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The use of human deceased donor skin allograft in burn care

Jorge Leon-Villapalos · Mohamed Eldardiri · Peter Dziewulski

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Abstract Burns are tissue wounds caused by thermal, electrical, chemical cold or radiation injuries. Deep injuries lead to dermal damage that impairs the ability of the skin to heal and regenerate on its own. Skin autografting following burn excision is considered the current gold standard of care, but lack of patient's own donor skin or unsuitability of the wound for autografting may require the temporary use of dressings or skin substitutes to promote wound healing, reduce pain, and prevent infection and abnormal scarring. These alternatives include deceased donor skin allograft, xenograft, cultured epithelial cells and biosynthetic skin substitutes. Allotransplantation is the transplantation of cells, tissues, or organs, sourced from a genetically non-identical member of the same species as the recipient. Human deceased donor skin allografts represent a suitable and much used temporizing option for skin cover following burn injury. The main advantages for its use include dermoprotection and promotion of reepithelialisation of the wound and their ability to act as skin cover until autografting is possible or re-harvesting of donor sites becomes available. Disadvantages of its use include the limited abundance and availability of donors, possible transmission of disease, the eventual rejection by the host and its handling storing, transporting and associated costs of provision. This paper will explore the role of allograft skin in burn care, defining the indications for its use in burn management and the future potential for allograft tissue banking.

Keywords Burn injury · Human skin allograft

J. Leon-Villapalos · M. Eldardiri · P. Dziewulski (✉)
St Andrews Centre for Plastic Surgery and Burns, Court Road, Broomfield, Chelmsford CM1 7ET, UK
e-mail: peter.dziewulski@meht.nhs.uk

Introduction

Burn injuries disrupt the ability of the skin to physically protect the underlying tissues from mechanical, heat, cold, and biological insult, prevent excess water loss and act as a temperature regulator. The skin also assists in electrolyte homeostasis, serves as a sensory organ for pain, heat, cold, pressure and touch and prevents entrance of foreign bodies and microorganisms.

Both the epidermal physical protection layer and the dermal regeneration layer may be affected by the burn in both extent and depth. This has implications in the surgical management of the burn wound. Early burn excision and autografting has been acknowledged as one of the major determinants in the decreasing mortality of extensively burned patients (Tompkins et al. 1988). The seminal work of Janzekovic (1970) established tangential excision of deep burns and immediate grafting as the current method for acute burn wound management.

This course of action is nevertheless limited by the availability of autograft skin despite the possibility of skin expansion and repeated skin harvesting. This necessitates the use of biological or synthetic skin substitutes, and specifically deceased donor allograft skin (Eisenbud et al. 2004), the focus of this paper.

The choice of temporary skin cover must be careful and judicious amongst the vast array of options (Jones et al. 2002; Phama et al. 2007), as the use of deceased donor allograft skin for burns has very clear indications, advantages and disadvantages (Kagan et al. 2007).

Deceased donor allograft skin provides temporary cover of the burn wound when autograft is not available in both partial thickness and full thickness burns; in addition, it can be used as a cover layer for widely meshed grafts (Alexander et al. 1981), in exfoliative disorders of the skin like toxic epidermal necrolysis or as an optimising step in the excised burn wound bed prior to autografting. This improves wound healing and reduces heat and fluid loss and scarring by restoring the dermoprotective role of the skin (Brychta et al. 2002).

Disadvantages include graft rejection once the immunosupressor effect of the burn has subsided, its limited availability and reliance on tissue banks, providing donors of low risk of disease transmission and the ethical implications and cultural issues for both donation and recipients (Burd and Chiu 2005).

Historic perspective

Ancient civilizations have left the historic legacy and graphic description of primitive but also frequently ingenious attempts to cover soft tissue with a variety of dressings and soft tissue flaps as shown in the Sushruta Sameta (Rana and Arora 2002) and also by Tagliacozzi (Tagliacozzi 1597; Gnudi and Webster 1950) but the modern skin graft impetus in humans was started by Paul Bert establishing the initial understanding of graft survival and stating that neovascularization is necessary for graft survival (Bert 1863). Reverdin (1871), a young Swiss student is credited as the first to harvest and use both autografts and allografts.

The use of allograft skin specifically for burn defects was described in 1881 by Girdner (1881) and a wide spread use of skin grafts of variable thickness by Thiersch (1886). Schone (1906) and Lexer (1911) demonstrated at the beginning of the twentieth century the limited survival of allografts and xenografts following transplantation in humans. This was confirmed by the work of Padgettt in a larger allograft rejection series (Padgett 1932). Padgett is also credited with establishing the biocompatibility and lack of rejection of grafts between identical twins (Andrew Lee et al. 2007).

The need for establishing an adequate and successful method to preserve allograft skin led to efforts of preservation by refrigeration over variable periods of time as performed by Wentscher (1903) and the addition of glycerol as a cryopreservant as stated by Billingham and Medawar (1952). These brilliant investigators also described the phenomenon of second-set rejection of allogenic tissue because of the presence of humoral antibodies from prior exposure to the same allogenic source.

Further research in the 1950s and 1960s led to the foundations of the current use of allograft as a biological skin treatment for major burns thanks to the work of Zaroff et al. (1966), Jackson (1972) and Mowlem (1952).

Burn depth classification

A burn is defined as coagulative destruction of the surface layers of the body.

The skin is made up of the epidermis and dermis with adenexal structures such as the hair follicles, sweat and sebaceous glands residing in the deeper parts of the dermis. These adenexal structures are important as they are the source of proliferating epithelial cells (keratinocytes), which resurface wounds when the skin has been injured.

Burn injury to the skin can be classified as partial or full thickness. If the epidermis and the superficial part of the dermis have been injured (superficial partial thickness injury), the majority of adenexal structures are preserved, epithelialisation is rapid (10–14 days) and the risk of hypertrophic scarring is low. If the burn extends down into the deeper parts of the dermis (deep partial thickness) more adenexal structures are destroyed, epithelialisation is slower (3–6 weeks) and there is a high incidence of hypertrophic scarring. Full thickness burns involve destruction of all constituents of the skin and usually require surgical intervention to achieve wound healing.

Burn wound closure

Options for skin replacement in burn care include

- Autograft: Tissue transplanted from one part of the body to another in the same individual. Also called an autotransplant. Represents the gold standard for cover as it replaces like with like but lacks enough dermal component to provide full skin pliability
- Allograft: is the transplantation of cells, tissues, or organs, sourced from a genetically non-identical member of the same species as the recipient. Allograft, the focus for this paper, is described as the use of human deceased donor skin as temporary cover for excised burn wounds. It can be classified into:
  - *Viable*: This contains viable cells including keratinocytes, fibroblasts, endothelial cells and Langerhans cells (dermal macrophages). It may be fresh or cryopreserved.
  - *Non-Viable*: This may be glycerolised or gamma irradiated, freeze dried or ethylene oxide treated
- Xenograft: The cells or tissue of one species transplanted to another species. For this paper, the term xenograft mainly relates to the use of non-viable porcine skin
- Cultured Epithelial Cells: Clonal growth of keratinocytes grown in vitro applied to the burn wound for cover
- Bioengineered skin substitutes

Uses of deceased donor allograft skin in burn injury

Superficial partial thickness burns

These are burns with epithelial and papillary dermis involvement with blistering as one of its characteristic features. Clinically they are sensate, blanch when examined and their potential for self-healing is enhanced by the presence of spared dermal elements. Their assessment and management can be difficult if these burns reach intermediate depth and careful monitoring with a watchful waiting approach for up to 3 weeks may be necessary until the wound declares its true healing potential. It is in these situations when the use of allograft becomes useful following debridement as its application as a biological dressing in a freshly debrided partial thickness burn promotes epithelialisation (Vloemans et al. 2002; Atiyeh et al. 2005)

Exfoliative disorders such as Stevens-Johnson Syndrome/toxic epidermal necrolysis and Staphylococcal Scalded Skin Syndrome where there is separation at the dermo-epidermal or intraepidermal level leaving intact dermis and the potential for full reepithelialisation can also be considered as superficial partial thickness burns.

Once the burn has been identified clinically as a partial thickness burn, the burn treatment plan starts with preparation of the wound by means of mechanical debridement either by thorough removal of necrotic epidermis by scrubbing in superficial partial thickness wounds or through tangential excision mid-dermal partial thickness wounds. Punctate bleeding following tangential excision represents the point of adequate debridement and the existence of a viable dermal plexus.

After ensuring strict haemostasis, allograft is then applied to the wound and fixed by the surgeon's choice of suture material, fibrin glue, tissue glue or staples, the wounds are dressed with a petrolatum-based gauze material or any other non adherent dressing material that allows rapid inspection of the wound. A non-circumferential layer of dressing with antiseptic properties follows and finally an abundant soft layer that can soak any discharge from the wound complete the dressing.

The allografted wound is inspected every 48 h for adequate cover and early surveillance of hematomas, seromas or infection. The staples, if present, are removed by day five and the wound is autografted if necessary a week from the initial surgery. It has been reported that the usage of allograft skin has been associated with slightly increased number of operative procedures per percent of Total Body Surface-Area (TBSA) burn (Blome-Eberwein et al. 2002). The reason for this includes larger number of dressing changes and eventually the need to substitute the allograft for autograft.

In areas of particular anatomical or cosmetic significance such as the face in which a watchful waiting approach for the wound is preferred to avoid overzealous debridement or excessive deformity,

allografts have proved to provide a better wound healing than topical wound management (Horch et al. 2005)

Deep dermal/full thickness burns

The use of allograft for large, deeper burns has contributed to a reported increase in survival rates (Burke et al. 1974; Wolfe et al. 1983). Involvement of the deepest dermal layer (reticular dermis) or the full thickness of the skin removes the potential for self-regeneration of the burn wound. These are non-blanching, fixed-staining coloured or leather looking injuries that will only heal by disorganised scarring; therefore full excision of the burn tissue down to healthy bleeding or to the next fascial layer is imperative.

If autograft is not an option due to lack of donor skin, prompt coverage of the excised burn wound with allograft will protect the debrided area and promote vascular ingrowth that will optimise future autograft take (Burd 2002). Temporary allografting will provide wound cover until autograft becomes possible. Once biointegration of the allograft is completed, the suitability for successful autograft will have been optimised (Tenenhaus and Rennekampff 2007)

The wound preparation, debridement and surgical technique for application is similar to mid dermal burns, but here the debridement is necessarily more radical to ensure an absolutely healthy wound bed for the temporizing allograft if autograft is not immediately available.

Debridement techniques in this case include tangential or fascial excision down to healthy tissue, and once hemostasis is secured, closure of the wound depends on the availability of donor autograft. If autograft is not available in enough quantities, the allograft temporizes and protects the wound bed. If autograft is available to achieve wound cover but only by means of meshing and over expansion of the autograft, then a sandwich technique as originally described by Alexander et al. (1981) can be used. In this technique, widely meshed autograft is covered by unmeshed or non expanded allograft; this provides a physical protective layer that prevents underlying tissue desiccation and contamination. Both the autograft and allograft adhere to the wound bed and as autologous epithelium grows across the interstices of the mesh graft the allograft separates off the wound bed, a process known as creeping substitution.

Even though this technique is widely used by burns surgeons in cases of massive burn excision, concerns have been raised regarding delayed reepithelialisation of the underlying autograft because of the influence of the overlying allograft, as this may incorporate into the wound due to the transient immuno-suppression caused by the burn (Hierner et al. 2005)

The different ways in which the allograft is preserved can greatly influence the biological behaviour of the allograft. Fresh and cryopreserved grafts exhibit greater adherence to the wound bed when compared to glycerol preserved allografts (Kealey et al. 1996).

In cases of potential life threatening epidermal loss such as in the exfoliative disorders Stevens-Johnson Syndrome or Toxic Epidermal Necrolysis Syndrome (TENS), allograft usage represents an extremely useful tool to achieve temporary tissue cover until spontaneous reepithelialization is completed (Spies et al.2001; Pianigiani et al. 2002).

Meningococcal septicaemia and purpura fulminans can cause similar wounds to full thickness loss. The protocol of management for these patients in our unit involves admission of the patients from regional Pediatric Intensive care Units (PICU's) following resolution of the acute meningitis episode. The skin defects are treated conservatively until they clearly demarcate. Once this occurs and the patient is clinically improved, stable from the sepsis and nutritional point of view and able to withstand surgery, we proceed to excision of the necrotic tissue and allograft the defects with a view to subsequent autografting (Lowery et al. 2008).

Allograft for reconstruction

Deceased donor skin can be de-epithelialised and rendered acellular leaving a dermal scaffold that can be used as a dermal substitute in both acute burn (Gore 2005) and reconstructive surgery (Tsai et al. 1999), for soft tissue augmentation (Byrne and Hilger 2004), dural repair (Barret et al. 1999), hernia repair (Buinewicz and Rosen 2004) and eyelid reconstruction (Taban et al. 2005). Once such product is Alloderm (LifeCell, Woodlands, TX, USA). It can be used as a dermal substitute combined with thin

autografts for wound cover. This is a one-step technique that provides pliability and dermal support to the treated areas (Callcutt et al. 2006).

Conclusion

Allograft skin is a fundamental weapon in the armamentarium of the burns surgeon. Its versatility and capacity to improve the environment of the burn wound makes deceased donor skin an indispensable tool in situations of sparse autograft availability. Future directions for research and improvement may involve the reversal of its current disadvantages. Any project that aims to provide a less antigenic, more readily available and completely free from the already remote risks of disease transmission allograft will increase the value of this already extremely useful tool in burns surgery.

There have been a few studies comparing allograft skin to other skin substitutes and conventional wound care in the management of burn wounds (Horch et al. 2005; Wang et al. 1984; Purdue et al. 1987, 1997; Demling and DeSanti 1999) Reports have been mixed, however, human deceased donor allograft remains a key tool in major burn wound management.

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