

Executive Summary

Bioengineered Skin Substitutes for the Management of Wounds

(Adapted from the report of the Review Group by Christine Barber)

Background

The objective of this review was to make recommendations on the safety and efficacy of bioengineered skin substitutes for the management of wounds based on a systematic assessment of the peer-reviewed literature. Bioengineered skin substitutes (BSS) either epidermal, dermal or both were compared to standard care/dressings or autografts.

Methods

Search strategy – Studies were identified by searching MEDLINE, EMBASE, The Cochrane Library, Science Citation Index and Current Contents from inception to April 2006. The Clinical Trials Database (US), NHS Centre for Research and Dissemination, NHS Health Technology Assessment (UK), National Research Register (UK), National Institute of Health (US) and Meta Register of Controlled Trials were also searched in April 2006.

Study selection – Only randomised controlled trials in humans were included for review. Only studies comparing a BSS as a physical layer, which would integrate into the wound (not lysate), were included. Efficacy outcomes included wound closure, wound healing time, pain, exudate, and cosmesis. Safety outcomes included complications such as infection and local allergic reactions.

Data collection and analysis - Data were extracted from the included studies by the ASERNIP-S researcher using standardised data extraction tables developed *a priori* and checked by a second researcher. Statistical pooling was not appropriate due to the study and result heterogeneity.

Results

In total, 23 RCTs were identified for inclusion in this review. These included eight studies for venous leg ulcers, six studies for diabetic foot ulcers and nine studies of other wounds. Collectively, the definition of success was defined as complete wound closure across all studies; however other outcomes such as wound healing time and percentage of wound closure were not consistently reported, making comparisons between studies difficult.

For the indication of venous leg ulcers, Apligraf®, cryopreserved cultured allografts, cultured keratinocyte allografts, Dermagraft®, EpiDex™, OASIS™ Wound Matrix and Promogran™, were comparable with the standard treatment in terms of wound healing time, wound closure and decreased ulcer area. There was no difference for pain, recurrence, and wound infection.

For the indication of diabetic foot ulcers, the use of BSS appeared to offer an advantage over standard care. Wound healing time appeared to be better overall with the use of BSS (Apligraf®, Dermagraft®, GraftJacket®, Hyalograft™ and Laserskin™, OrCel™ and Promogran™) and wound closure appeared to be favourable with the use of Apligraf®, GraftJacket®, and OrCel™. Infection rates were lower and where reported, there was no difference in recurrence between the BSS groups and the comparator.

Healing across different wounds was no better with BSS than the relevant comparator, although the evidence suggested that pain might be lower with their use. The evidence suggested that Apligraf® used for micrographic and post excisional wounds produced similar results to standard therapy, and Biobrane® used for donor sites was not as good as the standard therapy. The evidence for Promogran™ in the treatment of pressure sores suggested it was as good as the standard therapy, and cultured epidermal allografts were more favourable than the standard therapy in terms of wound healing time and pain, however in several studies the small sample sizes may limit the validity of the conclusions which may be drawn.

The BSS with more favourable outcomes commonly had a dermal matrix component in their composition, possibly offering a scaffold in which granulation tissue and angiogenesis may proceed. This may have contributed to the faster time to closure reported in these studies.

Based on the evidence presented in this systematic review, the ASERNIP-S Review Group agreed on the following classifications and recommendations concerning the safety and efficacy of bioengineered skin substitutes for the management of wounds.

Classifications and Recommendations

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Classifications

Evidence rating

The review panel rated the evidence-base in this review as average, limited by generally small sample sizes, short follow-up periods, and lack of methodological rigour. Additionally, the evidence was limited across three indications.

Safety

The evidence suggests bioengineered skin substitutes for the management of venous leg ulcers, diabetic foot ulcers and other wounds are at least as safe as standard therapies for these indications.

Efficacy

The efficacy of bioengineered skin substitutes for the management of venous leg ulcers, diabetic foot ulcers and other wounds could not be determined based on the available evidence. Insufficient data on treatment durability were available to establish long-term efficacy.

Clinical and research recommendations

Additional high quality, prospective, randomised controlled trials with longer follow-up periods would strengthen the evidence base for the use of bioengineered skin substitutes, particularly in terms of recurrence. Standard outcome measures should be developed so that investigators and clinicians can report primary outcomes (specifically in terms of ulcer healing) consistently. Cost-effectiveness studies, taking into consideration the Australian healthcare context, should also be considered.

Review Group Membership

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Important note

The information contained in this report is a distillation of the best available evidence located at the time the searches were completed as stated in the protocol. Please consult with your medical practitioner if you have further questions relating to the information provided, as the clinical context may vary from patient to patient.

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