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## *Review Article*

### *Treatment of Chemical Burn with Topical Silver Zinc Sericin Sulfadiazine Cream*

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#### **INTRODUCTION**

The ultimate aim of burn wound care is the closure of burn wound with patient's own epidermis. Physicians have to know the types of burn, extent and wound depth in order to treat burn wounds efficiently. The depth of burn is divided into three groups: First degree ( $1^\circ$ ), second degree ( $2^\circ$ ), and third degree ( $3^\circ$ ). Moreover the  $2^\circ$  burn can be categorized into two subgroups: superficial partial thickness burn and deep partial thickness burn. In this degree, it extends into dermal layer with plenty of micro vessels and nerves so it looks red, swell, and moist and patients feel very painful. Deep dermal burns heal slower than superficial burns. Unfortunately, there is a tendency toward hypertrophic scar formation in some cases. Nowadays, it is still ambiguous between treatment methods for

the initial treatment of deep partial thickness or secondary degree burn injuries. The initial method is the topical application of medication onto the wound 1-2 times a day and 1% silver sulfadiazine is the one of popular drug used in these wounds.<sup>1,2</sup> This method usually lasts longer than three weeks and the wound might prone to healing with scar contracture.

An alternative treatment is surgery called "skin graft". Early burn wound excision is done, followed by rapid skin graft to close the wounds to promote wound healing and reduce burn wound contraction and scar formation. This method still has some difficulties: skin is needed from another area for transplantation onto the burn site. Thus additional wound will be caused in other areas in order to harvest the skin graft to the burn wound.<sup>3</sup> At the Siriraj Hospital, there is a program

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for burn patients with deep partial-thickness burns. The popular treatment method for the burn wound is the application of 1% silver zinc sulfadiazine 1-2 times to the affected area. If the wound is not healed within three weeks, the surgeon will proceed with burn wound excision and then followed by skin grafting.

There was a report on the effectiveness of a glycoprotein isolated from silk (SERICIN) which is used in many cosmetics industry.<sup>4,5,7</sup> This form of protein is very safe and non-toxic to the body. It binds well to human tissue which contains no substances that may cause inflammation.<sup>6</sup> It was found that the sericin is effective in accelerating wounds and tissue healing. The drug-topical silver zinc sericin sulfadiazine cream is a new formula that was developed by mixing sericin with 1% silver sulfadiazine. This article reports on patients with scald injuries that were treated with this cream.

#### A Case

The patient is a 31-year-old Thai male weighed 57 kilograms with 160 centimeters in height presented with chemical burn from a spilled caustic soda onto the body and both arms and legs one hour before hospitalization. He was using sodium hydroxide to clean pipes in the bathroom. Unfortunately, he fell while holding the bottle of caustic soda, and the caustic soda spillage contacted the body causing burn wounds around the legs and chest and both arms, approximately 15 percent of total body surface area (Figure 1).

The patient was in pain with extensive burn wounds when admitted to the hospital. Upon examination, a mixed pink and yellowish eschar over burn wounds was observed on both arms and legs. Between admission at the Burn Unit, Siriraj Hospital,



**Figure 1** Chemical burn wounds on both legs from sodium hydroxide

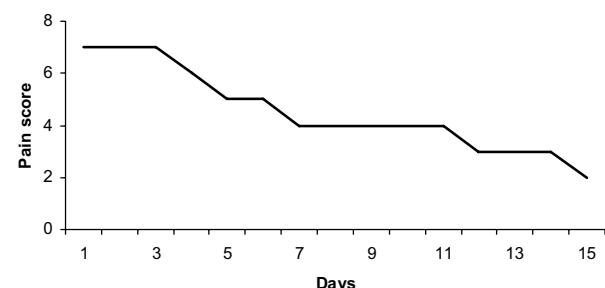
the patient showed the following vital signs: BP of 120/80 mmHg, temperature of 37 °C, heart rate of 90/min and respiratory rate of 20/min. Chemical burn wounds were mixed between deep- and superficial-partial thickness burns. The wounds were cleaned with NSS (normal saline solution) and dead tissues were removed. The 1% silver zinc sericin sulfadiazine cream was applied to the wound and covered on top with sterile gauzes.

During the treatment, the patient did not show any irritation or allergic reaction to this drug and there was no evidence of bacteria presence. The patient responded well to the treatment. Wound pain assessment was done using visual analog scale, which was evaluated at 30 minutes after wound dressing. The maximum score of 10 indicates that the patient has severe pain on the other hand the minimum of 0 implies no pain. The patient had pain score of 7 on the first day and gradually decrease to 2 on discharged day. The pain score in each day is shown in Figure 2.

The wounds begin to heal and narrow, respectively (Figure 3-4). The completely wound closure was diagnosed by attending burn surgeon. It determined by complete epithelialization cover all wound area. The patient was discharged on day 15 after the treatment in the hospital. There were no side effects; like allergy to the drug.

#### DISCUSSION

Wounds from burns can be classified into three different levels according to extent of injuries. First-degree burn, the injury is limited in the epidermal layer and has no clinical significance. The wound heals with no scar formation. Third-degree burn implies a destruction of whole skin layer by heat. The standard treatment is surgery with burn wound excision followed by skin grafting.



**Figure 2** Visual pain analog score in each day



**Figure 3** Complete epithelialization. Second-degree burn on chest after applying silver zinc sericin sulfadiazine cream.



**Figure 4** Burn wound healing within 15 days after applying silver zinc sericin sulfadiazine cream

There are two types of second-degree burns - superficial & deep secondary degree burns. Wounds with superficial secondary degree burns often recover in less than 2-3 weeks so surgery is not required. Wounds with deep secondary degree burns suffers longer traumatic period of time and take more than 2-3 weeks to heal or longer if any complication or infection sets in. Therefore the treatment for this type of wound is up to the discretion of doctor in attendance.<sup>1,8</sup> The current popular method of treatment is the topical application of 1% silver sulfadiazine (silver sulfadiazine) 1-2 times daily to the wound. If the wound does not heal within a period of three weeks, surgical excision should be done, followed by skin graft transplantation.

The 1% silver sulfadiazine is a standard drug for protection and prevention of infection of burn wounds which is widely used up to today.<sup>2</sup> Sulfanamides is known to act on the cell wall and membranes of bacteria.<sup>9,10</sup> It is also active against fungal, gram-positive and gram-negative bacteria such as Methicillin Resistant Staphylococcus aureus (MRSA), and Vancomycin Resistant Enterococci (VRE).<sup>11</sup> Topical sulfadiazine is easily available in the market. It is easy to use and causes no pain, burn feeling or precipitation of silver chloride which can stain clothing when used on the wounds. Silver sulfadiazine is particularly useful in wound care for burns although it is reported that silver sulfadiazine can slow the healing process, hypersensitivity of sulfa drugs, and may be toxic to cells and cause severe low white blood cell.<sup>12,13</sup>

Zinc plays an important role in the process of creating tissue and epithelium. The zinc activates the matrix metalloproteinase enzymes (MMPs), collagenase enzymes to generate and increase collagen in the tissue. This process accelerates cell proliferation and reduces the duration of wound healing. It is generally believed to play a role in promoting wound healing. Experts at the Faculty of Medicine, Siriraj Hospital, Mahidol University developed a mixture of topical zinc with 1% silver sulfadiazine cream to be used for burn wound care. This formulation has been widely accepted and used for patients with both shallow and deep wounds at Siriraj Hospital and other hospitals in the country. It may be concluded that topical zinc is anti bacteria and has anti-inflammatory effect and promotes tissue granulation in burn wound.<sup>14,15</sup>

Sericin is mainly composed of amino acids, serine, glycine and aspartic acid.<sup>16,17</sup> In addition sericin is the main component of natural moisture factor (NMF) in human skin.<sup>18</sup> Padamwar et al, in 2005, studied about the potential and safety of sericin on healthy volunteers. The results showed increase in moisture without any adverse effect.<sup>19</sup> Sericin has useful application in the food and cosmetic industry. Developments in cosmetics continue to take advantage of its medicinal properties.<sup>20-21</sup> Because of the essential amino acids, methionine and cysteine, sericin was investigated in cell studies and experiments on animals for several years.<sup>22</sup> Silk increases the rate of cell proliferation and accelerates the growth of cells in rat and human skin tissue.<sup>23</sup> In 2007, Aramwit et al. found that a cream for wound containing eight percent sericin stimulates

wound healing. A layer of collagen developed in the skin of mice.<sup>7</sup> It is also good for human tissue as it does not cause any inflammation.<sup>6,24</sup> Teramoto did a study on developing and testing the effectiveness of silk gel sheet on wound healing, by stimulating wound healing, increasing moisture with no toxic effect on cells.<sup>25</sup> Nagai et al. reported that the corneal healing rate of rats instilled with 10% sericin solution was significantly higher than that of rats instilled with saline.<sup>26</sup>

Topical silver sulfadiazine is commonly available in Thailand for the treatment and prevention of wound infection. It is capable of killing the bacteria but does not help stimulating wound healing. Therefore there is a need for a product that has two components in ordered to optimize the treatment of burn wounds. Sericin does not have antibacterial properties but has stimulating effects for wound healing. It is interesting that wound heals quickly due to stimulation from accelerated skin cell division (epithelialization) and new collagen production. When combined with 1% silver sulfadiazine and zinc, the mixture has antimicrobial and accelerates wound healing properties. These two effects of cream may help standard wound treatment more efficiently. If the wound heals quickly then the patient does not need to undergo further surgery. This reduces the duration of treatment in the hospital and reduces complications such as wound infection. Wound contraction and scarring are also reduced. Therefore the mixture of sericin and silver sulfadiazine and zinc may be seen as a faster wound healing treatment compared to non drug compounds. This may be useful in wound healing for burns in the future.

#### REFERENCES

- Heimbach D, Mann R, Engrav L. Evaluation of the burn wound management decisions. In: Total burn care, 2<sup>nd</sup> ed. New York: WB Saunders Co; 2002.
- Baxter CR. Topical use of 1.0% silver sulfadiazine. Contemporary burn management. Boston: Little, Brown and Co; 1971.
- Bessey PQ. Wound care. In: Total Burn Care, 3<sup>rd</sup> ed. New York: WB Saunders Co; 2007.
- Dash R, et al. Silk sericin protein of tropical tasar silkworm inhibits UVB-induced apoptosis in human skin keratinocytes. *Mol Cell Biochem* 2008;311:111-9.
- Dash R, Acharya C, Bindu PC and Kundu SC. Antioxidant potential of silk protein sericin against hydrogen peroxide-induced oxidative stress in skin fibroblasts. *BMB Reports* 2008;41:236-41.
- Aramwit P, et al. Monitoring of inflammatory mediators induced by silk sericin. *J Biosci Bioengineer* 2009;107:556-61.
- Aramwit P and Sangcakul A. The effects of Sericin Cream on Wound Healing in Rats. *Biosci Biotechnol Biochem* 2007;71:2473-7.
- Papini R. ABC of burns: management of burn injuries of various depths. *Br Med J* 2004;329:158-60.
- Stanford W, Rappole BW, Fox Jr CL. Clinical experience with silver sulfadiazine, a new topical agent for control of pseudomonas infections in burns. *J Trauma* 1969;9:377-88.
- Russell AD, Hugo WB. Antimicrobial activity and action of silver. *Prog Med Chem* 1994; 31: 351-70.
- Carr HS, Włodkowiński TJ, Rosenkranz HS. Silver Sulfadiazine: In vitro antibacterial activity. *Antimicrob Agents Chemother* 1973;4:585-7.
- Fuller FW. The Side Effects of Silver Sulfadiazine. *J Burn Care Res* 2009;30:464-70.
- Vincent KM, et al. In vitro cytotoxicity of silver: implication for clinical wound care. *Burns* 2004;30:140-7.
- Fox JR, Rao TN, Azmeth R, Gandhi SS, Modak S. Comparative evaluation of zinc sulfadiazine aims silver sulfadiazine in burn wound infection. *J Burn Care Rehabil* 1990;11:112-7.
- Agren MS. Studies on zinc in wound healing. *Acta Derm Venereol Suppl (Stockh)* 1990;154:1-36.
- Takasu Y, Yamada H and Tsubouchi K. Isolation of Three Main Sericin Components from the Cocoon of the Silkworm, *Bombyx mori*. *Biosci Biotechnol Biochem* 2002;66:2715-8.
- Tokutake S. Isolation of the Smallest Component of Silk Protein. *Biochem J* 1980;187:413-7.
- Kurioka A, Kurioka F, and Yamazaki M. Characterization of sericin powder prepare from citric acid degraded sericin polypeptides of the Silkworm Bombyx mori. *Biosci Biotechnol Biochem* 2004;68:774-80.
- Padamwar MN, et al. Silk sericin as a moisturizer: an in vivo study. *J Cosmetic Dermatol* 2005;4:250-7.
- Sobajo C, Behzad F, Yuan XF and Bayat A. Silk: a potential medium for tissue engineering. *Eplasty* 2008;8:47.
- Altman GH, et al. Silk-based biomaterials. *Biomaterials* 2003;24:401-16.
- Aramwit P, et al. The effect of sericin with variable amino-acid content from different silk strains on the production of collagen and nitric oxide. *J Biomater Sci* 2009;20:1295-306.
- Tsubouchi K, Igarashi Y, Takasu Y. Sericin enhances attachment of cultured human skin fibroblasts. *Biosci Biotechnol Biochem* 2005;69:403-5.
- Zhaorigetu S, et al. Silk protein, sericin, suppresses DMBA-TPA-induced mouse skin tumorigenesis by reducing oxidative stress, inflammatory responses and endogenous tumor promoter TNF-α. *Oncol Rep* 2003;10:537-43.
- Teramoto H, Kameda T and Tamada Y. Preparation of gel film from *Bombyx mori* silk sericin and its characterization as a wound dressing. *Biosci Biotechnol Biochem* 2008;72:3189-96.
- Nagai N, et al. Enhancing effects of sericin on corneal wound healing in Otsuka Long-Evans Tokushima fatty rats as a model of human type 2 diabetes. *Biol Pharm Bull* 2009;32:1594-9.