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Comparison Epithelialization of Moist Exposed Burn Ointment and Silver Sulphadiazine for Treatment Superficial Partial Thickness Burns.

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ABSTRACT

This study aim to evaluate the epithelialization of application Moist Exposed Burn Ointment (MEBO) and Silver Sulphadiazine (SSD) on Superficial Partial Thickness Burns. This study utilizes *Wistar* rats in a controlled laboratory setting. Rats are divided into 3 groups: A(n=6) receiving MEBO, B (n=6) receiving SSD, and C (n=6) as control negative. Superficial partial thickness wounds were made, and either MEBO, SSD and nothing were given on the wound. On 3rd, 7th day sample were taken each group, and last day 14th, all rats were sacrificed and excision the wound for histologic examinations, observed histologic assessment scale. The data showed a significant histologic scale in MEBO compare to the SSD and placebo groups (p=0.001). .

Keywords: MEBO, SSD, Epithelialization, Histology.

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INTRODUCTION

Wound healing is a complex physiological process that dependent on a number of inter-related factors. All body tissues have the capability to healing wound through two mechanisms, regeneration or repair. Regeneration is the replacement of tissue that is damaged by identical cells. The second wound healing mechanism is repair where the damaged tissue replaced by the connective tissue and then forms a scar [1]. Tissue regeneration and repair processes appear after lesions. Lesions occur due to stimuli that damage the physical continuity of functional tissue. A stimulus that can cause the lesion could be external or internal, including physical, chemical, electrical or thermal [2]. A burn is a coagulative necrosis of the skin and some times of deeper tissues caused by the dissipation of thermal energy into it [3]. Following successful resuscitation, patients with severe burns will experienced hypermetabolic coditions, chronic inflammation and lean body mas wasting, all of which may impair wound healing [4]. The severity of burn injuries depends on the depth of the wound injury and the extent of the body area affected. As a result of burn wound, the skin loses its protective function against the microorganism that causes the risk of infection infection of microrganism is a major cause morbidity associated with length of hospital stay and high cost [5]. 1% silver sulfadiazine (SSD) is the most commonly used agent worldwide. SSD has been shown to decrease bacterial contamination, to hasten epithelization and to delat wound contraction. However SSD is also known to delay wound healing and separation of scar tissue, to cause atrophic and hyperthrophic scars, to have renal toxicity, leukopenia and risk of resistance [6]. Moist exposed burn ointment (MEBO), an oil based ointment containing sesame oil, beta-sitosterol, beberine and other small quantities of plant ingredients has been proposed as the ideal burn wound treatment. It is thought that this oil based ointment providess a moits environment for epithelial regeneration to occur, with the added anti inflammatory effects of beta sitosterol and the antibacterial effects of berberine [7].This paper presents the results of an experimental study on a rats model designed to observe the different epithelial repair of same degree but treated with MEBO, SSD and dry exposed therapy.

MATERIALS AND METHODS

The experimental animal-model study utilized the *Wistar* rats, with ethical clearance obtained from the Health Research Ethical Committee of Sumatera Utara, Medical School Universitas Sumatera Utara. Eighteen healthy male rats with body weight between 200-250 g were equally divided into three groups; the Moist Exposed Burn Ointment group (MEBO), the Silver sulphadiazine group (SSD), and the control group (CTR). Rats weighing less than 200 g were excluded. Subject is dropped out if death occurs within five days after intervention.

Prior to any procedure, they were acclimatized in laboratory in equal light darkness periodicity with liberal access to food and water. They were housed in separate hygienically maintained cages. Rats were weighed on the day of surgery, then anesthetized by trans-peritoneal injection of 0,05 mg Ketamine per 20 mg body-weight, and placed prone with four limbs taped onto an operating field. Hair was removed from some area on dorsum of the rats manually by razor, and skin disinfected using 10% povidone iodine scrub followed by sterile saline rinse.

Using steel plate with 2 cm^2 and 2 mm thick 100^0c heated. then applied on dorsum by contact for 4 seconds, superficial partial thickness burn wound was inflicted on each side. Wound depth was verified by pathological examination on day 3,7 and 14 by full thickness biopsy at edge of each wound. Rats were then allocated as either group I were treated with MEBO every *8h*, MEBO ointment was supplied by the Beijing Guangming Chinese Medicine Institute for Burns, Wound and Ulcers, China, group II were treated with silver sulfadiazine, 35 mg, expiry date on 30 June 2015), and group III were not treated with anything as negative controls. Treatment were given on the day of wound infliction to fourteen.

On the 3^{rd}, 7^{th}, 2 rats each group were anesthetized ketamine, wound margin were biopsy full-thickness, including health skin and fixed in a 10% paraformaldehyde solution. On the14^{th} day, rats were euthanized by Ketamine overdose. Sample were prepared into paraffin blocks, sliced onto specimen slides and underwent the hematoxyllin-eosin staining. Using a handy taller on 100x and 400x magnification under microscope.. Each item was graded by a blinded pathologist according to a semi quantitative approach as absent (0) and present.

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Wounds size were recorded on the day 3rd, 7th and 14th. Data were then analyzed using the SPSS tested by one-way ANOVA, with a p value <0.05 considered as significant.

RESULT AND DISCUSSION

The animals were generally well preserved and active, No clinical infection was recorded on MEBO group. On the day 3rd , dark-brown necrotic tissue were recorded, MEBO group 5 rats noted the necrotic skin had spontaneously partial detached, leaving pink tender skin either 3 rats on SSD group and 2 rats on CTR group, the rest 4 rats were underwent deep thickness wound. On the 7th day 3 samples had removed necrotic tissue for CTR group, total removed on MEBO group, and 5 samples detached on SSD group. Clinical detached all necrotic tissue were recorded for total group on day 14.The characteristic histologic finding was denudation of the epidermis with superficial dermis. Re-epithelialization proceeded by proliferation in deep layer (Fig 1)

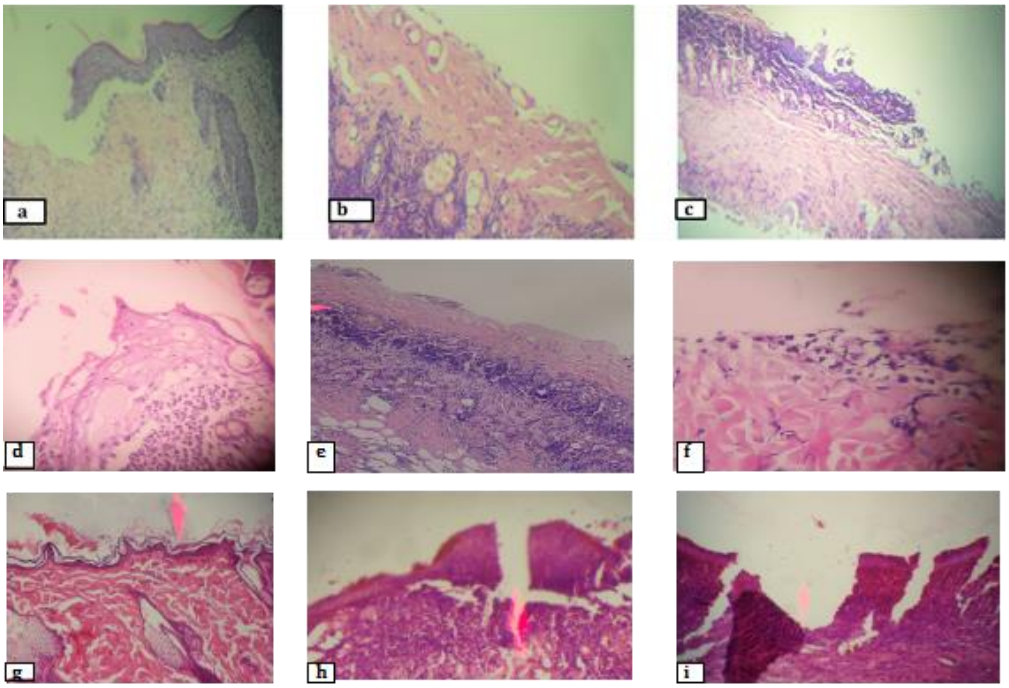

Figure 1: Histological of healing skin on day-3 with hematoxillin-eosin staining (100x). Noted the fully detached necrotic tissue on MEBO group, and increase number of fibroblast, hair follicle (b) necrotic tissue still attached on control (b) and SSD group (c). On the 7th day control group showed denudation of epidermal layer (d), MEBO group showed epidermal growth (e). SSD showed abnormal collagen cell, on 14th day MEBO group showed healing(g) SSD still discontinuity epidermal layer(h) and large discontinuity on control group with increased inflammatory cells (i) .

Table 1: Histologic Assessment Scale result for MEBO, SSD, CTR

Group	Hyperkeratosis	Epidermal Hyperplasia	Hair follicle	Apocrine gland	Smooth Muscle	Collagen	Fibroplasia	Vascular
MEBO	1	0	1	0	1	3	1	1
	1	1	1	1	0	3	1	1
	1	1	1	1	1	3	1	1
	1	1	1	1	1	3	1	1
	1	1	1	1	1	3	1	1
	1	1	1	1	1	3	1	1

SSD	1	0	0	0	0	0	0	1
	1	1	1	0	1	3	0	0
	0	1	0	0	1	1	1	0
	1	0	1	0	0	2	0	1
	1	1	0	1	0	1	1	0
	0	1	0	0	0	3	0	0
CTR	0	0	0	0	0	0	0	0
	0	0	0	0	0	0	0	0
	0	0	1	1	1	1	0	0
	0	1	1	0	1	1	0	0
	0	0	0	0	2	2	1	1
	0	0	0	0	1	1	0	0

Based on table 1, mean histologic scale on 14 day for MEBO was 9.50 (range,8-10;SD,0.83), and for SSD was 4.50 (range, 2-7;SD,1,64) and for CTR was 1.83 (range,1-4;SD,1.72). These differences were statistically significant.

Silver sulfadiazine is one standar antimicrobial topical ointment with advantages such as easy and convenient use. It is not causing pain during administration, yielding low toxicity and sensitivity [8]. It is used to prevent and treat infections of second and third grade burns. It is harmful to a wide variety of bacteria including Gram-positive cocci, S. aureus and Gram-negative bacilli. Silver sulfadiazine have some side effects including alllergic reactions to its sulfadiazine muiety, silver staining of the treated burn wound, hyperosmolality, methemoglobinemia and hemolysis due to a congenital lack of glucose – 6 phospate dehydrogenase. Early post burn leukopenia, once thought to be side effect of the use of SSD in burn wound therapy, is no longer regarded as such since it has been found to occur with the use of other burn topical agents. Its presence is no longer an indication to discontinue SSD burn wound therapy [9]. Yaman et al [10] reported the effects of natural ointment, Nigella sativa (NS) and SSD on heling burn wound in rats. It reported that, histopathologically on the 14th day of experiment, the scab had fallen of in all groups and epidermis was observed to have developed completely. However the epithelial layer in the NS group had a better appearance when compared with SSD groups. Moist Exposed Burn Ointment (MEBO) is a widely used topical agent applied on skin burn. In this experiment, the result showed a significant histologic scale in MEBO compare to SSD and placebo groups (p=0,001).in this study, from histologic changes, MEBO showed increasing amount in fibroblast and good collagen thickening without increasing inflammatory cells. But in 14 days collagen appear stable and epidermal and keratinocyte covered the discontinuity of that tissue injured normally with the significant difference (p<0,001) than SSD. It might be due to the activation and proliferation of epidermal stem cells induced by MEBO. El-Hadidy et al [10] reported the histoloical study of burn wounds with partial thickness burn 1,4,7,14,21 and 28 days after treatment with MEBO. Burned skin showed necrosis of full thickness epidermis that extended to dermis. Gradual regeneration of skin accompanied with an enhancement in CK19 immune reactivity was noted 4,7,14 and 21 days after treatment. On day 28 a complete regeneration of skin was observed. Tang et al [11] reported MEBO significantly promoted the formation of granulation tissue in wounds, shortened the time of wound healing and increased neovascularization and the number of fibroblast. MEBO application also increased the gene expression of vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (bFGF). VEGF stimulastes hydrogen sulfide synthesis and release from endothelial cells, thus leading to subsequent endothelial cell growth, migration and permeability and wound healing. bFGF induced angiogenesis, endothelial cell and fibroblast proliferation.

CONCLUSION

As topical agent to treat superficial partial thickness burn, this study showed the MEBO is better dressing agent compared to SSD application, in terms of faster healing and the better scar.

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