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Role of Phenytoin Therapy in Burns

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Abstract

Background: Thermal burn injuries are relatively common in developing countries which produce more physical and psychological damage. By promoting early healing these complications can be minimised. Phenytoin is one of the easily available drug that promote early wound healing. *Objective:* To assess the effect of healing of topical phenytoin in burn wounds caused by 2nd and 3rd degree burns. *Method:* It is a prospective study done in tertiary burn centre from the period of December 2015 to November 2016. Total 9 patients (3 males, 6 females) were included in the study based on the inclusion and exclusion criteria. All patients were treated with topical application of intravenous phenytoin solution once 3 days. The data collected include demographic details, tissue culture, wound discharge, severity of pain, appearance of granulation tissue, wound contraction. *Results:* Majority of burn wound caused by self-inflicted. At the time of starting of phenytoin therapy majority of wounds were colonised with pathogenic bacteria which were not affecting the phenytoin induced wound healing. Wound discharge got significantly reduced after 3 -5 sittings of phenytoin therapy. Severity of pain got significantly reduced as per patient's self-assessment of pain. All wounds showed progressive wound contraction as documented and assessed by digital planimetry. *Conclusion:* In our study topical application of phenytoin caused progressive wound contracture, re-epithelialisation, reduce in discharge and pain, leads to early wound healing. Bacteriostatic effect also noted in few cases, further controlled trials is required to validate the same.

Keywords: Phenytoin; Burns.

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Introduction

Burn injuries produce major physiological and psychological damages than any other type of injury. These patients needs special care and management such as dealing with ûuid shifts, monitoring electrolyte imbalances, proper wound care, respiratory support, nutritional support, treating infections, and sometimes treating sepsis and multiple organ failure syndrome [1]. Faster healing of the wound decreases the severity of burn wound complications such as hypertrophic scarring, joint contractures, and stiffness [1,2]. The percentage of total body surface area is calculated by using rule of nines/ Lund and Browner chart which is used to calculate the patient's ûuid and nutritional requirements [3]. Assessing the burn depth is necessary for further conservative/surgical treatment of burn wounds. Depth of the burn wounds are measured as epidermal first-degree burns, superficial partial-thickness second-degree dermal burns, deep partial-thickness second degree dermal burns, and full-thickness third-degree burns [3].

For successful management of a burns patient, it is important to properly evaluate, assess and manage the burn wound [4]. Superficial epidermal as well as partial-thickness dermal burns usually will heal spontaneously. Treatment of deep second-degree and third-degree burns requires early surgical intervention [1]. Infection of the burn wound is the main cause for morbidity and mortality from extensive burn injury. Infected wounds heal more slowly that leads to delayed

wound bed preparation for soft tissue cover and also lead to systemic infections. There are lots of topical therapy measures are being used in the treatment of burn wounds they include topical antibiotic creams, silver/iodine ion releasing dressings, biological dressings that include various forms of collagen and other skin substitutes, synthetic dressings that include alginates, hydrocolloid, foam dressings etc [1]. And there are drugs (insulin, phenytoin) which were primarily used to treat other specific diseases are found to have accelerated wound healing properties which can also be used in burn wounds [5,6].

Phenytoin (diphenylhydantoin) was introduced into therapy in 1937 for the treatment of seizure disorders [5]. A common side effect with phenytoin treatment for epilepsy is the development of fibrous overgrowth of gingiva and mild skin and skull thickening may also occur. This apparent stimulatory effect of phenytoin on connective tissue suggested an exciting possibility for its use in wound healing [5].

Methodology

Study was carried out in JIPMER tertiary burn care center between the periods of Dec 2015 to November 2016. Total 9 patients with burn raw area caused by 2nd and 3rd degreethermal burns were studied (6 females, 3 males). Inclusion criteria include patients who are all admitted as inpatients between 18-60 years of age and less than 45% thermal burns (Table 1).

Patients who are on oral/systemic phenytoin and having hypersensitivity to phenytoin are excluded from the study. Topical phenytoin application therapy started between 7-10 days. Surface area of raw area calculated (digital planimetry software)and the tissue culture was done before the commencement of phenytoin therapy. Topical application of phenytoin therapy was given every 3rd day till discharge/skin grafting/discharge (Table 2). 100–300 mg of intravenous solution (50mg/1ml) of phenytoin sprinkled (Figure 2) over the wound surface and covered with Vaseline gauze dressings and patients were assessed for wound discharge, pain, granulation tissue, wound contraction once in 3 days. Other systemic nutritional support, antibiotics, analgesics were given accordingly to the patients.

Fig. 1: 2nd degree burns on day 7

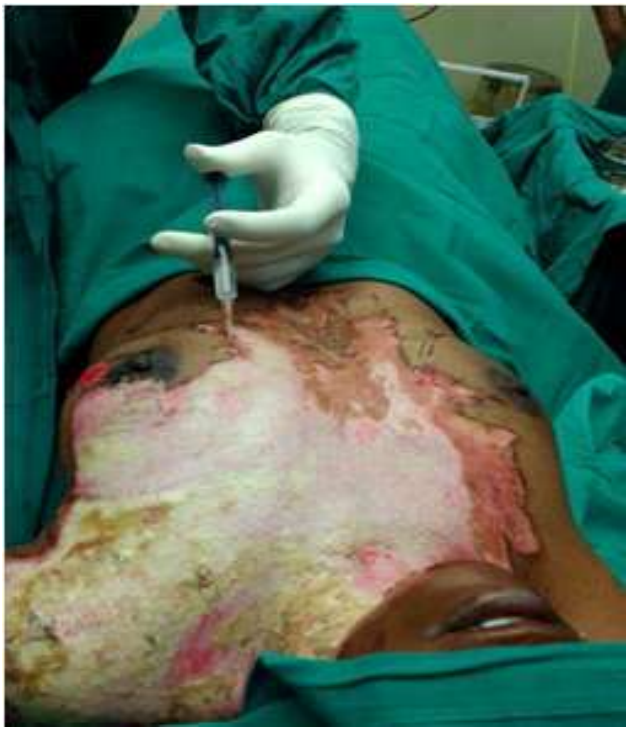

Fig. 2: Day 13 – 3rd sitting of phenytoin instillation

Table 1: Demography of the patients

S. No	Age in years	Sex	Percentage(%) of total surfaces area of Burns	Percentage (%)of 2nd& 3rd degree burns	Tissue culture	Duration of hospital stay
1	25	M	30%	10%	Pseudomonas	32 days
2	24	F	20%	8%	Acinetobacter	25 days
3	32	M	45%	18%	Pseudomonas	43 days
4	30	F	40%	15%	MRSA	37 days
5	45	F	25%	10%	Klebsiella	29 day
6	56	M	13%	7%	No growth	25 days
7	37	F	43%	20%	E.coli	42 days
8	21	F	28%	13%	Acinetobacter	33 days
9	28	F	40%	15%	Pseudomonas	29 days

Table 2: Effect of phenytoin therapy

S. No.	Surface area before application (sq.cm)	Post burn day(PBD) of starting phenytoin therapy	No of Applications	Surface area after application (sq.cm)	Final culture	Healed by secondary intention/Healed with split skin grafting(SSG)
1	150	10	5	50	Pseudomonas	Healed with SSG
2	146	8	5	20	No growth	Healed by secondary intention
3	244	9	8	52	No growth	Healed with SSG
4	84	10	5	28	MRSA	Healed with SSG
5	108	8	5	30	Proteus	Healed with SSG
6	64	7	5	15	No growth	Healed by secondary intention
7	138	8	8	48	Pseudomonas	Healed with SSG
8	88	8	5	24	Acinetobacter	Healed by secondary intention
9	140	8	5	32	Pseudomonas	Healed with SSG

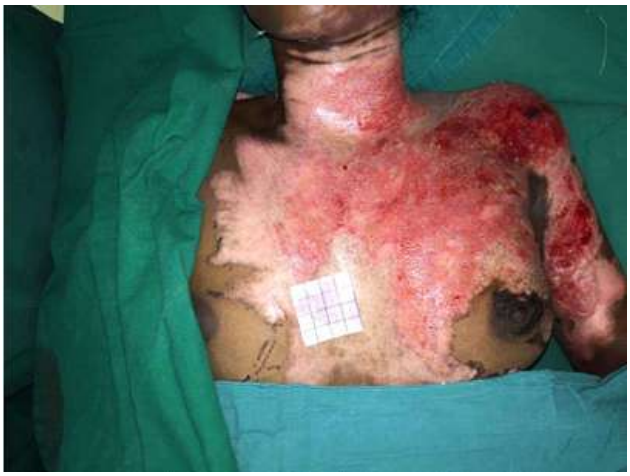

Fig. 3: After 5 sittings

Fig. 4: Day 15, 2nd and 3rd degree burns

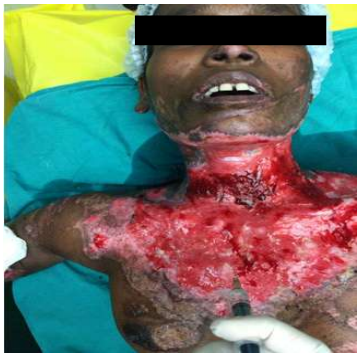

Fig. 5: 7th sitting of phenytoin instillation

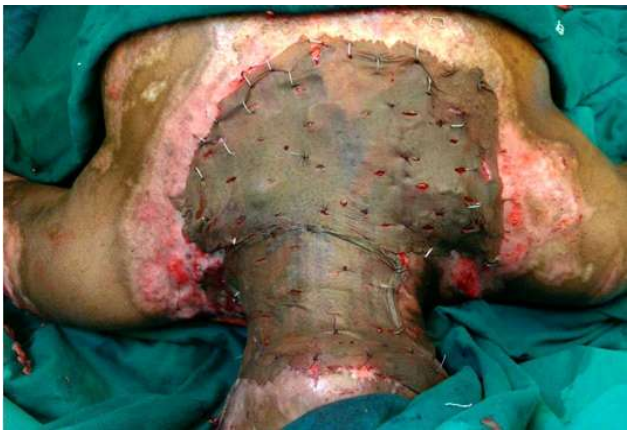

Fig. 6: SSG fixed

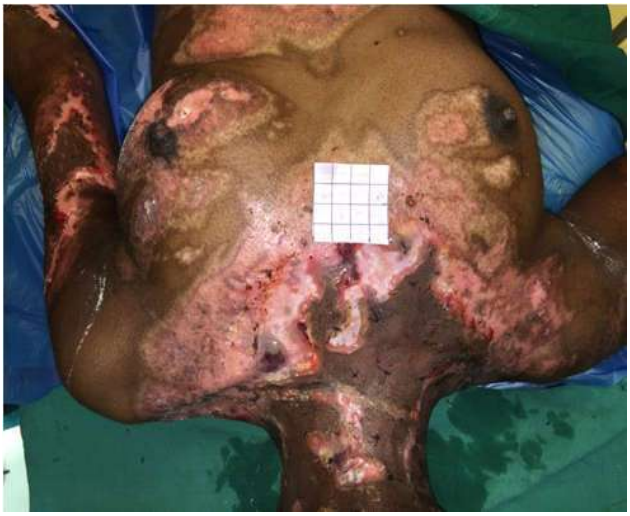

Fig. 7: 9th POD after SSG

Results

This study included 9 patients (3 males, 6 females) of thermal burns less than 45%. Major cause of the burn was self-inflicted. 5-8 sittings of intravenous solution phenytoin application given. All wounds showed progressive improvement by increase in the amount of granulation tissue, increased re-

epithelialisation which was measured by the wound contraction using digital planimetry software. Wound discharge progressively reduced from moderate to mild. Patient subjective feeling of pain also got reduced from severe to mild/no pain. All of the wounds were healed completely by secondary intention/ skin grafting. All patients experienced mild burning sensation while sprinkling of phenytoin which lasted only for few minutes. No systemic or local adverse effects noted in all these patients.

Discussion

Phenytoin is one of the pharmacological agents that have been used for their antiepileptic activity and also it is found to promote wound healing in diabetes ulcers, decubitus ulcers, traumatic ulcers, venous ulcers, tuberculous ulcers, epidermolysis bullosa, burns etc [5, 7]. Phenytoin increases neovascularization, myofibroblast and fibroblast proliferation, collagen production and deposition, extracellular matrix production, and growth factors and their mediators activity [5,7,8,9]. Phenytoin reduces oedema, wound exudate, bacterial load, pain and promotes re-epithelialisation [8,9]. The mechanism of action is not clearly known, probably due to causing increasing in the gene expression of platelet derived growth factor in the monocyte and macrophages and net the effect of inhibition of collagenase [7,9]. Topical application of phenytoin results in direct access of the drug to the target site and avoids the risk of getting systemic side effects. Phenytoin can be applied on the wound as powdered form of the commercially available tablets, can be used in dissolved saline, IV solution, cream, ointment, lotion, aerosol forms [5].

Firmino F et al has explained the beneficial effects in wound healing and wound bed preparation for grafting following topical phenytoin application on various types of ulcers [5].

Carneiro et al. has conducted a comparative study on the effects of topical phenytoinwith silver sulfadiazine for the treatment of acute burns. He has concluded that topical phenytoin use produced significant reduction in pain which is similar to the results of this study [10].

Another randomised prospective study done by Carneiro et al has proved the beneficial effects of topical phenytoin application in chronic leg ulcers which accelerated wound healing, decreased pain and discharge which is similar to the results of this study done on acute burn wounds [8].

Conclusion

In our study topical application of phenytoin used as an adjunctive measure caused progressive wound contracture, re-epithelialisation, reduce in discharge and pain, leads to early wound healing. Bacteriostatic effect also noted in few cases, further controlled trials is required to validate the same.

Conflicts of Interest: Nil

Source of Funding: Nil

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