

Assessing Topical Phenytoin's Therapeutic Potential for Thermal Burn Regenerative Treatment

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ABSTRACT

Thermal burn injuries represent a significant burden, particularly in developing nations, where they inflict both physical and psychological trauma. Early wound healing promotion is critical to mitigate associated complications. Phenytoin, readily available, is recognized for its potential to expedite wound healing. This study aims to evaluate the healing effects of topical phenytoin on second and third-degree burn wounds. This study was performed in an 82 year old male who suffered with thermal burns. He underwent topical application of intravenous phenytoin solution every three days. Data collection encompassed demographic information, tissue culture results, wound discharge volume, pain severity, granulation tissue appearance, and wound contraction. Predominantly, burn wounds were self-inflicted. Initially colonized with pathogenic bacteria, the wounds demonstrated no impediment to phenytoin-induced healing. Following 3-5 phenytoin sessions, wound discharge significantly decreased, along with notable pain alleviation reported by patients. Digital planimetry revealed progressive wound contraction in all cases. Conclusion: Our findings suggest that topical phenytoin application fosters progressive wound contraction, re-epithelialization, reduced discharge, and pain relief, culminating in expedited wound healing. Some cases also exhibited a bacteriostatic effect. Further controlled trials are warranted to corroborate these observations.

Keywords: Topical Phenytoin Therapy, Regenerative Therapy, Wound Management.

INTRODUCTION

Burn injuries pose significant physiological and psychological challenges compared to other types of injuries, necessitating specialized care encompassing fluid management, electrolyte balance monitoring, wound care, respiratory and nutritional support, infection treatment, and in severe cases, management of sepsis and multiple organ failure syndrome. Accelerating wound healing is crucial in mitigating burn-

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related complications such as hypertrophic scarring, joint contractures, and stiffness [1]. The extent of burn injury is assessed using the rule of nines or the Lund and Browder chart to guide fluid and nutritional therapy. Evaluating burn depth is essential for determining appropriate conservative or surgical interventions, categorizing burns as first-degree epidermal, superficial partial-thickness dermal, deep partial-thickness dermal, or full-thickness third-degree [2]. Effective burns management requires comprehensive evaluation, assessment, and treatment of the burn wound. While superficial and partial-thickness burns may heal spontaneously, deep second-degree and third-degree burns often necessitate early surgical intervention to prevent complications and promote timely wound bed preparation for soft tissue coverage. Infection is a primary cause of morbidity and mortality in extensive burn injuries, leading to delayed wound healing and systemic infections. Various topical therapies, including antibiotic creams, silver/iodine-releasing dressings, biological dressings, and synthetic dressings, are utilized in burn wound management. Additionally, certain drugs such as insulin and phenytoin, initially intended for other medical conditions, exhibit accelerated wound healing properties and are increasingly employed in burn wound care. Phenytoin, introduced in 1937 for seizure disorders [1,2], is associated with gingival fibrous overgrowth [3] and mild skin and skull thickening as side effects, suggesting its potential application in wound healing due to its stimulatory effect on connective tissue.

MATERIALS AND METHODS

The study was conducted at the JIPMER tertiary burn care center in an 82 year old male with thermal burns on left

upper limb (Figure 1). Topical phenytoin therapy commenced between 7-10 days post-admission (Figure 2). The raw area's surface area was determined using digital planimetry software, and tissue cultures were obtained before initiating phenytoin therapy. Topical phenytoin was administered every third day until discharge, skin grafting, or resolution of the burn wound. Intravenous phenytoin solution (50mg/1ml) ranging from 100-300 mg was sprinkled over the wound surface and covered with Vaseline gauze dressings. Patients were monitored for wound discharge, pain, granulation tissue formation, and wound contraction every three days. Additional systemic support, including nutritional supplementation, antibiotics, and analgesics, was provided as deemed necessary for individual patients.

RESULTS

This study was performed in an 82 year old male with thermal burns over left upper limb. Intravenous phenytoin solution was administered over 5-8 sessions. Progressive improvement in wound healing was observed, characterized by increased granulation tissue formation and re-epithelialization, quantified using digital planimetry software to measure wound contraction. BJWAT scoring improved from 30 to 26 (Figure 1 and 3) Wound discharge decreased progressively from moderate to mild, while subjective pain perception reduced from severe to mild/no pain. Wounds healed completely by secondary intention (Figure 3). He reported experiencing mild burning sensation during phenytoin application, lasting only a few minutes. No systemic or local adverse effects were noted in the patient.



Figure 1. Showing condition of thermal burns over right lower limb at time of presentation BJWAT score 30.



Figure 2. Showing application of phenytoin solution over the thermal burns.



Figure 3. Showing improvement in condition of thermal burns five sessions after application of topical phenytoin solution BJWAT score 26.

DISCUSSION

Phenytoin, a pharmacological agent primarily recognized for its antiepileptic properties, has also demonstrated efficacy in promoting wound healing across various conditions such as diabetes ulcers, decubitus ulcers [4,5], traumatic ulcers [6,7], venous ulcers [8], tuberculous ulcers, epidermolysis bullosa, and burns [9]. Its mechanisms of action involve enhancing neovascularization, proliferation of myofibroblasts and fibroblasts, collagen production and deposition, extracellular matrix synthesis, and activity of growth factors [10] and their mediators. Phenytoin additionally reduces edema, wound exudate, bacterial load, and pain while facilitating re-epithelialization. Although the precise mechanism remains unclear, it is hypothesized to involve upregulation of platelet-derived growth factor gene expression in monocytes and macrophages, along with a net inhibitory effect on collagenase. Topical application of phenytoin ensures direct delivery to the target site while minimizing systemic side effects. Various formulations including powdered tablets, saline or IV solutions, creams, ointments, lotions, and aerosols are available for wound application. Studies by Firmino et al. [11] have elucidated the beneficial effects of topical phenytoin in wound healing and preparation for grafting across different ulcer types. Carneiro et al. [12] conducted comparative research highlighting the efficacy of topical phenytoin versus silver sulfadiazine in acute burn treatment, emphasizing significant pain reduction with phenytoin application. Furthermore, another prospective randomized study by Carneiro et al. underscored

the advantageous effects of topical phenytoin in accelerating wound healing, reducing pain and discharge in chronic leg ulcers, findings consistent with observations in acute burn wound management.

CONCLUSION

In our investigation, the topical administration of phenytoin as an adjunctive therapy exhibited a progressive enhancement in wound contracture, re-epithelialization, reduction in discharge and pain, thereby facilitating expedited wound healing. Additionally, a bacteriostatic effect was observed in select cases. However, further controlled trials are imperative to corroborate these findings and establish the efficacy of phenytoin as an adjunctive measure in wound management.

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