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A COMPARATIVE STUDY ON EFFICACY OF TOPICAL PHENYTOIN AND SILVER SULPHADIAZINE IN PATIENTS WITH 20% TO 30% BURNS

General Surgery

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ABSTRACT

Introduction:- 20% to 30% burns remains a frequent clinical problem amongst people of country. The aim of this study is to evaluate and compare the benefit of topical phenytoin and topical silver sulphadiazine in these patients. **Material & Methods:-** Hospital based prospective study conducted at Dept. of Surgery, S.P. Medical College and P.B.M Hospital, Bikaner. 100 patients of 20% to 30% burns without any comorbid conditions were selected. **Results:-** Mean age of phenytoin group was 33.24±11.25Yrs and SSD group was 33.34±12.60 Yrs. Male patients in phenytoin group were 60.00% and in SSD group were 56.00%. Culture conversion rates from positive culture on day 2 to negative culture on day 7 is more in phenytoin group compared to SSD group and difference is statistically significant ($p<0.05$). Reduction in burn wound area on day 7 compared to initial wound on day 1 was significantly more in phenytoin group compared to SSD group ($p<0.01$). Hospital stay was significantly less in phenytoin group compared to SSD group ($p<0.01$). Pain reduction on day 7 compared on day 1 was significantly more in phenytoin group compared to SSD group ($p<0.01$). **Conclusion:-**We conclude that topical phenytoin is safe and effective in dressing of burn wounds and its efficacy is more than topical silver sulphadiazine

KEYWORDS

SSD- Silver Sulphadiazine

INTRODUCTION

Burns are a serious public health problem. A burn is defined as an injury to the skin or other organic tissue primarily caused by heat or due to radiation, radioactivity, electricity, friction or contact with chemicals. Heat burns occur when some or all of the different layers of cells in the skin are destroyed by a hot liquid (scald), a hot solid (contact burn) or a flame (flame burn).

According to WHO, estimates about 2,65,000 deaths occur each year from fires alone globally, with more deaths from scalds, electrical burns, and other forms of burns for which data are not available. The majority of these deaths occur in developing countries, with almost half occur in the South-East Asia Region.[1]

Treatment plan for burns includes surgical debridement of wound, special dressings, iv fluids and antibiotics. The burn injury causes devitalising injury to skin surface and forms extensive raw areas, which if not taken care of properly can become colony of microbes and subsequently lead to sepsis.[2]

Numerous topical medications are promoted for burns care and healing. Relatively few have proved to be more efficacious. Since the introduction of SSD into clinical use, it has been used extensively in the topical treatment of infected burns however topical silver sulphadiazine is usually considered to delay wound healing due to cytotoxic effects[3]

Silver sulfadiazine (SSD) cream stood the test of time because of its broad spectrum range, ease of application, minimal side effects and extremely low systemic absorption properties. But of late, bacterial resistance to SSD has emerged. Since superficial burns have shown satisfactory outcome even with other topical antibiotics, like framycetin (soframycin) & neosporin, the use of SSD has to be judicious.[4]

Phenytoin has been widely used in the treatment of epilepsy since 1937 due to its sodium channel blocking activity. However it has been used topically for the treatment of various non-healing ulcer like decubitus ulcers, venous stasis ulcers, traumatic wounds and also in burns.

Few studies shows topical phenytoin revealed similar therapeutic results compared to silver sulphadiazine in treatment of superficial dermal burns.[5]

The mechanism by which phenytoin accelerates wound healing is unknown. Clinical, animal and in vitro studies suggest that phenytoin may be involved in the healing process by several mechanisms stated below.

Stimulation of fibroblast by phenytoin causes fibroblast proliferation and enhancing the formation of granulation tissue. At low concentration and short incubation time, phenytoin markedly enhanced fibroblast cell proliferation.[6]

Antibacterial effect of topical phenytoin was reported to eliminate Staphylococcus aureus, Escherichia coli, Klebsiella spp. and Pseudomonas spp. from wounds within 7-9 days. In a guinea pig model of wound healing, it was found that phenytoin cleared gram negative organisms from the wounds more readily than gram-positive bacteria. It is unknown if phenytoin has intrinsic antibacterial activity, or if the effect of phenytoin on the bacterial load of wounds may be mediated indirectly by effects on inflammatory cells and neovascularisation and decreasing wound exudates.[7]

Decreasing collagenase activity by reducing collagenase production or secretion or both not by direct enzyme inhibition, but by decreasing the synthesis centrally via the pituitary-adrenal axis or by competitive antagonism of the glucocorticoid receptor and thus promoting deposition of collagen and other connective tissue components.[8]

Analgesic effect and Local pain relief has also been observed with topical phenytoin therapy, which can be explained by its membrane-stabilizing action; the reduced inflammatory response may also contribute[9]. Facilitation of nerve regeneration has also been reported with phenytoin.[10]

MATERIAL AND METHODS

Study design: Hospital based prospective study.
Study duration: 12 months
Study place: Dept. of Surgery, S.P.Medical College and P.B.M Hospital, Bikaner
Study population: Patients having 20% to 30% burns were included in this study
Sample size: 100 patients
Sampling Method: Random sampling
Inclusion Criteria: Patients with age group between 15-60 years & having burns ranging from 20- 30%, with less than 48 hours duration and without comorbid conditions like diabetes mellitus and hypertension were included.

Exclusion Criteria:
- Patients with age <15 years & >60 years
- Burns <20% or >30% body surface area
- Allergic to phenytoin
- Pregnant patients
- Patients with shock or sepsis

Data Collection: After obtaining permission from institution research board, the present study was conducted at Department of Surgery, P. B. M. Hospital, Bikaner including 100 patients by random sampling, of 15-60 years age group, reporting to Surgery department with 20-30% burns. Out of these 100 cases, using single blind technique, patients were randomly distributed in 2 groups- Control (SSD) group and study (phenytoin) group both containing 50 patients. All patients were explained objectives of study and prior written consent was obtained from them.

At time of reporting to department for treatment, initial evaluation of burn and resuscitation was done as per ATLS principles.

All patients underwent detailed clinical examination and relevant investigations. The wounds were thoroughly cleaned and debrided. Burns dimensions as well as the surface area were assessed immediately and reassessed every day till 7 days in either type of dressing. Wound cultures were obtained using sterile culture swab on the day 2nd of initiation of treatment and on 7th day of treatment. The patients were followed up on a daily basis for 7 days in both the study and the control groups.

Group A was dressed with topical phenytoin (study group) and group B with silver sulphadiazine (control group)

Phenytoin sodium tablet of 100mg was crushed and dissolved in 5ml of sterile normal saline to form a solution. This solution was sprayed on the wound with a sprayer and then wound was covered with sterile gauze pad and dressing was done.

Dosage of phenytoin:
Dosage of phenytoin was calculated at 2mg per cm^2 of body surface area. Control group dressing was done with silver sulphadiazine once a day. Before applying both dressing daily wound is cleaned with normal saline and debridement is done if necessary.

Assessment of wound healing in both group done on the based on the following parameters
- Wound contraction and epithelialization (size of wound)
- Culture and sensitivity
- Pain scale Duration of hospital stay

Wound size was measured initially at day 1 and at the end of 7 days, size was recorded. Size was measured twice and mean of two was taken. Wound was also observed for granulation tissue and discharge every day and wound discharge was sent for culture and sensitivity on day 2nd and 7th of treatment. Pain was assessed at day 1 and 7 using visual analogue scale. Duration of hospital stay of both group was also compared.

The following formula was applied to calculate % reduction in area of wound after 2 weeks period in both cases and controls.

% Reduction of burns BSA after 1week = (Initial % BSA– Final % BSA) ÷ (Initial % BSA) X 100 .

Statistical analysis: Independent-Student T Test.
Investigations:-
- Blood: CBC , random blood sugar , fasting blood sugar , blood urea, serum creatinine, serum electrolytes.
- Pus: culture and sensitivity.

Data Analysis
To collect required information from eligible patients a pre-structured pre-tested proforma was used. For data analysis microsoft excel and independent student's T test was used and data was analyzed with the help of frequencies, figures, proportions and measures of central tendency.

RESULTS
Mean age of phenytoin group was 33.24±11.25Yrs and SSD group was 33.34±12.60 Yrs. Male patients in phenytoin group were 60.00% and in SSD group were 56.00%. Culture conversion rates from positive culture on day 2 to negative culture on day 7 is more in phenytoin group compared to SSD group and difference is statistically significant ($p<0.05$). Reduction in burn wound area on day 7 compared to initial wound on day 1 was significantly more in phenytoin group compared to SSD group ($p<0.01$). Hospital stay was significantly less in phenytoin group compared to SSD group ($p<0.01$). Pain reduction on day 7 compared on day 1 was significantly more in phenytoin group compared to SSD group ($p<0.01$).

OBSERVATION TABLES

Table 1. Age wise distribution of study subjects

Age in years	PHENYTOIN	SSD	p-value
Mean	33.24	33.34	>0.01
Standard deviation (SD)	11.25	12.60	

Table 2. Sex wise distribution of study subjects

Sex	Phenytoin group	SSD group	p-value
Male	30	28	>0.01
Female	20	22	

Table 3. Culture conversion on day 7 among study groups

	DAYS OF BURN WOUND	Phenytoin Group	SSD group	p-value
POSITIVE	DAY 2	25	26	<0.01
CULTURE	DAY 7	8	17	

Table 4. Hospital stay wise distribution of study subjects

Hospital stay (days)	Phenytoin group	SSD group	p-value
Mean	9.12	12.54	<0.01
Standard deviation (SD)	1.90	2.76	

Table 5. Comparision of pain on day 1 and day 7 in study subjects

		PHENYTOIN GROUP	SSD GROUP
DAY 1 PAIN	MEAN	5.84	5.88
	STD DEVIATION	0.91	1.02
DAY 7 PAIN	MEAN	1.58	2.86
	STD DEVIATION	0.7	0.83
REDUCTION IN PERCENTAGE (MEAN)	73.33%	51.23%	

Table 6. Comparision of wound area on day 1 and day 7 in study subjects

WOUND BODY SURFACE AREA		PHENYTOIN GROUP	SSD GROUP
DAY 1	MEAN	25.02	26.64
	STD DEVIATION	2.37	2.53
DAY 7	MEAN	17.82	20.54
	STD DEVIATION	2.69	2.51
REDUCTION IN WOUND BSA PERCENTAGE (MEAN)	28.90%	16.70%	

DISCUSSION
Burn injuries constitute a major health problem causing considerable morbidity and mortality in India. Inappropriate treatment facilities lead to severe complications like wound infections and septicaemia and delayed wound healing.

Phenytoin dressing has shown great promise as a procedure for healing of wounds (Venous ulcers, pressure sores, superficial burn wounds, small donor site wounds and minor abrasions). Phenytoin acts by stimulating fibroblasts enhancing granulation tissue formation, decreasing collagenase activity.5

In the present study, an attempt has been made to establish better healing rates with use of phenytoin dressing in 20-30% dermal burns. There is no significance of gender of the patient in this study.

This study is a comparative study which is aimed to document the safety and performance of phenytoin dressing in the treatment of burns.

In our study we found that in age distribution of patients of burns in both groups there were more of young patients than older ones. The mean age of patients in phenytoin group was 33.24 years while for SSD

group it was 33.34 years. The difference between ages among two groups was statistically insignificant. Thus both groups were matched equally for age.

In our study we found that in both groups there were more of male patients than female patients. In phenytoin group we had 30 male patients and 20 female patients while in SSD group we had 28 male patients and 22 female patients.

Menezes et al in his study compared topical phenytoin to immobilization in trophic leprosy ulcer and found that both groups showed a significant reduction in depth and surface dimensions of the ulcers (p<0.0l). The decrease in ulcer depth in the phenytoin group was not statistically significant compared to the control group. However, the rate of decrease in surface dimensions was significant (p<0.05) in the phenytoin group compared to the control[11] while Bansal and Mukul in their study found that the mean decrement in ulcer volume after 4 weeks in the phenytoin group was 72.1 % compared to 55.5% in the control(normal saline dressing) group (p<0.001). [12]

This is consistent with our results where the mean wound area reduced from 25.02% to 17.84 % in patients dressed with topical phenytoin compared to 24.64% to 20.54% in the SSD group. Percentage of reduction in % BSA of burns is 28.9% in study group compared to 16.7% in control group. This study demonstrates that treatment of burns with topical phenytoin dressing results in considerable and rapid burns area reduction and this difference was statistically significant (p =<0.001). .

El Zayat in his study reported reduction of wound contamination with topical phenytoin and postulated it is not a direct anti-bacterial effect, but rather a change in the pH and improvement in local circulation[13]. However Lodha et al suggested that phenytoin may have a direct antibacterial effect[14]. Pendse et al in his study found that 50 % of the phenytoin-treated wounds showed negative cultures by day 7 vs 17% of the saline-treated group at the end of the 4-week treatment period, 29 of 40 phenytoin-treated ulcers had healed in comparison to 10 of 35 controls.[15] PMR Carneiro, LRJ R Wan Yuma, CA Mknoy in their study found that pus discharge was recorded in 59% of Phenytoin-treated and 75% in Silverex-treated patients after day 10. [16]

These results were consistent with our results which showed that culture conversion rates on day 7 of phenytoin group were more compared to SSD group. In our study group, 25 patients in phenytoin group are culture positive on day 2 and are reduced to 8 patients on day 7 and in control group 26 culture positive patients on day 2 are reduced to 17 patients on day 7.

PMR. Carneiro in his study showed that 78% of patients in the Phenytoin group reported mild or no pain/discomfort compared to 47% in the SSD group.16

In our study, we noticed that reduction in the pain on day 7 was more in patient dressed with phenytoin 73.33% compared to SSD 51.23% this difference was statistically significant(p<0.05). In our study based on VAS score the difference between pain on day 1 in both phenytoin and SSD group is insignificant with mean pain score in phenytoin group at 5.84 and that of SSD group at 5.88, however after 1 week of application of dressing over wound mean pain score on day 7 stood at 1.58 for phenytoin group and 2.86 for SSD group.

Duration of hospital stay in our study group (9.12 days) is less compared to control group (12.54 days). The average hospitalization period was statistically significant in our study, however, this difference was not statistically significant in study conducted by PMR Carneiro and LRJ Wan Yuma at al.16

In our study we did not notice any systemic side effects of phenytoin. Very few about 4 patients complained of burning sensation during 1st dressing of wound however during subsequent dressing such complaints were not reported.

Overall, this study shows that phenytoin dressing is safe and effective in treating 20-30% dermal burns. This study was conducted only for 1 week and complete epithelialization and wound reduction was not awaited.

CONCLUSIONS

With the use of topical phenytoin dressing in comparison with the silver sulphadiazine dressing for the treatment of 20-30% dermal burns , the following conclusions were derived;

- The frequency of burn wounds were more in young age group.
- The frequency of burns in male were more that female in our study.
- Topical phenytoin dressing showed faster and better healing rates among the study group.
- Area reduction and percentage reduction was better in topical phenytoin dressing group.
- Pus culture conversion is more with topical phenytoin dressing group. Topical phenytoin dressing may have anti-infective effect
- Significant reduction in pain compared to silver sulphadiazine.

Duration of hospital stay is less in phenytoin group..

Disclosure Statement

This study is investigator initiated. The authors declare that they have no competing/conflict of interests in relation to this article.

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Consent For Publication

- Not applicable.
- Ethics approval and consent to participate.
- The study protocol was approved by the medical ethics committee of the Rajasthan University of Health Sciences, Jaipur, Rajasthan (State), India.

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