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A comparison of topical Phenytoin with Silverex in the treatment of superficial dermal burn wounds

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Abstract

Objective: To compare topical diphenylhydantoin (Phenytoin) with silver sulphadiazine/chlorhexidine (Silverex) in terms of rate of wound healing, analgesic and antibacterial properties in small to moderate-sized (<30% TBSA) superficial dermal (second degree) burn wounds.
Design: A prospective randomized controlled study.
Setting: Surgical wards, Muhimbili National Hospital from July 2000 to February 2001.
Subjects: Sixty four patients with acute burns, 32 in each group.
Interventions: Study group treated by sprinkling Phenytoin powder and control group by sprinkling Silverex powder on the wounds for 14 days or until the wound epithelialised or was ready for skin grafting. The data collected included demographic characteristics of patients, aetiology of burn injury, circumstances of injury, site and extent of burns, pus discharge and smell from the wound, pain and discomfort from the wound, bacterial cultures of wound swabs, rate of reduction in wound size and outcome of treatment.
Results: The study enrolled 33 male and 31 female patients, 69% being children under five years of age. Hot liquids (80%) and open flames (20%) were the only causes of burns. In 97% of patients injury was due to domestic accidents. In half of the patients burns involved the trunk, and 52% of all patients had less than 15% total body surface burnt. Pus discharge was recorded in 59% of Phenytoin-treated and 75% in Silverex-treated patients while foul smell was noted in 19% and 31% of cases respectively. There were more negative bacterial wound cultures in Phenytoin-than Silverex-treated wounds on day five and day 10 of treatment, the difference being statistically significant ($p < 0.01$ and 0.001 respectively). There was also a statistically significant difference in wound pain in favour of Phenytoin ($p < 0.01$). There was no statistically significant difference in the rate of healing in the two groups.

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Conclusion: Phenytoin is a cheap and easy-to-use medicament, effective in suppressing burn wound bacteria and relieving pain thereby promoting healing, and may be advocated for the purpose in resource-scarce environments.

Introduction

Burn injuries constitute a major health problem causing considerable morbidity and mortality in Tanzania[1] and around the world.[2,3] It is a common surgical problem and leading cause of death (20% mortality) in our paediatric surgical ward (Morbidity/Mortality report 2000 — Muhimbili National Hospital). Mzezewa et *al.*[4] reported an overall mortality of 22% in a three year study at the Harare Burn Units. Inappropriate treatment facilities lead to severe complications like wound infections and septicaemia, anaemia and contracture deformities resulting in prolonged hospitalization with enormous economic impact in medical cost and loss of time from school and work. Socio-economic factors contributing to increased incidence of burns especially in children include domestic accidents resulting from explosion of cheap kerosene stoves, poor architectural design of the kitchen in low-income families and cooking on open fires at floor level often in the open where children are playing.[5,6]

While deep, extensive burns are a specific entity requiring specialized intensive care, the more common small to moderate size superficial dermal (second degree) burns can be a major cause of morbidity due to complications. Our standard topical burn wound therapy like the use of sofratulle gauze dressings, silver sulphadiazine cream/ powder (Silverex) have not been very effective in preventing complications like wound infections and the average hospitalization period has been about three to four weeks.

Diphenylhydantoin (Phenytoin) powder when used topically on burn wounds has been found to be very effective.[7,8] Phenytoin, a hydantoin derivative, was first synthesized in 1908, but its anticonvulsant activity was not discovered until 1938 when it was used for epilepsy.[9] Since then it has been employed in the treatment of many conditions including cardiac arrhythmias, muscle disorders, trigeminal and related neuralgias and other types of pain. Recently, Phenytoin has been found to have a distinct beneficial role in the biology of wound repair,[9,10] reducing pain and promotes healing and is thereby useful in acute burns.[7,11] Biopsies of the Phenytoin-treated burns showed increased fibroblast proliferation,[12] increased neovascularization and capillary patency, and increased collagen content.[13] Decreased wound water loss and bacterial contamination and infection were also noted. Apart from a case of generalized rash in one study[14] no adverse reactions (including contact dermatitis or other manifestations of hypersensitivity or chemical toxicity) have been noted.[7-14] Given the strong laboratory[10,15-17] and clinical[7,15,18] evidence, a clinical trial to compare topical Phenytoin with Silverex on the rate of wound healing, analgesic and anti-bacterial properties in small to moderate size superficial dermal burns in our environment is indicated.

Materials and Methods

This was a randomized, controlled, prospective study. The study group consisted of 32 patients with small to moderate size (10 to 30%) superficial dermal burns treated with Phenytoin and the control group consisted of the same number of patients treated with Silverex. The latter is an antimicrobial agent used commonly as a topical therapy in burns and consists of a combination of silver sulphadiazine and chlorhexidine hydrochloride. The study was carried out in all adult and children surgical wards in Muhimbili National Hospital where burn patients are admitted. Patients taking oral Phenytoin or hypersensitive to it and those on immunosuppressive or steroid therapy were excluded. Also not included were pregnant women and subjects with any other condition or therapy which might pose a risk to the subject.

The burn site was cleaned with normal saline and debrided as required each day for 14 days. Dry Phenytoin powder and Silverex powder was then sprinkled topically on to the wounds in the study and control group respectively. This was done daily until complete healing occurred or uniform granulation tissue appeared when skin grafting was done. Wound swabs were taken on admission, day five, and day 10 and transported to the Microbiology Laboratory in Stuart transport medium on the same day for culture and sensitivity.

Patients were interviewed and the burn wounds were inspected daily by the same investigator to assess presence of discharge (pus) and/or odour and severity of wound pain using the analog scale. Children were assessed on how comfortable they were with the assistance of their parents/ guardian. Rate of wound healing was assessed by measuring the decrease in size of the wound calculated approximately by multiplying the longest vertical and horizontal dimensions of the wound. Determination of wound area was done on admission (baseline), days three, seven, 10 and 14.

Ethical clearance and patient consent was obtained, the results analyzed and subjected to statistical tests (Chi-square test for categorical variables and Student t-test for means).

Results

The study period was from July 2000 to February 2001 whereby 64 patients were enrolled, 32 in each group. Children under five years were the majority (69%) but there was no significant difference in the distribution of

patients by age in the two groups. Thirty three were males and 31 female patients; there was no significant difference in the sex distribution. Scalds (from hot liquids) which were the majority (80%), and open flames were the only causes of burns in the study and a significant difference in the distribution of patients according to aetiology ($p< 0.01$) was noted. Nearly all burns resulted from domestic accidents (97%). The remainder were due to assault (non-accidental injury). In half of the patients the burns were on the trunk and the extent of burns ranged from 10 to 24%. In 52% of cases it was less than 15%. Both treatment groups were comparable regarding extent of burn injury. Pus discharge was seen in 67% of all patients, 59% in burn wounds treated with Phenytoin and 75% in those treated with Silverex but the difference was not statistically significant. Foul smell from burn wounds was noted in 25% of all patients. There was, however, no statistically significant difference in the two groups. Table I shows the burn wound bacterial culture results on admission, days five and 10 of treatment; two patients in the Phenytoin group and one in the Silverex group were already discharged by the 10th day of treatment as their wounds had healed. While there was no significant difference on wound cultures between the two groups on admission, there were more patients with negative wound bacterial cultures in the Phenytoin group than in the controls on days five and 10, the difference was highly statistically significant ($p< 0.01$ and $p< 0.001$ respectively). Common pathogens isolated in both groups included *Pseudomonas aeuriginosa, Klebsiella* spp., *Escherichia coli, Proteus* spp. and *Staphylococcus aureus.*

Table I: Burn wound bacterial cultures.

Day Swab taken	Phenytoin		Silverex	
	Positive N	Negative N	Positive N	Negative N
On Admission	13	19	14	18
Day 5	12	20	23	9
Day 10	3	27	15	16

Seventy eight percent of patients in the Phenytoin group reported mild or no pain/discomfort compared to 47% in the Silverex group (Table II), the difference being statistically significant ($p < 0.01$). Table III correlates treatment outcome with aetiology and shows that complete healing was observed in all the Phenytoin-treated burns due to scalds whereas six patients in the Silverex group healed poorly. Overall, seven patients (22%) in the Silverex group progressed poorly and had to have their treatment changed compared to only one patient (3%) in the Phenytoin group. This difference was statistically significant ($p< 0.05$).

The average hospitalization period was 14.2 days in the Phenytoin group compared to 16.25 days in the Silverex group, however, this difference was not statistically significant.

Table II: Presence of wound pain/discomfort.

	Phenytoin	Silverex	Total
Pain/discomfort	N	N	N
Moderate-Severe	7	17	24
Mild or None 25	15	40	
Total	**32**	**32**	**64**

Table III: Treatment outcome in relation to aetiology.

Treatment	Phentoin		Silverex		Total
Outcome	Scald N	Flame N	Scald N	Flame N	N
Complete healing	21	8	24	0	53
Skin grafting	0	2	0	1	3
Poor healing	0	1	6	1	8
Total	**21**	**11**	**30**	**2**	**64**

Discussion

Young children were the majority in this study as it only included small to moderate size superficial dermal burns that often result from hot liquids following domestic accidents.[1,19,20] The sex distribution was fairly equal thereby avoiding gender bias on the outcome of study. Similarly the site and extent of burn injury were comparable in the study and control groups. Though there was a statistically significant difference in aetiology of burns in the two groups ($p< 0.01$), the authors did not feel that this finding contributed to bias in the study as the local management of superficial dermal burn wounds is the same irrespective of its aetiology.

There were fewer cases of pus discharge and foul smell from wounds in the Phenytoin group but the difference was not statistically significant. However, pus swabs taken from the wounds for culture and sensitivity on the fifth and 10th day of treatment showed a significant reduction in wound contamination in the Phenytoin group ($p<0.01$ and $p<0.001$ respectively) as was also seen in other studies.[7,14,21-3] The mechanisms by which Phenytoin reduces wound bacterial contamination are not known. Improvements in wound pH and local circulation appear likely to be responsible.[14] In addition, Lodha *et al.*[23] attributed it to Phenytoin direct antibacterial effect.

Phenytoin-treated patients appeared significantly more comfortable and reported less wound pain ($p<0.01$) correlating other studies.[8,14,21-4] The local analgesic property of topical Phenytoin is thought to be due to its membrane stabilizing actions including modulation of ion flux with selective depressions of repetitive neuronal activity and synaptic transmission.[24] Phenytoin analgesic properties minimized the need for pain medications. In addition the sodium-free Phenytoin has been reported to avoid the initial burning sensation on wounds.[14]

Lodha *et al.*[8] found the healing of second-degree burn areas was consistently faster in the Phenytoin

group ($p < 0.001$) but this was not evident in this study. However, significantly more patients in the Silverex group ($p < 0.05$) had to have their treatment changed as the wounds were not healing well. Average hospitalization period was two days less in the Phenytoin group as was also reported in another study[22] thereby reducing hospital admission costs.

Given Phenytoin antibacterial and analgesic properties in promoting burn wound healing, as well as its availability, low cost, ease of use and apparent safety, the authors recommend its use as a treatment modality for burn wounds especially in developing countries.

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