International Surgery Journal
Koshariya M et al. Int Surg J. 2018 Sep;5(9):2995-3001
http://www.ijsurgery.com
pISSN 2349-3305 | eISSN 2349-2902

Original Research Article

DOI: http://dx.doi.org/10.18203/2349-2902.isj20183409

Role of topical Sucralfate in healing of burn wounds

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Received: 23 July 2018
Accepted: 26 July 2018

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ABSTRACT

Background: Sucralfate is a basic aluminum salt of sucrose octasulphate which was orally taken for prevention and treatment of several gastrointestinal diseases. This study primarily aims to analyze whether sucralfate accelerates wound healing process in burn patients. The incidence of infection & relieve in pain in burn patients was also compared.
Methods: This is an observational study carried out in the Department of General Surgery, Hamidia Hospital Bhopal on 50 patients divided into group 1 (sucralfate)and group 2 [a-sucralfate; b-silver sulfadiazine (SSD)]. Demographics, history, physical, and systemic examinations of the patients were recorded.
Results: It was observed that sucralfate augments the formation of granulation tissue (in 6-17 days) as compared to SSD (14-22 days). It was noticed that faster healing by re-epithelialization was present in sucralfate group (11-22 days) as compared with SSD group (15-30 days). By the end of 3rd week 50-75% of wound was healed in sucralfate group as compared with 35-50% in SSD group. Incidence of secondary infection was less when topical sucralfate was used (group 1 = 25%; group 2a = 16.6%; group 2b = 66.66%). There was a marked relief in pain and discomfort after sucralfate application as compared to SSD.
Conclusions: Using topical sucralfate expedite the burn wound healing process, significantly decreases pain with no local or systemic adverse reactions to the topical application therefore it can be used as an adjunctive or alternative agent in the future. However, multicentric trials with larger sample size are needed to insure the concept.

Keywords: Silver sulfadiazine, Sucralfate, Wound healing

INTRODUCTION

The burn of scald differs from other types of physical trauma in that they affect primarily one of the most vascular and richly innervated tissue of the body, the skin. Usually they are extensive and associated with profound shock and wounds are prone to infection and varying degrees of toxemias are usual.[1] Inspite of dynamic developments in the art of medicine, the management of burns still remains a problem to the treating surgeon.[2] With improved understanding of mechanism and treatment of shock, attention within recent years has been directed towards altered pathophysiology of burn which includes shock, metabolic imbalance, protein disequilibrium, toxemia, anemia, endocrine disturbance and possibility of infection and its sequel.[3] Availability of better facilities and specialties, early hospitalization and team approach in burn units has virtually reduced the mortality but morbidity has thus increased considerably. The morbidity is mainly due to extensive raw area and their healing sequelae.[4] In the management of burn wound prevention and treatment of infection is the primary aim. The multiplicity of systemic and topical regime in use is a good indication that none is completely satisfactory. Topical therapy coupled with other measures has proved to be the mainstay of

treatment. The burn wound has been victim of assault by practically every substance known, the only limiting factor has been the imagination of attending medical man. Substance used for topical application have ranged from powdered unicorn's horn to tannic acid and antibiotics and antiseptics of modern era.

Pruitt has listed the following characteristics of an ideal topical applicant in burns:

- The compound is stable over a wide range of temperature and pH and is not inactivated by pus, tissue fluids or blood.
- It diffuses rapidly through eschar and shows no long storage in visceral organs, being excreted primarily by renal route, without tubular precipitation.
- It permits wound to be treated by open technique with extremities accessible for inspection and physical therapy.
- It is not cytotoxic.
- The compound is easily applicable and easily removed from the burn wound and thus simplify, the treatment of both inpatient and outpatient cases of burns.
- No anaerobic infection has occurred in patient treated with the medication.
- The application should not be irritating and producing stinging effect.

Studies have shown that sucralfate accelerates cell proliferation in the skin layers leading to clear thickening of the epidermis and dermis. This finding suggested that sucralfate is active also on the skin and has anti-inflammatory and cell proliferative activities.[5] Based on these studies and on the role of sucralfate in protection of gastric mucosa we performed a study on the role of topical sucralfate in the healing of burn wounds.[6-8] We speculate that properties that effect prevention and healing in peptic ulcer disease may act similarly in the prevention and healing of burn wounds.[9] Sucralfate is a complex salt of sucrose sulfate and aluminum hydroxide. It has been widely used in the protection and healing of gastric mucosa in acid peptic disease.[10]

METHODS

The present study was carried out in Hamidia Hospital associated to Gandhi Medical College, Bhopal. A total of 50 patients of burns were studied, 5 of them of superficial burn, 5 were of full thickness burn and 40 of them were of partial thickness burns of less than 50 per cent BSA and who reached the hospital within 48 hours following burns. All the patients were admitted to the surgical ward Burn and Plastic and Pediatrics Surgery Ward. Patients of both sexes and all age groups were studied, out of 50 patients, 10 were treated as outdoor patients. The total of 50 patients were divided into two groups as following. Group I, 25 cases taken as test subjected to topical application of Sucralfate. Group II, 25 cases having bilaterally almost symmetrical burns, one side treated as (A) topical sucralfate and other as (B) taken as control with silver sulphadiazine. First of all, necessary resuscitatory measures were carried out, detailed enquiry and examination was carried out under following

Registration of the cases

This is important for hospital records and medicolegal purposes.

History

Type of burn

Dry flame burns or burns due to electricity or chemicals

Duration of burn

For the calculation of fluids for replacement and the prognosis of the patient.

Local examination

This is done to know:

- Extent (surface areas) of burns, calculated by Wallace's rule of nines
- Parts of body involved
- The depth of burns.

Systemic examination

Patients were evaluated for respiratory and circulatory functions. Accompanying pre-existing disease were excluded.

Investigation

Complete blood picture**,** urine for sugar and albumin, Weekly cultures from the wound. Other special investigations were done as and when indicated, e.g., serum electrolytes, blood urea, serum proteins, etc.

The cases were regularly reviewed clinically from time of admission to the time of complete healing. Reports of investigations, condition of the wound and the patient were recorded. Parameters taken into consideration for the comparative evaluation of efficacy of the treatment and the following events were noted.

- Disappearance of pain and discomfort
- Appearance of red granulation tissue
- Starting of epithelization from the periphery
- Reduction of size/depth
- Rate of healing
- Complete healing time
- Incidence of infection
- Duration of hospital stay
- Comparison of effects in the study and control group

- Appearance of any side effects or complications
- Healing of burn wounds was assessed by me and following observation was made
- Faster healing in superficial burn
- Marked healthy granulation tissue in second degree burn with marginal epithelization with reduction in size of wound.
- Marked evidence of healing with >50% epithelial covering
- Disappearance of the discomfort like burning sensation and itching.

Preparation of topical sucralfate

Emollient form

Prepared as 7 gm% sucralfate in a eucerin-glycerin water based 7 tablets of 1 gm each were crushed into a fine powder and added to 100 gm of glycerol. Glycerol is a syrupy liquid having a sweet taste with hygroscopic properties.

Creamform

Sucralfate 7 gm% water miscible cream base Initially in some cases sucralfate was used as an emollient form later on after availability of sucralfate cream, it was used.

RESULTS

Table 1 shows that out of 50 patients 30% had burns of less than 15% BSA and 40% had 15-30% BSA and rest 30% had burns of 30-45% BSA or more.

Table 1: Distribution of cases in different groups according to extent of burns.

Group	Below 15% BSA burn	15-30% BSA burn	30-45% and above BSA burn
I	11	10	4
II	4	10	11
Total no.	15	20	15
Percentage	30	40	30

Table 2 shows: **s**calds are more common in paediatric age group, females predominate over males in adults age group, most of the females are victim of stove accidents dry flame, burn due to dry flame constitutes 82% of cases.

Table 2: Age and sex wise aetiological distribution of cases.

Etiology	>12 years	Above 12 years		Total
		Males	Females	
Scalds	4	0	1	5
Dry flame	0	14	27	41
Electrical	0	4	0	4
Total	4	18	28	50

Table 3: Distribution of cases in different groups according to depth of burn.

Group	Superficial burns	Partial thickness burn	Deep burn
I	5	15	5
II	0	25	0
Total	5	40	5

Table 3 shows that in the present study 10% of cases were of superficial burn, 80% of cases were of partial thickness burn and 10% of cases were of deep burn.

Table 4: Incidence of anaemia in the cases of different groups.

Group	Haemoglobin in Grams%		
	Less than 8	Between 8-10	More than 10
I	0	8	17
II	4	5	16
Total	4	13	33

Table 4 shows that in most of the case (66%) haemoglobin was above 10 gm% and 34% were anaemic.

Table 5: Incidence of albuminuria and glycosuria.

Sugar		Albumin	
Present	Absent	Present	Absent
9	41	6	44
18%	82%	12%	88%

Table 5 depicts that 18% of total patients had glycosuria and 12% had albuminuria but in none of the cases any organic cause could be detected on follow-up and further investigation.

Table 6: Average duration of hospital stay in days.

Group	Duration of stay in days		
	0-15 BSA burn	15-30 BSA	30-50 BSA burn
I	2.9 days	14.2 days	25.5 days
II	3.4 days	16.3 days	29.0 days

Average duration of hospital stay was found to be higher in Group II as compared to Group I over different range of burn surface area.

Table 7: Average healing time in test (I) and control (II) group.

Group	Duration of stay in days		
	0-15 BSA burn	15-30 BSA	30-50 BSA burn
I	10.5 days	16.3 days	20.27 days
II	14.0 days	21.2 days	24.81 days

On an average healing has faster by 22.4% in the test (I) as compared to that of control (II) group.

Table 8: Incidence of infection in different groups.

Group	Positive Culture					
	I Week		II Week		III Week	
	No.	%	No.	%	No.	%
I	20	80	11	44	4	16
II A	22	88	6	24	1	4
II B	25	10	22	88	5	20

Table 8 depicts that 4 (16%) cases were primarily infected by III week in group I, Test Group (IIA) culture was positive in 4% and in 20% cases of control group (IIB). Culture was positive by III week.

Table 9: Incidence of infection in primarily sterile cases.

Group	Primary culture Sterile	Secondary culture +ve	Incidence of secondary infection
I	4	1	25.00%
II (A)	6	1	16.6%
II (B)	6	4	66.66%

Table 9 shows that incidence of secondary infection is less when topical sucralfate was used.

Table 10: Type of organism isolated.

Bacteria	Culture (first week)	
	Total No.	Percentage
Staphylococci		
Coagulase +ve	13	38
Coagulase –ve	2	4
Pseudomonas	3	6
Coliform	8	12
E. coli	4	2
Proteus	2	2
Contaminants	10	25
Growth of multiple organism	42	84

Table 10 shows multiple organisms were present in large number in culture at 1st week out of which Coagulase positive *Staphylococci* preceded all.

DISCUSSION

The difficulty and the unpredictability in the treatment of burns have been lamented by all workers. Burn patient's exhibit heightened susceptibility to infection which predisposes them to microorganism infection.[11,12] Effective topical therapy results control of bacterial population of the burn wound and this provides to rapid healing of wounds. Sucralfate is one that deserves such consideration for the treatment of burns. The present study has been carried out with an idea to evaluate its effectiveness and assess the clinical and economical superiority, if any, of it over other conventional topical application used in the treatment of burns. In this study we have picked up lead from findings and works of many medical predecessors which has shown that sucralfate cream accelerates cell proliferation in the superficial skin layers leading to a clear thickening of the epidermis and dermis.[13-17]

Figure 1: Partial thickness burn with topical sucralfate.

Figure 2: After topical sucralfate application on 11th day.

Figure 3: Partial thickness burn showing red granulation after topical sucralfate application.

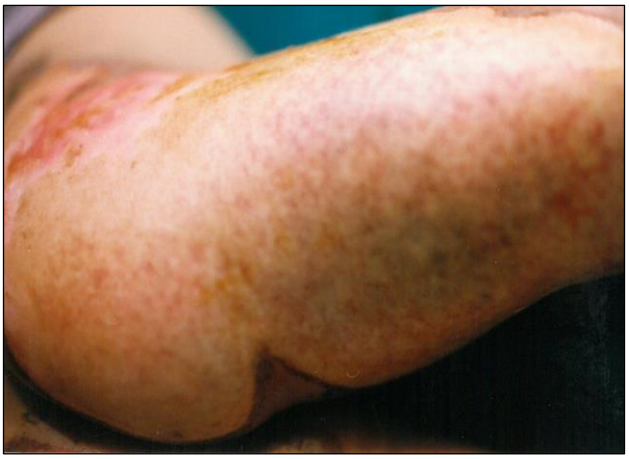

Figure 4: Complete healing.

These findings suggested that sucralfate is also active on the skin. The present study was carried out to evaluate the topical therapy of sucralfate in a soluble base like glycerol and cream.[18,19] Some of the early cases were treated with sucralfate in glycerol case (7 gm%) and later on after the availability of sucralfate cream, majority of the cases are treated with sucralfate cream. Results obtained were equally effective with use of both the preparation. The concept of this therapy is based on the knowledge that sucralfate binds to surface proteins and physically protects normal and injured tissues from exposure to noxious agents. Sucralfate exerts both protective and healing/repair actions through multifactorial process. The management of continuous discharge from the burn wound was done with the use of sucralfate cream. The mess which is being observed with the use of other topical agents on burn wounds is not there. Cleaning of the patient is not difficult as it comes out easily with the toilet of burn wound. After the cleaning of the burn wound, there is always a burning sensation with the feeling of discomfort observed. This leads to the patient to avoid a daily toilet of the wound.

With the use of sucralfate, the minimum of discomfort after cleaning and application has led to the patient a choice of topical applicant. The healing of burn wounds is probably by the provision of a physical barrier to protect the wound from break down products obtained from burn trauma and other toxic irritants, thus promoting healing and re-epithelization. Sucralfate binds epidermal growth faster and causes it to accumulate in the wound areas and stimulate epithelial cell proliferation. It also stimulates angiogenesis which increases the granulation tissue and helps in wound healing (Table 11 and 12).

It also helps in the protection of the wound because of its antibacterial activity in other words it has got cyto-protective activities. These actions of sucralfate are speculated to play an important role in healing of burn wounds. Hayashi AH, Lau HYC and Gillis DA showed that topical sucralfate is an effective therapy for the management of resistant peristomal and perineal excoriations.[20] This role of sucralfate is further supported by studies of Burch RM and McMillan BA.[5] Sucralfate induces proliferation of dermal fibroblasts and keratinocytes in culture and granulation tissue formation in full thickness skin wounds. A cream vehicle or sucralfate in the cream vehicle (10 % by weight) was applied to full thickness wound daily for 12 days. At the end of this time, thickness of granulation tissue was found to be markedly augmented with sucralfate cream. Further sucralfate induced PGE2 synthesis and IL-6 release from cultured skin cells which augment the healing process. The effect of sucralfate was also observed on macrophages, another cell type prominent in healing of skin wounds. The above studies show that sucralfate has definite skin healing properties.

Clinical assessment

Appearance of red granulation tissue

The appearance of red granulation tissue was the criteria for its clinical assessment with the topical application of sucralfate.

In the present study, the appearance of red granulation tissue was also compared with other topical agents used.

Table 11: Appearance of red granulation tissue (in days).

Topical agent	Indication	Days (average)
Sucralfate	Partial thickness	6-11 days
Sucralfate	Full thickness	11 -17 days

Table 11 shows that red granulation tissue appears early in partial thickness burn as compared to full thickness burn on sucralfate application.

It was observed that results using topical sucralfate were better in comparison to other topical agents (SSD) used as depicted in the Table 12.

Table 12: Appearance of red granulation tissue (in days).

Topical agent	Days (average)
Sucralfate	6-17 days
Silver sulphadiazine	14-22 days

Appearance of epithelialization

In burn wounds, it was observed that faster healing by re-epithelialization with production of collagen tissue was more when it was compared with other topical agent used in treatment of burn wounds. In the present study, the appearance of epithelialization was compared with other topical agent (SSD) used and sucralfate was found to be superior.

Table 13: Appearance of epithelialization (in days).

Topical agent	Days (average)
Sucral fate	11-22 days
Silver sulphadiazine	15-30 days

Rate of healing

The rate of healing was evaluated when complete re-epithelialization occurred, and it was found that sucralfate showed faster rate of healing as compared to other topical agent (SSD) in the present study.

Table 14: Rate of healing.

Topical agent	Duration (by the end of three weeks)
Sucralfate	50-75%
Silver sulphadiazine	35-50%

Pain and discomfort

Topically applied sucralfate was found to have a very soothing effect and was very effective soon after application. There was a marked relief in pain and discomfort like burning sensation, irratation and itching after sucralfate application as compared to silver sulphadiazine.

Biopsy

- Although skin biopsy was not done in all the patients. It was done in 4 patients of partial thickness wound. Biopsy was taken from both the study (Sucralfate) and control side
- It was noticed that by 7 days by application of sucralfate some dermal regeneration has occur and delicate new epidermis formed over it
- After 2nd week many young fibroblasts were seen lying with their long axis in a horizontal plane together with many new capillaries
- By the end of three weeks a great deal of collagen was laid down under the dermal belt
- On comparison of biopsy taken from wound treated with sucralfate tissues than with the biopsy of area treated with silver sulphadiazine. It was found that Re-epithelization was faster in patients treated with Sucralfate than the treated with silver sulfadiazine.

Side effects

All studies done till now using sucralfate either systemically or topically have shown that it is a very safe drug. There were no local or systemic adverse reactions to the topical application of sucralfate. In the present study, topical sucralfate was found to be effective and hence we advocate its use in healing of burn wounds, by prevention of infection, formation of healthy granulation and faster re-epithelization.

- Sucralfate is effective in the regeneration of human skin
- Sucralfate induces proliferation of dermal fibroblasts and keratinocytes and augmentation of granulation tissue in full thickness skin wounds
- Sucralfate is effective in healing burns and non-healing burn ulcer when other agents are unsuccessful
- Sucralfate is soothing and reduces patient discomfort and is very effective in elimination of burning sensation in burn patients which is a very challenging problem. Thus, sucralfate is an efficient and excellent alternative to traditional topical agents used in the treatment of burns till now for healing of wounds.

CONCLUSION

Using topical sucralfate expedite the burn wound healing process, significantly decreases pain with no local or systemic adverse reactions to the topical application therefore it can be used as an adjunctive or alternative agent in the future. However, multicentric trials with larger sample size are needed to insure the concept

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Koshariya M, Shitole A, Agarwal V, Dave S. Role of topical Sucralfate in healing of burn wounds. Int Surg J 2018;5:2995-3001.