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Glyaderm® dermal substitute: Clinical application and long-term results in 55 patients

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ABSTRACT

Introduction: Glycerol preserved acellular dermis (Glyaderm®) consists of collagen and elastin fibers and is the first non-profit dermal substitute derived from glycerol-preserved, human allogeneic skin. It is indicated for bi-layered skin reconstruction of full thickness wounds.
Methods: A protocol for clinical application and optimal interval before autografting with split thickness skin graft (STSG) was developed in a pilot study.

A phase III randomized, controlled, paired, intra-individual study compared full thickness defects engrafted with Glyaderm® and STSG versus STSG alone.

Outcome measures included percentage of Glyaderm® take, STSG take, and scar quality assessment.

Results: Pilot study (27 patients): Mean take rates equaled 91.55% for Glyaderm® and 96.67% for STSG. The optimal autografting interval was 6 days (±1 day).

Randomized trial (28 patients): Mean Glyaderm® take rate was 88.17%. STSG take rates were comparable for both research groups ($p = 0.588$). One year after wound closure, Glyaderm® + STSG was significantly more elastic ($p = 0.003$) than STSG alone. Blinded observers scored Glyaderm® treated wounds better in terms of scar quality.

Discussion: The efficacy of Glyaderm® as a suitable dermal substitute for full thickness wounds is attested. Currently a procedure for simultaneous application of Glyaderm® and STSG is adopted, allowing for further widespread use of Glyaderm®.

1. Introduction

Dermal substitution has become an integral part of surgical burn care and many commercial dermal equivalents have emerged on the market since the introduction of Integra® dermal substitute (Integra LifeSciences Corporation) some two decades ago [1–3].

We extensively reported on the various cellular, acellular, temporary and permanent skin replacements available for burns and full thickness defects in a previous publication [4].

Glycerol preserved acellular dermis (Glyaderm® – Euro Skin Bank, Beverwijk, The Netherlands) is the first non-profit dermal substitute derived from glycerol preserved, human allogeneic skin [4–6]. Glycerol preserved allogeneic skin (GPA)

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is routinely utilized as a temporary biologic dressing on partial thickness burns and as a means of wound bed preparation on excised burns. Allograft coverage prevents dehydration and infection of the wound and stimulates granulation formation to prepare the wound for closure with autologous skin [5,6]. Allografts contain donor cells, which are ultimately rejected and can therefore only be used as temporary wound coverage. Glyaderm®, which is decellularized by treatment with sodium hydroxide (NaOH), can be used to replace lost dermis in full thickness wounds serving as a dermal substitute. Glyaderm® consists of a collagen and elastin fiber network with native collagen and can ensure a bilayered skin restoration in combination with a thin autologous split skin graft. It is intended to be cost-effective and easy to use for widespread application in full thickness wounds such as full thickness burns. Glyaderm® is placed in a wound bed prepared with allografts, after which, a thin autologous split thickness skin graft (STSG) will close the wound following Glyaderm® ingrowth. Animal studies showed favorable results in terms of tissue integration and wound contraction and scar quality [6].

We first initiated a phase I pilot study to elucidate the most practical protocol for Glyaderm® application and to further investigate the scope of use of the dermal matrix in the clinical setting.

The second study was a phase III randomized, controlled, paired, intra-individual comparison of full thickness skin defects engrafted with Glyaderm® and STSG versus STSG alone.

2. Materials and methods

2.1. Enrollment

Between September 2005 and October 2010 27 patients were recruited for the pilot study and 28 patients met the criteria for inclusion in the randomized controlled, paired, intraindividual trial.

Study protocols were approved by the Ghent University Hospital Ethics Committee.

Glyaderm® was produced and provided by Euro Skin Bank, Beverwijk, The Netherlands. The preparation steps of Glyaderm® have been described previously [6].

2.2. Phase I pilot study

The pilot study was initially performed to assess the scope of clinical applications of Glyaderm® as a dermal substitute and to optimize usage protocol. Patients with full thickness burns, but also other full thickness skin defects were considered eligible for this study.

All burn wounds that were not clearly full thickness on clinical assessment were treated during the first 48 h with an enzyme alginogel (Flaminal® Forte – Flen Pharma) [7] and covered with a paraffin gauze dressing (Jelonet® – Smith & Nephew). Flaminal® Forte combined with Jelonet® ensured maintenance of a moist wound environment [7] for the first 48 h prior to assessment by laser Doppler imaging (LDI). This is the standard treatment for all burns admitted to the Ghent Burn Center.

In our burn center we use the moorLDI2-BI imager (Moor Instruments Ltd., Axminster, UK) to objectively determine the healing potential of the burn [8]. LDI is now becoming a standard of care for early diagnosis of healing potential, which is a main determinant of subsequent treatment policy. In clinical trials LDI ensures exact comparison between two burns without depth difference bias.

In this study, besides clinical observation, LDI was also intended to monitor the rate of vascularization into the dermal substitute and thereby to delineate the optimal time between the application of Glyaderm® and the final coverage with an autologous STSG. Ingrowth of blood vessels into Glyaderm®, resulting in increased blood flow through the dermal substitute, was assessed by means of LDI at day 1, 3, 5 after the application of Glyaderm® to the wound. An increase in flux values over the measurement period was interpreted as increased blood vessel ingrowth. Biopsies were harvested before autografting to support this hypothesis. In order to visualize blood vessel ingrowth into Glyaderm® the sections taken from the biopsies were colored with antibodies against alfa-smooth muscle actin (ASMA) in order to demonstrate the presence of myofibroblasts and pericytes, which are supporting cells for blood vessels.

Efficacy of the protective open pore structure polyamide dressing (Surfasoft® – MediProf) and finally the coverage with a 10% povidone iodine (PVP-I) gel (iso-Betadine® Gel – Meda-Pharma Belgium) in combination with Jelonet® was tested.

Outcome measures were percentage of Glyaderm® take and percentage of STSG take.

Patients were invited for a long-term follow-up after complete scar maturation. The long-term scar assessment included objective measurement of elasticity with the DermaLab® (Cortex Technology, Denmark) and measurement of scar erythema and pigmentation with the DermaSpectrometer® (Cortex Technology, Denmark), as well subjective scar evaluation by means of the adapted Vancouver Scar Scale (aVSS) and the Patient and Observer Scar Assessment Scale (POSAS). The aVSS, besides scar color, pigmentation, pliability and scar height also takes into account scar itching and the presence of defects.

In 4 patients biopsies were taken at 1 month and sent for histological analysis. Biopsies were fixed in 4% formalin and were further processed into paraffin. Sections were prepared and stained with Haematoxilin–Eosin and Elastica von Giesson to study the presence of Glyaderm®.

3. Phase III study

3.1. Study design

This was a randomized, controlled, paired, intra-individual comparison of full thickness skin defects engrafted with Glyaderm® and STSG (experimental treatment) versus STSG alone (conventional treatment).

3.2. Study objective

Primary outcome measure was comparison of autograft survival at one week between full thickness defects treated with Glyaderm® plus STSG versus STSG alone.