INTRODUCTION

Leg ulcers generally represent a chronic recurrent state, which involves high costs for both the patient and society. Since most leg ulcers are of venous origin, they can be healed with compression therapy alone or combined with local treatments. In recent years, the concept of a clean, moist environment has been widely accepted in the treatment of leg ulcers. In some cases, however, a moist environment and compression therapy are not sufficient for the ulcer to heal, and for these hard-to-heal ulcers, the development of tissue-engineered products can offer new options for treatment. Over the past years, the problem of creating new, more effective treatment methods, resulting in the rapid epithelialization of ulcers and increasing the rate of healing, has raised.

New materials derived from biological sources have been proved to be effective in the process of granulation and epithelialization of the dermis. These also play a role in the regulation of evaporation and exudation at wound level and in the protection against bacterial infections. The latest products are represented by cell cultures (human fibroblast-derived dermal substitutes), bioengineered skin grafts, or other biological materials of animal origin (porcine intestinal submucosa). Human Fibroblast-Derived Dermal Substitutes: A tissue-engineered human dermal substitute (HDS) is designed to replace the dermis and to provide essential stimulatory growth factors for wound healing. It contains living human fibroblasts obtained from neonatal foreskins seeded onto a bioabsorbable polyglactin mesh. The HDS pieces are stored frozen at -70°C until used. Although the precise mechanism of action of tissue-engineered dermis is not completely understood, it has been shown to provide elements to the wound bed that are believed to be important in the repair process. HDS provides live, nonsenescent fibroblasts capable of colonizing the wound bed and persisting in situ for several weeks. The fibroblasts are capable of secreting a number of cytokines and growth factors, including platelet-derived growth factor, insulin-like growth factors I and II,

SUMMARY

The aim of this paper is to review the most recent trends in the treatment of chronic ulcers with the latest products prepared from cell cultures (human fibroblast-derived dermal substitutes), bioengineered skin grafts or other biological materials of animal origin (porcine intestinal submucosa), as well as to evaluate their efficacy compared to traditional standard methods.

Key words: ulcer treatment

SUMMARY

The aim of this paper is to review the most recent trends in the treatment of chronic ulcers with the latest products prepared from cell cultures (human fibroblast-derived dermal substitutes), bioengineered skin grafts or other biological materials of animal origin (porcine intestinal submucosa), as well as to evaluate their efficacy compared to traditional standard methods.

Key words: ulcer treatment

TRATAMENTUL ACTUAL AL ULCERULUI DE GAMBĂ

Rezumat

Lucrarea de faţă îşi propune o trecere în revistă a celor mai noi tendințe de tratament a ulcerelor cronice cu produse de ultimă oră preparate fie din culturi de celule (substituenții dermați din fibroblasti umani), fie grafe de piele obținută prin bioingenierie, fie alte materiale biologice de proveniență animală (submucosă intestinală porcine), precum și o evaluare a eficienței acestora în comparație cu metodele standard, tradiționale.

Otilia Bărbos1, O. Andercou 2

Received for publication: 07.07.2008
Revised: 25.08.2008

1- “Ion Chiriac” Oncological Institute,  
2 - “Iuliu Hațieganu” UMPh, Cluj-Napoca

Correspondence to: Otilia Bărbos, e-mail: otliabarbos2006@yahoo.com
heparin-binding epidermal growth factor, vascular endothelial growth factor, transforming growth factors a and b, and keratinocyte growth factor. Growth factors are known to stimulate fibroblasts, granulation tissue, matrix deposition, angiogenesis, and skin cell maturation. The fibroblasts also produce matrix proteins like collagen types I and III, fibronectin, and tenascin, as well as glycosaminoglycans, which bind growth factors and enhance their activity.

They are indicated in chronic ulcers with a duration of more than 3 months, more than 1 cm² in diameter, refractory to conservative treatment, of various etiologies: venous, diabetic, rheumatic, vasculitic, posttraumatic, arterial or mixed.

HDS are administered by weekly application associated with compressive bandage; the mean duration of application is 9 weeks, depending on the etiology and the size of the ulceration. Results show in 60% of the cases healing of ulcer (depending on size and duration) and after 2 years, 47% of ulcers remained epithelized [3].

Skin grafts are of several types. The oldest form is the homograft harvested from a cadaver (since the 19th century), which was initially used for burns[4]. The gold standard is still the autologous skin transplants for accelerating healing in cases of extensive skin loss.

Use of allografts to treat these patients has recently become accepted in clinical practice and has been extended to conditions characterized by extensive skin loss, such as ulcers, post-traumatic and post-surgical wounds, pressure ulcers, Lyell syndrome, congenital epidermolysis diseases, and other autoimmune diseases.[5] Administration: daily for 5-7 days, then weekly for 1-12 months

FDA has recently approved the use of bioengineered skin substitutes.

Indications: chronic ulcers of venous, arterial, mixed or diabetic etiology, which do not respond to conventional treatment.

Application: single application, then weekly follow-up for 8 weeks and monthly follow-up for at least 22 months.

Results: 64% complete healing after 5-6 months 36% non-response to treatment[6]

**Biologic materials**: The latest biomaterials consist of a thin translucent layer of porcine intestinal submucosa, 0.15 mm thick. This contains an extracellular collagen matrix enriched with glycosaminoglycans, proteoglycans, fibronectin, growth factors which favor the granulation and epithelialization process, play an antibacterial role and thus decrease the duration of healing.

Their indications are particularly in reconstructive plastic surgery, as well as in large sized chronic venous ulcers.

Application: once weekly + compressive treatment; mean duration 12 weeks

Results: 73% of cases complete epithelialization in 3 months, versus 46% epithelialization by standard therapy.[7]

Colagen biological dressings: Collagen plays a relevant role in cutaneous tissue repair and represents a valid therapeutic option when used as a bioactive advanced dressing in chronic wound management. It improves fibroblast deposition in the dermal matrix and stimulates angiogenesis, granulation tissue formation, and reepithelization.[8] Fibroblasts mainly participate in the biosynthesis of collagen, which acts as a mold, precursor, plastic material, and cementing substance in the wound healing process.

**CONCLUSIONS**

The long duration of healing of leg ulcers involves high treatment costs. Over the past years, the application of new products for ulcer healing has been attempted. When considering the number of available wound healing products, achievements made within the tissue engineering field become clear. A wide range of products are commercially available today.[10] Progress has been made in the tissue engineering field resulting in a variety of skin substitute products, yet no autologous bilayered skin substitutes are currently available—ideally to further minimize the risk of host versus graft reactions. Research still focuses on stem cells. Through learning more about the fundamentals of stem cells, they might some day be used as cellular therapy for local tissue repair.
REFERENCES
9. Maria Stefania Bertone, RN; Valentina Dini, MD; Paolo Romanelli, MD; Franco Rizzello, DI; Marco Romanelli, MD, PhD :Objective Analysis of Heterologous Collagen Efficacy in Hard-To-Heal Venous Leg Ulcers.Wounds. 2008;20(9):245-249