

Autologous cell treatment of problem wounds

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Non-healing and chronic wounds pose a huge problem to both patients and staff within the NHS (National Institute for Clinical Excellence, 2004). There are at least 400 000 leg ulcer sufferers in the UK at any one time, with approximately 100 000 patients receiving treatment (UK Health Episode Statistics 2004–5). Furthermore, large numbers of burns, trauma and post-operative wounds do not heal as a result of infection, poor underlying pathology (i.e. diabetes mellitus), or poor vascularisation (McCampbell et al, 2002).

Split skin grafts (SSG) (Ahnlide and Biellerup, 1997) and cultured epithelial autografts (CEA) (Elliott and Vandervord, 2002) have been used in the treatment of chronic wounds and burns (Hefton et al, 1986; Phillips and Gilchrist, 1990; Horch et al, 2005).

These procedures are not always successful and are susceptible to mechanical damage as well as blistering and infection (Herzog et al, 1988; Williamson et al, 1995). They also require a patient biopsy or graft site, leaving the patient with a second wound that is also potentially non-healing.

Myskin™ (CellTran, Sheffield) cell therapy is an autologous cell therapy treatment that enables the patient's own cultured keratinocytes to be delivered back to the wound bed on a sterile, medical-grade polymer dressing (Zhu et al, 2005). Unlike those required for CEAs and SSGs, the biopsy size for a Myskin™ graft is only 2cm x 2cm and from this biopsy an indefinite number of cells

can be cultured for repeated graft applications. A local anaesthetic is used to obtain the thin-shave biopsy, which is taken by a qualified clinician in the clinic and promptly returned to the Myskin™ clean room laboratory. The first graft is returned to the patient within two weeks of taking the biopsy. In this time, the wound care team can ensure the wound is clean and any infection is controlled, maximising the healing efficacy of the grafts.

The keratinocyte cells are provided on the Myskin™ patented transfer surface, enabling them to be applied in the clinic or in the patient's home. The surface encourages the keratinocytes to transfer from the Myskin™ graft to the wound bed and to promote re-epithelialisation, a process that takes about four days from application. The Myskin™ dressing and its protective secondary dressings can then be removed, leaving a thin layer of the patient's own keratinocytes in the wound bed. A suitable dressing is then applied until the next application of cells, three days later.

Hydrocolloid and silver-containing dressings should not be used on top of the transferred skin cells as their mode of action is too harsh to allow the new skin cells to grow into the wound bed. Treatment is then continued until the wound has fully re-epithelialised. This normally occurs following 4–6 weeks of cell application.

Myskin™ cell therapy treatment has proven applications in chronic wounds, burns and plastics arenas with both clinical trial and case study data being available (Moustafa et al, 2004; Zhu et al, 2005).

This article highlights the case of Mrs L, a 68-year-old female with diabetes, who had a large post-operative wound to her foot, and who was precluded from skin grafting treatment because of her poor general health.

Initial treatment

Mrs L presented to Accident and Emergency in September 2005 with painful black areas and blisters on the top of her right foot. She was pyrexia and had general malaise. She was admitted onto the vascular ward with cellulitis of the right foot and necrotic areas on the fourth toe, fifth toe and right forefoot. A subsequent X-ray confirmed osteomyelitis in four toes of the right foot and blood tests revealed previously undiagnosed type 2 diabetes.

On admission, Mrs L was given intravenous antibiotics for her cellulitis and insulin for blood glucose control. She then underwent angiography, which diagnosed bilateral peripheral vascular disease. Four days after admission she underwent a right femoropopliteal bypass (using a below knee, non-reversed vein graft from the left leg), and also amputation of her right second, third, fourth and fifth metatarsals. The necrotic areas on her forefoot were also debrided. Post-operatively, the wound was covered with Mesitran™ honey dressings (Medlock Medical, Oldham) to minimise the risk of infection (Cooper et al, 1991; Molan, 1999). The wound area at this point measured 68cm² (Figure 1).

Maggot therapy

Five days post-operatively, some slough and a small amount of necrotic tissue remained on the wound border. Maggot therapy (Zoobiotic Ltd, Bridgend) was initiated to thoroughly clean the wound. Maggots not only remove the dead tissue but have also been found to remove bacteria from the wound, including methicillin-resistant *Staphylococcus aureus* (MRSA) (Thomas et al, 1999). This treatment was continued twice weekly for four weeks until the necrotic areas had been removed along with the majority of the slough (Figure 2).



Figure 1. The wound area measured 68cm² following surgical debridement.



Figure 2. The wound after maggot therapy.



Figure 3. The wound after VAC treatment.

Following the maggot therapy, the wound area measured 60cm² and although clean, showed no further signs of healing independently. During this time, a second ulcer had formed on the outer ankle with a diameter of 5cm. This was treated with MesitranTM dressings.

Vacuum assisted closure

Vacuum assisted closure therapy (VACTM; KCI Ltd, Oxford) was utilised on the larger wound to control exudate and promote vascularisation. VACTM therapy uses negative pressure to remove fluid, reduce oedema and increase blood flow to the wound (Joseph et al, 2000). Reduced bacteria counts within the wound have also been reported (Morykwas and Argenta, 1997). As Mrs L had only recently received a femoropopliteal bypass it was considered the reduced pressure on the wound bed would also aid revascularization of both the right leg and foot.

Mrs L responded well to the VACTM and after two weeks of treatment, the wound area measured 55cm² (Figure 3). The wound bed showed signs of healthy granulation tissue with reduced exudate, so VACTM therapy was discontinued. MesitranTM was applied for a further two weeks, however, granulation continued without a reduction in the wound area.

Mrs L's general condition and her diabetes precluded her from having an SSG to cover the wound as it was considered the graft donor site could easily become a

chronic wound. It was decided that MyskinTM autologous cell grafting, with its small biopsy size, would be a more suitable alternative to achieve wound closure.

MyskinTM

The wound was assessed by personnel from CellTran to ensure its suitability for treatment with MyskinTM and the treatment was explained in depth to Mrs L, as her cooperation was essential to ensure success. At this point amputation of the right foot was considered a likely course of action; a situation Mrs L was desperate to avoid.

Before treatment, swabs from the wound, mouth, and biopsy site were taken and sent for culture and sensitivity testing. This ensures that the cells are treated appropriately in accordance with the UK Human Tissue Act in the laboratory and also so any wound infection can be treated before the first application of MyskinTM.

In Mrs L's case, a thin biopsy of skin (approximately 0.6mm thick) was taken from the thigh and transported to the MyskinTM laboratory in sterile saline solution. It was decided to keep Mrs L as an inpatient during the treatment due to the size (55cm²) and position of the wound and her general poor health. The MyskinTM graft was delivered to the clinic once a week by courier service and applied to the wound within an hour of its delivery (Figure 4). The wound was prepared by washing with saline solution



Figure 4. MyskinTM as it arrives at the clinic.



Figure 5. The wound after two applications of MyskinTM.



Figure 6. The wound four weeks after completion of MyskinTM treatment.

before the Myskin™ surfaces were gently placed into the wound ensuring contact was made between the cell layer and the wound bed. Mesitran™ dressings were then placed over the Myskin™ grafts to keep them in position, remove exudate and protect the wound from infection before the foot was wrapped in a conventional bandage.

Four days later, the Myskin™ graft transfer surface was removed, leaving a thin layer of the patient's own keratinocyte cells in the wound bed. For three days before the next application of Myskin™, Mesitran™ and a conventional bandage were again used over the treated area to prevent any damage to the new skin cells and prevent the wound from becoming contaminated. After just two applications of Myskin™ and overlaid Mesitran™, the wound measured 48cm² (Figure 5). The wound bed showed healthy granulation tissue and the wound edges were clearly coming together, and no further grafts were required.

Two days following the removal of the final Myskin™ treatment, Mrs L was discharged home. As the patient and wound showed no reaction to the antimicrobial Mesitran™, its regular application to the wound was continued by the district nurse visiting Mrs L.

At the first follow-up (four weeks post-discharge) the wound area measured 25cm² and the wound bed remained clean and healthy (Figure 6). Mrs L also responded well to her diabetes treatment, maintaining an HbA_{1c} of 5.8%. She continued to attend the outpatient's clinic on a two-weekly basis.

Discussion

Mrs L's wound was treated using a variety of conventional treatments before the application of Myskin™ grafts. These acted to debride, clean and revascularise the wound bed so it was in an optimum condition to receive the patient's cultured cells and provide the best possible healing outcome. Unfortunately, following maggot and VAC therapy, although healthy granulation tissue was observed, the wound did not decrease in size. As Mrs L was not eligible for a SSG to cover the wound, a Myskin™ graft was considered. Amputation of the foot was considered a likely future course of action. In Mrs L's case only two applications of the Myskin™ graft were applied to instigate re-epithelialisation and wound healing, resulting in a rapidly closing wound and saving the foot from a costly and debilitating amputation.

This case study has shown that once the wound bed was clean, well prepared and had a good blood supply, Myskin™ grafts were used to successfully promote wound healing and closure in a patient where conventional grafting techniques were precluded. **WUK**

For further information on Myskin™ please contact s.fraser@celltran.co.uk

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