The Libyan International Medical University

Faculty of Basic Medical Science

Stem Cell Therapy for Burn Victims – As a Fast Growing Modality of Treatment

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Abstract

Burn injuries affect large segments of populations across the world. The current standard procedure for third degree skin burns is skin grafting. Skin grafting has posed several issues including graft rejection, exposure of new wounds, susceptibility to infections, and limited availability. With the discovery that burn derived mesenchymal cells can be utilized to regenerate skin, new doors will open with regards to regenerative medicine in the context of burn wounds.

Introduction

Acquiring a burn is a common form of injury. A burn is an injury to the tissue of the body, typically the skin, varying in severity from mild to life threatening. Frequently, thermal, chemical, electrical and radiation accidents affect segments of different populations across the world resulting in third-degree burns. Additionally, there are many non-accidental incidents such as child abuse, spousal abuse, and personal disputes in general. In some cultures, burning is used as a form of domestic violence, such as bride burning in India.

Burns are generally classified as; first-degree, second-degree, third-degree, and fourth-degree burns. Firstly, first-degree burns affect only the outer layer of the skin and cause redness, pain and swelling. Second-degree burns affect the outer and underlying layer of the skin, causing pain, redness, swelling and blistering. They are also known as partial thickness burns. Third-degree burns affect deep layers of the skin and are known as full thickness burns. They cause white or blackened burned skin and the skin itself becomes numb due to nerve damage. Lastly, fourth-degree burns extend through entire skin and into underlying fat, muscle and bone and require immediate amputation.[1]

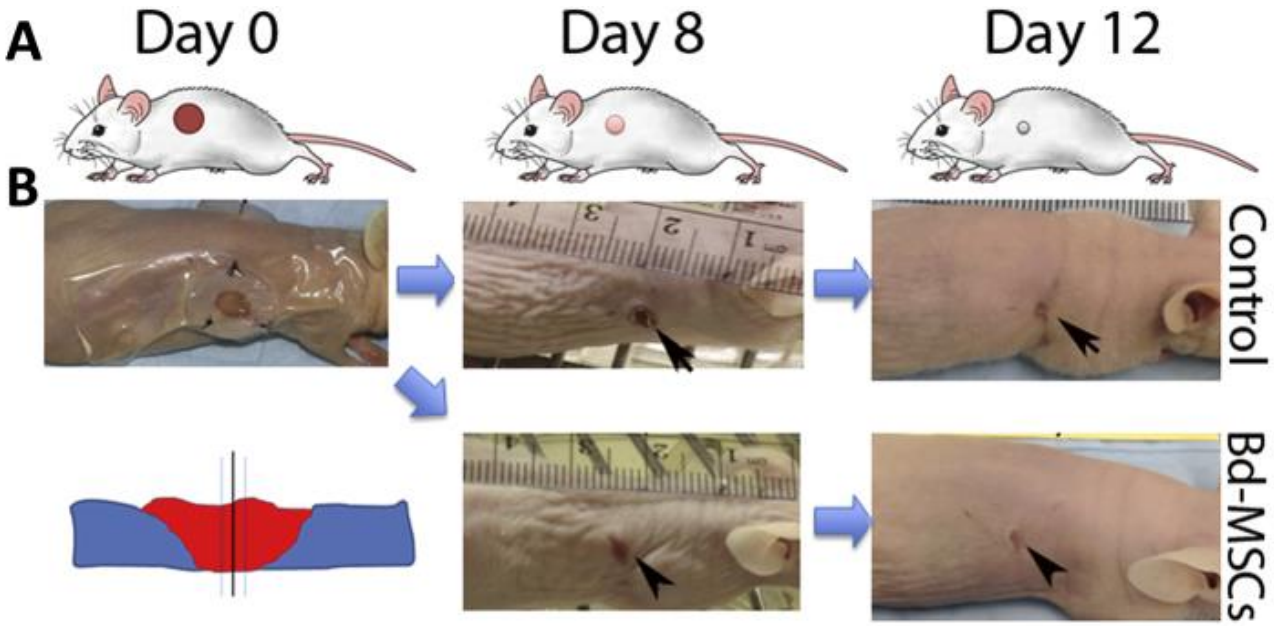
The treatment options for third degree burns have been quite limited. Skin grafting continues to be the golden option to treat burns. It involves the transplantation of skin to the patient, either from a donor or their own healthy skin. A more recent form of treatment is stem cell therapy, also known as regenerative medicine, promotes the repair response of injured tissue using stem cells or their derivatives. Surgeons are collaborating more than ever aiming to incorporate stem cells as a more efficacious treatment option to the current surgical management paradigm of burn injuries. They accelerate burn wound healing by inducing neo-angiogenesis, collagen deposition and granulation tissue formation. They modulate the inflammatory response and reduce the risk of infection. To add onto that, they can regenerate skin appendages and halt the zone of stasis in acute burn injuries[2]. Therefore, these findings indicate a promising future for regenerative medicine with regards to burn injuries, offering patients aesthetic outcomes.

Method and Material

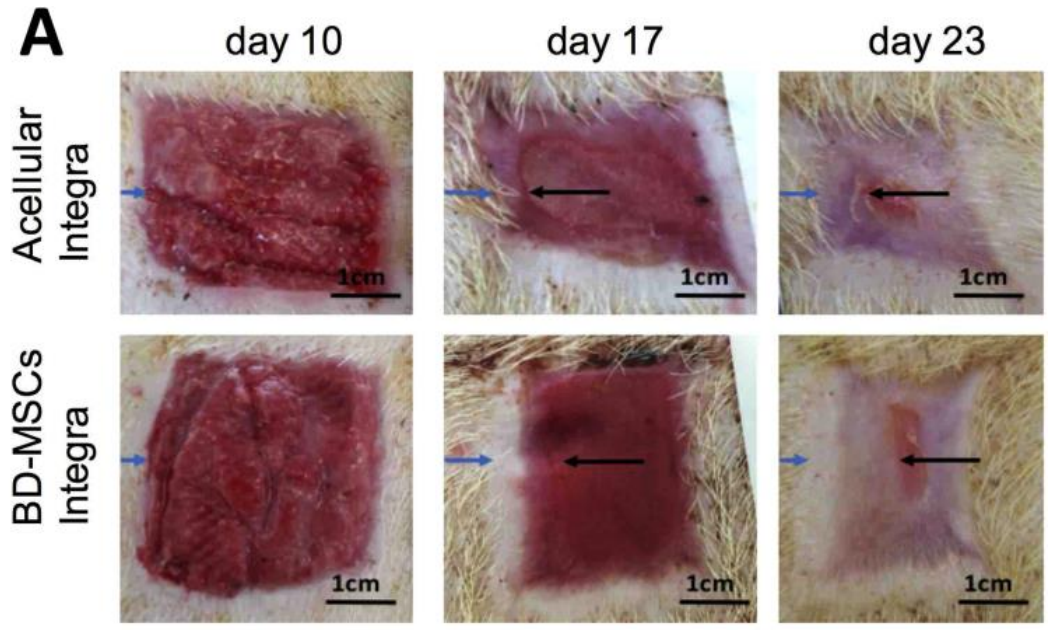
Burned derived-MSCs were extracted using two different methods that both were able to successfully isolate viable mesenchymal stem cells out of burned tissue. An enzymatic cell extraction method, for which burned skin was homogenized and incubated in collagenase I or a conventional extraction method that involves cutting the tissue into squares and placing them in a growth medium made up of High Glucose Dulbecco's Modified Eagle Medium (DMEM). These cells form colonies in a colony-forming assay and four differentiation staining techniques were utilized including: Oil Red O staining for Adipogenic differentiation, Alizarin red staining for Osteogenic differentiation, Alician Blue staining for chondrogenic differentiation and finally immunofluorescent adipogenic cell culture staining. Subsequently, the reparative and regenerative potential of these cells was evaluated in 10 mice and four pigs.[3]

Results

Mice treated with BD-MSCs visibly displayed faster healing. Histological examination of the healed wounds at day 12 post-wounding showed a significantly smaller wound size. At day 12, the mice that received BD-MSCs passed the proliferation phase and showed a lower proliferation profile which is characteristic of late proliferation phase and early remodeling phase. Ten immunodeficient mice were subjected to 4 mm excisional punch biopsy and randomly divided into two group of treatment and control. BD-MSCs embedded in Matrigel to assure cell adhesion to the wound bed, while the control mice only received Matrigel. After observing the mice over 12 days to allow all wounds to fully close, mice treated with BD-MSCs visibly displayed faster healing. Histological examination of the healed wounds at day 12 post-wounding showed a significantly smaller wound size. This data shows that topical BD-MSC treatment accelerated wound healing, reduced scar formation and did not lead to adverse side effects in mice. Additionally, BD-MSC treatment of excisional wounds in the porcine models showed the pro-wound healing properties of BD-MSCs obtained in the previous murine study without any adverse side effects and there was a higher number of blood vessels in the dermal component of reconstituted skin, another characteristic of enhanced skin healing.



(Figure 1)



(Figure 2)

Discussion

For decades, allogenic skin grafting has always been the standard procedure to restore the skin of burn victims. The single most crucial factor for burn patients in terms of survival is wound coverage and wound healing. The current standard for burn wounds that are extensive is to

excise the injury within 72 hours[4]. Extracting the nonviable tissue that would delay wound healing, due to the burn eschar's strong inflammatory response and increased risk of bacterial colonization and infection, and also to prevent pathological responses such as keloid formation and hypertrophic scarring. Excision is continued until a plane of well-vascularized tissue, with punctate bleeding, is reached and necrotic material or debris is removed. Subsequent to the removal of burned skin, allogenic skin grafting is the current conventional route. While grafting can be successful, it poses several limitations. Firstly, Grafting is an invasive procedure and creates a new wound in a healthy skin area. The body may reject a skin graft, necessitating the immediate removal of the graft. Graft rejection can occur if there is poor blood circulation to the graft or if blood fills up beneath the skin graft--called a hematoma--and prevents the graft from properly adhering and growing to the wound site. The transplantation of allogeneic skin grafts is always associated with a potent inflammatory immune response leading to the destruction of donor cells and the rejection of the graft. While current immunosuppressive treatments are effective in preventing early rejection of organ transplants, such as kidney, they have little or no effect in skin transplantation.[4]

On the other hand, an autologous stem cell transplants for burn patients are currently believed to be the most promising strategy for circumventing immune rejection. Autologous stem cells are generated directly from the patient seeking treatment and need to be differentiated into the cell type that needs to be replaced. Since the cells carry the same tissue antigens as the patient, they are tagged as "self," and so these cells are accepted by the immune system.

The autologous procedure of skin grafting also creates a new wound in a healthy skin area. The larger the burn, the less healthy skin remains for autologous skin grafting, limiting its overall availability for grafts. The new formed wounds that result from autologous skin grafting make the patient susceptible to infections, and so increasing the patient's suffering.

Realizing the limitations with skin grafting, scientists turned to stem cells as a new. Fibroblast-like cells from surrounding intact cells as well as recruited mesenchymal progenitor cells contribute to the reconstitution of the dermis. Recent data is showing that myeloid lineage cells may directly convert into fibroblast-like cells and assist in dermis reconstitution.

Full-thickness burned skin that is usually discarded to avoid further morbidities contains viable mesenchymal skin stem cells. These cells are abundantly available and can be extracted and utilized in vitro in a cost-effective incorporation process to regenerate skin on the patient. To add onto that, cell isolation from burned skin is a non-invasive with no added risk to the patient since debridement of affected burned tissues is part of routine and therapeutic practice. Consequently, the greater the body surface affected by burn injury the increased need for stem cells to regenerate and replace the lost skin and concomitantly, the higher the amount of excised skin is that can be potentially used to extract the stem cells.. This autologous availability of stem cells contrasts the standard autologous skin grafting procedure of physically removing healthy skin from the patients, which can lead to discomfort, pain, and a long recovery time.[3]

Burn-derived stem cells are a promising new source of skin stem cells for regenerative medicine and burn-wound management and this autologous method can potentially revolutionize the way we treat burn patients.

Conclusion

The severely burnt skin that is routinely excised and discarded should not be overlooked and regarded as medical waste as it contains viable burn-derived mesenchymal stem cells that can be used for skin regeneration and wound healing. The limitations of skin grafting should push medical practioners to utilize stem cells as a new alternative for wound healing to avoid potential graft rejection, and areas of exposed wounds that make the patient prone to infections. The thermally injured skin provides an ideal source of mesenchymal stem cells for regenerative medicine and is more cost efficient and easier to access.

References

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