with the recommended wound care regimen and the wound size had not decreased in several months for any of the patients. All seven patients reported improvements in pain levels within 15 minutes of TPD application. As a result, this cohort increased adherence with recommended treatment plans, reduced oral pain medication use, and exhibited a steady decrease in wound sizes and drainage, resulting in complete wound closure.[11]

Based on observations of the retrospective case series, TPD may be a safe and viable alternative for the management of nonhealing DFUs and VLUs. In these series, TPD both significantly improved and shortened the wound healing process without the need for skin grafting.

Conclusion

Early evidence suggests that TPD may provide a promising alternative to skin substitutes for the treatment of patients with hard-to-heal DFUs and VLUs, particularly in the post-pandemic environment faced by both healthcare providers and patients. Anecdotal evidence suggests the potential added benefit of pain reduction in VLU patients treated with TPD. While further studies (including a large multicentre prospective study) to confirm the efficacy of TPD in the treatment of hard-to-heal wounds are warranted, the early available evidence, combined with the potential to decrease the overall healthcare cost burden, indicates that TPD is an encouraging option for patients with these wounds. JWC

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