RCS ADVANCING SURGICAL STANDARDS

ONLINE CASE REPORT

Ann R Coll Surg Engl 2014; **96:** e20–e22
doi 10.1308/003588414X13946184903487

Combined use of hyperbaric oxygen and sprayed keratinocyte suspension to tackle a difficult wound

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ABSTRACT

This is the first reported case in the literature to combine the use of a well established therapy to achieve wound healing (ie hyperbaric oxygen treatment) and a novel sprayed keratinocyte suspension technique to treat a challenging wound successfully. The merits and potential issues associated with these treatments are outlined and the case is detailed.

KEYWORDS

Hyperbaric oxygen – Wound healing – Chronic wound – Sprayed keratinocytes

Accepted 5 December 2013; published online XXX

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Case History

A 40-year-old man presented to the plastic surgery department with a wound on his right lower leg following a fall 3 months previously. Attempted primary closure by the referring hospital was unsuccessful. His past medical history was complex with chronic renal failure and two previous renal transplants (requiring immunosuppression). He also had insulin dependent type 2 diabetes mellitus. The wound was initially treated conventionally with surgical debridement, regular dressings and negative pressure therapy on three occasions but it did not progress to a healthy bed for a skin graft (Fig 1A). Following each debridement, the wound deteriorated to a sloughy and necrotic state, and no healthy granulation tissue formed. The wound failed to make significant progress and the patient was considered for hyperbaric oxygen therapy (HBOT).

Following discussion with the local hyperbaric unit, a plan was made for 20 preoperative and 10 postoperative HBOT sessions. These treatments were delivered in 2-hour sessions as per the Marx protocol including a 10-minute descent to 2.2 atmospheres, two 45-minute sessions of 100% oxygen with a 5-minute break between them and a 15-minute decompression. As a result of the hyperbaric treatment, the wound began to make progress and arrangements were made for a skin graft to be performed 12 weeks after presenting to our department (Fig 1B).

As the patient was known to have wound healing problems, it was recognised that performing a conventional split-thickness skin graft (STSG) may result in two non-healing wounds and the decision was taken to use sprayed keratinocyte suspension (ReCell®; Avita Medical, Royston, UK) therapy in combination with a widely meshed (3:1) conventional STSG (Fig 1C). The keratinocyte solution was applied to both the donor site and recipient bed. The patient subsequently underwent ten further sessions of HBOT. Assessment in clinic eight weeks following surgery demonstrated that the wound and donor site were fully healed (Fig 2).

Discussion

HBOT is a well established treatment and works by providing a pharmacological dose of oxygen to tissues. While breathing 100% oxygen at normal pressures will saturate haemoglobin, providing oxygen at higher pressures results in oxygen dissolution in plasma. The action of high concentrations of oxygen includes vasoconstriction to reduce oedema, shifting the oxygen dissociation curve right, hyperoxygenation of ischaemic tissues, downregulation of cytokines (including interleukins 1 and 6, and tumour necrosis factor) and upregulation of growth factors (including fibroblast growth factor, platelet derived growth factor and vascular endothelial growth factor).

Oxygen is also key to neutrophil phagocytosis and polymorphonuclear leucocyte function,[1] and HBOT therefore has a role to play in tackling infection.[2,3] Other mechanisms of action in the treatment of infection include inhibition of endotoxin release, and inhibition of bacterial growth due to the production of oxygen radicals and superoxides. Evidence suggests that the effects of HBOT may continue for many years following treatment[4] as research has linked the mobilisation of progenitor cells after HBOT to the recovery of damaged tissues.[5]

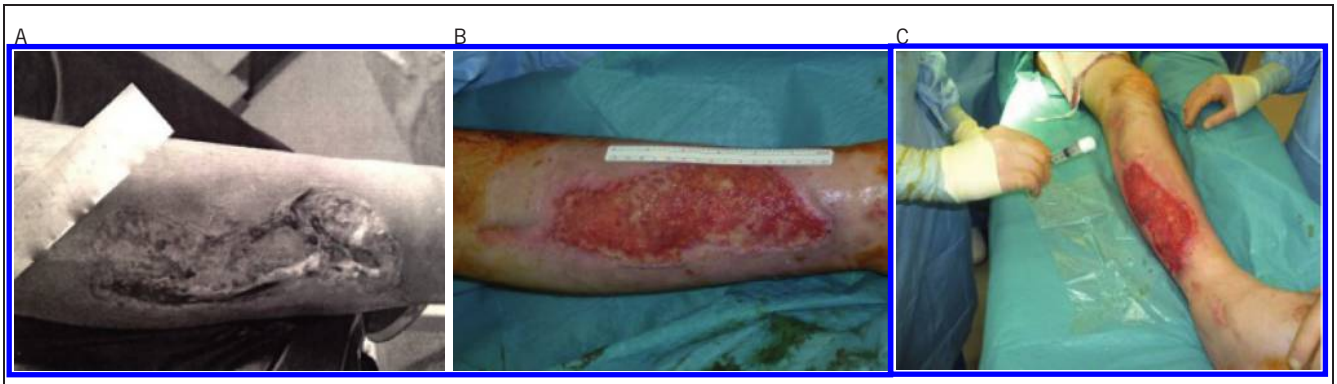

Figure 1 Right lateral leg wound following 3 surgical debridements showing evidence of unhealthy wound bed (A), right lateral leg wound following 20 sessions of hyperbaric oxygen therapy demonstrating healthy granulation and filling in of defect immediately prior to application of split-thickness skin graft (B), and application of ReCell® via spray system after 3:1 meshed split-thickness skin graft applied with Telfa™ dressing (C)

There are, however, complications and contraindications to HBOT, and these include ear and sinus barotrauma, which may occur in 2–17% of cases.[6] Temporary myopia and exacerbation of cardiac failure (due to increased peripheral vascular resistance and decreased cardiac output) have been reported as well as oxygen induced seizures (incidence 1 in 10,000) and pulmonary barotrauma. Furthermore, there is limited access to hyperbaric chambers and patients may require relocation to access the facility.

Sprayed keratinocyte suspension therapy

Available commercially since 2002, sprayed keratinocyte suspension therapy (ReCell®) involves the use of autologous cells harvested in the same fashion as STSG surgery, which are processed to be applied within minutes to a recipient site up to 80 times larger than the donor site. Harvested skin is added to a trypsin solution for approximately 20 minutes whereupon the keratinocytes, melanocytes, Langerhans cells and fibroblasts separate from the epidermis and dermis. These cells are then suspended in a lactate solution, at which stage they are ready to be applied in a spray formulation.

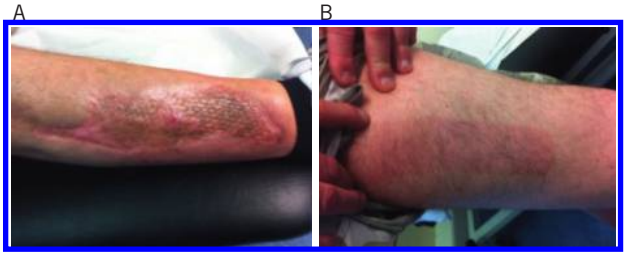

Figure 2 Eight weeks following surgery: fully healed recipient wound bed on right lateral leg (A) and fully healed donor site on right lateral thigh (B)

This technology eliminates the need for expensive and time consuming keratinocyte culture in a laboratory, and requires only a small sample of donor skin. Current uses of this technology include treatment of burns, accelerated healing of donor sites, and treatment of hypopigmented skin and acne scars. It can be also used in combination with aesthetic procedures such as dermabrasion and laser resurfacing. Treatment of leg ulcers with cultured keratinocytes has been documented previously[7,8] and sprayed keratinocytes may provide a viable, cheaper alternative with fewer risks of morbidity.

The literature supporting ReCell® and other autologous non-cultured skin cell techniques is in its early stages. Gravante *et al* compared ReCell® with conventional STSG surgery in adult burn patients and showed similar healing times but with smaller donor sites (and less pain) in the ReCell® group.[9] More recently, Wood *et al* have shown benefits of earlier intervention with ReCell® and biological dressings compared with STSG surgery in the management of paediatric scald injuries.[10]

The cost of this treatment is a key component and should be addressed. Thirty sessions of HBOT, provided over six weeks on an outpatient basis, come to £3,500 per patient. In addition, the cost of a single application kit of ReCell® therapy is £950. A study from 2012 examining the cost of chronic leg ulcers demonstrated that ulcers that are static, deteriorating (ie increasing in size, exudate or odour) or severe (ie requiring hospital admission and surgical intervention) cost between £100 and £637 per week.[11] When this figure is taken into account alongside the costs of HBOT and ReCell® in the context of a severe ulcer (average £637 per week), the cost of our treatments, excluding bed occupancy, would be negated after just seven weeks.

Conclusions

This is the first report in the literature using sprayed keratinocyte suspension in combination with HBOT to treat a hard-to-heal leg ulcer. The advantages to this treatment

have been minimising donor site morbidity, achieving wound healing and thereby reducing ongoing cost to our department.

Acknowledgements

With thanks to Dr Gerry Purdy (Medical Director, North of England Hyperbaric Services).

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