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Effect of Different Formulations of Silver Sulphadiazine Cream on experimentally Induced Burn Wound Healing

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ABSTRACT

To study the healing effect of various formulations of silver sulfadiazine cream of Apex laboratories Chennai, on experimentally induced burn wound in male Wistar rats in comparison to Silverex. Partial thickness burn wounds were inflicted on Wistar rats (180-200g) under pentobarbitone anesthesia (30mg/kg/i.p), By pouring hot molten wax at 80C into a metal cylinder of 300mm² placed on shaven back of the rat and were divided into 5 groups (n=10). Group 1 did not receive any drug and served as control group. Group 2, 3 and 4 were applied topically silver sulfadiazine A, B, C creams of Apex lab and group 5 Silverex AV creams once daily for 21 days or till complete healing whichever was earlier and results were analyzed by one way ANOVA. Mean period of epithelialization was found to decrease significantly in silver sulfadiazine C treated group when compared to control and it is in line with Silverex. Wound contraction was significantly better in silver sulfadiazine A, B, and C treated groups in comparison to the control groups. In the present study Silver sulfadiazine C is superior to other three creams testing in healing burn wounds.

Key words: Wound healing, silver sulphadiazine, epithelialization, wound contraction

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INTRODUCTION

Burn is a coagulative destruction of the part or whole of the skin, and sometimes of the deeper tissues as well. It is caused by heat which may be dry as flame or moist as boiling water, tea, milk etc. The lesion caused by dry heat is called burns whereas that produced by moist heat is called scald. There is no essential difference in pathology and clinical features between burns and scalds. However, the effects of scald are usually less in severity. Similar lesions may also be produced by electric current, lightning, X-rays, Radium emanations and various chemical agents such as acids and caustics. Burns are classified as: simple erythema, superficial burn and deep burn. Deep burn may involve whole skin or involvement of whole skin and deeper structures. One of the complications of burn injuries is life threatening infection [1, 2], nearly 15% of which are caused by anaerobic bacteria [3]. Silver sulphadiazine is routinely used topically in burn wound patients. Apex Laboratories, Chennai has prepared Silver sulphadiazine in cream base (A, B, & C). Whether these cream based agents are superior/ comparable to available market preparation (Silverex) in healing burn wounds is not precisely known. Hence a study is planned to compare the effect of these agents on experimentally induced burn wound healing.

MATERIALS AND METHODS

Study design

An in vivo Experimental Study

Study Settings

The study was conducted in the Department of Pharmacology, Kasturba Medical College, Manipal University, Manipal.

Selection and animal handling

Fifty male Wistar rats were selected for the study, which were bred locally in the central animal house of Manipal University, Manipal. These animals were of 150-200g and 6 months old, housed under controlled condition of temperature $23 \pm 2^\circ\text{C}$, humidity of $50 \pm 5\%$ and 10-14hr of light and dark cycle respectively. The animals were housed individually in polypropylene cages containing sterile paddy husk (procured locally) as bedding throughout the study and had free access to sterile food (animal chow) and water *ad libitum*. The study was undertaken after obtaining the approval from the institutional ethics committee.

Animal groups

The animals were divided into 5 groups of ten animals each.

1) Control-No drug application

- 2) Silversulphadiazine (Apex product A)
- 3) Silver sulphadiazine (Apex product B)
- 4) Silver sulphadiazine (Apex product C)
- 5) Silverex of Rexcin Pharmaceuticals

Burn wounds

Partial thickness burn wounds were inflicted, on overnight starved Wistar rats (150-200 g) under pentobarbitone anesthesia (30mg/kg/i.p), by pouring hot molten wax at 80° C into a metal cylinder of 300 mm² circular opening placed on shaven back of the rat [4]. Immediately after the injury and on subsequent days Ringer lactate (1 ml/kg) was administered i.p., for resuscitation. Wound contraction was monitored by measuring wound area, planimetrically, on the alternate days till the wounds are completely healed and expressed as percent of wound contraction compared to original wound size. Time taken for full-epithelization was measured by recording the days required for fall of scab leaving no raw wound behind. Apart from the drugs under investigation no local/systemic chemotherapeutic cover was provided to animals. Animals showing signs of infection were excluded from the study and replaced with fresh animals.

Group 1 did not receive any drug and served as control group. Group 2, 3, 4,5, received Silver sulphadiazine (apex product A) , Silver sulphadiazine (apex product B) , Silver sulphadiazine (Apex product C) , Silverex of Rexcin Pharmaceuticals respectively once daily for 21 days or till complete healing whichever is earlier.

Assessment of burn wound healing: Animals were inspected daily and the healing was assessed based on the physical parameters, epithelization period and wound contraction.

- a) Epithelization period: It was monitored by noting the number of days required for the eschar to fall off from the burn wound surface without leaving a raw wound behind.
- b) Wound contraction: It was noted by following the progressive changes in wound area planimetrically, excluding the day of wounding. The size of wounds was traced on a transparent paper every two days, throughout the monitoring period. The tracing was then transferred to 1 mm² graph sheet, from which the wound surface area was evaluated. The evaluated surface area was then employed to calculate the percentage of wound contraction, taking the initial size of wound, 300 mm², as 100% , by using following equation:

$$\% \text{ of wound contraction} = \frac{\text{Initial wound size} - \text{Specific day wound size}}{\text{Initial wound size}} \times 100$$

c) Histopathology

On day 16, some of the animals in each group were sacrificed and the wounds were excised together with the surrounding skin. They were fixed in 10% neutral buffered formalin. Histological examination was performed on hematoxylin and eosin stained 5-6 μ thin paraffin sections of wound bed material.

Statistical analysis

Analysis of data was done by one way ANOVA followed by post hoc test using SPSS 12.0

RESULTS

The period of epithelization in control group is 19.00 \pm 0.68 days. Silversulphadiazine C and Silverex reduced the epithelization period significantly ($p < 0.001$) when compared to control group. There was no significant decrease in epithelization period in groups treated with Silver sulphadiazine A and Silver sulphadiazine B (Table 1).

Table 1. Period of epithelization in days (Mean \pm SE)

Groups	Mean \pm SE(days)
CONTROL	19 \pm 0.68
Silversulphadiazine A	17.66 \pm 0.33
Silversulphadiazine B	17.16 \pm 0.54
Silversulphadiazine C	15.83 \pm 0.30**
Silverex	15.66 \pm 0.33**

**P value \leq 0.001 is more significant

Table 2: Mean \pm SE of the percentage of wound contraction on 4th, 8th, 12th and 16th day.

Groups	4 th day	8 th day	12 th day	16 th day
CONTROL	9.14 \pm 1.99	26.40 \pm 4.28	34.55 \pm 4.85	52.77 \pm 12.16
Silversulphadiazine A	45.083 \pm 1.52**	66.59 \pm 3.26**	75.51 \pm 2.42**	86.14 \pm 3.36*
Silversulphadiazine B	43.43 \pm 5.47**	64.46 \pm 5.42**	74.37 \pm 4.06**	84.74 \pm 5.21*
Silversulphadiazine C	44.53 \pm 5.52**	61.31 \pm 2.77**	75.93 \pm 2.48**	91.40 \pm 2.71*
Silverex	32.66 \pm 6.10**	61.32 \pm 4.88**	71.19 \pm 3.45**	89.04 \pm 2.05*

*P values \leq 0.05 significant

**P value \leq 0.001 more significant

The wound contraction in control animals was 9.14 \pm 1.99% on 4th day, 26.40 \pm 4.28% on 8th day, 34.55 \pm 4.85% on 12th day and 52.77 \pm 12.16% on 16th day (Table 2). All four drugs namely Silver sulphadiazine A, B, C and Silverex cream have significantly favoured wound contraction when compared to control animals. On day 4th Silverex treated group was little behind in wound contraction but later on the wound contraction proceeded in the same fashion. Among the four drugs Silver sulphadiazine C has shown more significant wound contraction when compared to others.

Histopathology studies showed steady and progressive wound healing in the control group. Advanced healing with restoration of epithelium with high amount of collagen was seen in Silver sulphadiazine C and silverex treated groups (Fig.1, Fig 2, Fig. 3, Fig 4, Fig 5).

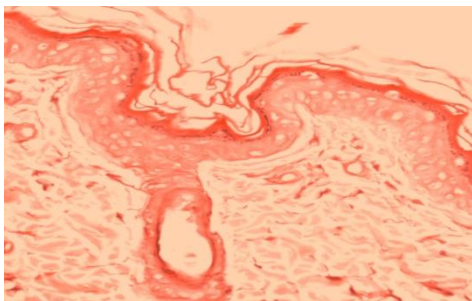


Fig. 1 Control

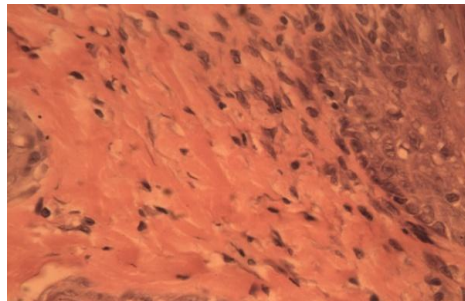


Fig. 2 Silversulphadiazine A

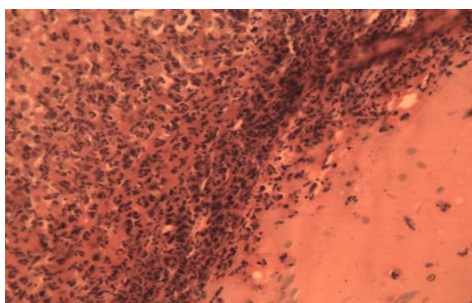


Fig. 3 Silversulphadiazine B

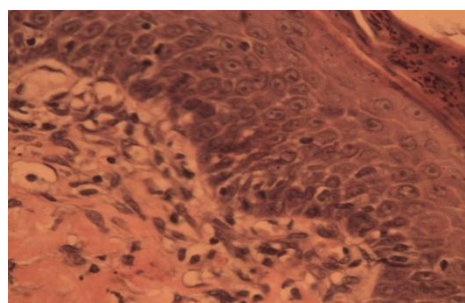


Fig. 4 Silversulphadiazine C

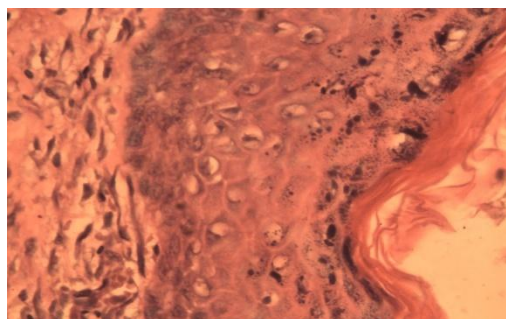


Fig. 5 Silverex

DISCUSSION

Silver sulphadiazine Cream (apex product C) and Silverex AV Cream significantly reduced the period of epithelisation and improved the wound contraction when compared to control group as well as other creams tested. Silver sulphadiazine Cream (apex product C) is slightly better than Silverex AV Cream as it is evident from its effect on wound contraction. The observed finding on wound healing is because of difference in base added to Silver sulphadiazine. This finding highlights the superiority of Silver sulphadiazine Cream (apex product C) in treating in burn wounds. A well planned clinical trial may through more light on this possible advantage of Silver sulphadiazine Cream (apex product C) in burn wound healing.



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