Original Article

Effectiveness of 1% Silver Sulfadiazine with Zinc versus 1% Silver Sulfadiazine in Burn Wound Healing

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Background: 1% silver sulfadiazine (1%SSD) cream is a well-known topical antibiotic used for first- and superficial second-degree burn wound treatment due to its good outcomes and reasonable price. Zinc (Zn) is an essential mineral in the cell proliferation process.

Objective: The primary objective was to compare the efficacies of the 1%SSD-with-Zn and the standard formula burn wound healing.

Materials and Methods: The present study was conducted as a prospective, double-blinded, randomized controlled trial.

Results: Twenty-seven superficial second-degree wounds of non-major burn patients were randomized to 2 groups: 13 patients were treated with 1%SSD-with-Zn, while 14 were treated with standard 1%SSD. In the group with wounds sized less than 100 cm^2, the complete healing days for the 1%SSD-with-Zn and control groups were 9 and 12 days, respectively (p-value = 0.193). For wounds sized over 100 cm^2, the complete healing days for the 1%SSD-with-Zn and control groups were 12 and 15 days (p-value = 0.307). The secondary outcomes of the groups (pain scores, infection complications, blood Zn levels, and wound swab cultures) were not significantly different.

***Conclusion*:** Although 1%SSD-with-Zn showed no statistical significance in burn wound healing compared with the standard formula, it demonstrated a clinical trend towards treatment cost saving.

Keywords: Silver sulfadiazine cream, Silver sulfadiazine cream with zinc formula, Zinc, Burn wound healing

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In Thailand, the incidence of patients with burns exceeds 10,000 per annum. The main treatment objective for these patients is to heal their wounds, which costs the public health system an estimated 4,000 million baht annually. The standard healing process for burn victims is related to the depth of their wounds. In cases of first- and superficial second-degree burns, the process involves the creation of a suitable recovery environment and the prevention of complications that would delay recovery, such as infections. The application of 1% silver sulfadiazine (1%SSD) cream to first- and superficial second-degree burn wounds is employed as the standard healing process throughout Thailand and worldwide for 2 reasons. Firstly, the cream exerts an antibacterial effect that helps prevent wound infections; moreover, the cream imparts the right amount of moisture to wounds, thereby helping them recover faster. In Thailand, the cream is also classified as an essential medicine under the Thai National Drug Information system; its costs are therefore fully reimbursable, which means that the financial burden on patients is lessened. 1%SSD is a relatively old medicine, and it has not undergone much development. The authors postulated that the addition of the element zinc (Zn) to 1%SSD cream may hasten healing. Zn is an essential mineral for the human body, being present in many enzymes that are involved in cell development, especially in the hair, skin, and nails. This study compared the results of using the 1%SSD cream both with, and without, Zn for the treatment of superficial second-degree burn wounds. The hypothesis was that the zinc-containing formula might aid in improving patients' quality of life by reducing the number of days that they were incapacitated by their wounds. Furthermore, it was speculated that the use of 1%SSD-with-Zn might reduce the public health care costs associated with the healing process.

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Background

The Epidemiological Report of Burn Patients in Fiscal Year 2018, published by the Community of Practice

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(CoP) Burn Nurses of Thailand, reported on 700 cases of burns[1]. In addition, the 2015 annual report of the Siriraj Burn Unit stated that 447 new burn victims were treated, with 385 being dealt with as outpatients and 62 as inpatients. From those data, we can extrapolate that the incidence of burns throughout Thailand exceeds 10,000 cases yearly. As well, the approximate length of stay of burn admissions has been estimated to be 23 days per patient, at a cost of approximately 400,000 baht per admission[1]. In other words, massive sums of money are being expended annually by the public health care system to treat burn patients. The main aim of burns treatment is to optimize the wound healing process. Its achievement is reflected in reductions in the lengths of hospital stay, the incidence of complications, and the mortality rate, coupled with an improvement in the quality of life of patients and a lowering of their treatment costs.

The burn wound treatment that is administered depends on the depth of wound and an assessment of the risk of an infection. Burn wounds are classified according to three degrees of severity. Partial-thickness burns are deemed to be either first-degree or second-degree burns; the former involve the epidermis only, whereas the latter affect the epidermis and dermis. Full-thickness burns are classed as third-degree burns. The healing processes of partial and full-thickness burns differ. Partial-thickness burn injuries that involve less than 20% of the total body surface area (%TBSA) are defined as minor burns that are self-limited if there is no infection. Consequently, the treatment of partial-thickness burns aims to create the optimum healing environment in order to achieve the fastest recovery and prevent infections. Conversely, the healing process for full-thickness burns focuses on performing an operation for debridement with skin grafting and the subsequent bandaging of the wounds.

1%SSD cream was first used in 1968 by Fox to cure wounds[2]. It has since been widely employed to cure burn wounds, especially those that are infected. Consequently, it has long been considered to be the first choice for the treatment of burn wounds. The cream has an antibacterial effect due to its silver salt (Ag^+) ingredient rather than the effect of sulfadiazine[3]. As the medication only has a low concentration of Ag^+ (1 to 2 parts per million), it is not suited for healing burn wounds in severe sepsis conditions involving a huge amount of empyema-forming bacteria. In cases of severe burn sepsis, wound bandaging cannot replace a debridement operation nor an operation to drain the infected tissue. There is much evidence supporting the antibacterial effects of 1%SSD on Gram-positive, Gram-negative bacteria and fungi[2,4–6]. Although the cream can be used to cure burn wounds of any degree these days, it provides different results for each degree of severity. With partial-thickness burns, the cream provides an antibacterial effect and moisture that facilitate quick and suitable recovery (i.e., the promotion of granulation tissue)[7]. In the case of full-thickness burns, surgeons use 1%SSD as a topical physical debridement agent in order that the cream's moisture can aggravate tissue maceration. The cream soaks the dry and hard eschar, transforming it into a macerated and soft eschar that is easier to peel off while changing dressings or performing debridement. Even though the medication has existed for a relatively long time and has had very limited development (only the addition of 0.2% of chlorhexidine gluconate in some brands), it is still an effective medicine for the healing of wounds aside from burn wounds[8-11]. Given that the cream is economical and, in Thailand, its costs are fully reimbursable, it is extensively used for the healing of wounds in present clinical practice. On the other hand, its action time is quite short, with it transforming after 6 to 12 hours into a thick, inactive form that requires the wound dressing to be changed at least once daily. In addition, the fluid that is formed from the cream after it reacts with the wound can cause perilesional skin maceration. Moreover, systemic complications (for instance, leukopenia[12], an unusual complication) may also occur.

Zn is an important mineral for the human body. Even though this trace element is found in small amounts, its presence is essential for the body to function. It acts as a part of many enzymes that are involved in many steps of cell life cycles. It also facilitates the normal functioning of the immunity and recovery systems. The recommended daily allowance for Zn in a healthy adult is 8 to 15 milligrams per day. Most of the Zn in the body is intracellular, with 85% of the total body Zn being present in the bones and muscles. The amount of Zn in the skin is 32 micrograms per tissue weight in grams (representing 6% of the total body Zn). The body mostly receives Zn through eating; it is absorbed through the intestinal epithelial cells at the distal duodenum and proximal jejunum. Later, it will pass through the cells by binding to metallothionein protein and entering the venous blood. Since Zn homeostasis in the human body is tightly regulated, only a huge zinc shortage would affect the zinc levels in the blood and tissues. Unlike other minerals that utilize the liver and kidneys to control their homeostasis, the Zn balance mainly results from the work of the alimentary system. Zn's balance is the consequence of an efficient counterbalance between absorption and secretion that occurs mainly in the gastrointestinal tract. As the serum Zn level is more sensitive to a zinc deficiency than the tissue Zn level, it is used to diagnose Zn deficiency[13,14].

Zn helps to stimulate new tissue formation. An increase in metallothionein protein and matrix metalloproteinase enzyme levels plays an important role in epithelium and fibroblast development through stimulating the proteolytic and collagenolytic generating processes. The protein and enzyme decompose tissues and cells that were damaged and died in the tissue repair process, and they activate cell migration to form new tissues that heal the wound. Moreover, Zn is an element of the integrins enzyme, which activates keratinization[15]. Aside from the recovery stimulation effect as mentioned previously, a superphysiological zinc level also has an antibacterial effect with gram-positive bacteria and some gram-negative bacteria[16,17].

As to Zn in burns, we have frequently found mineral and Zn deficiency after burn wounds; especially in cases where the wound size was large (post major-burn

hypozincemia). The post-injury body response changes the levels of zinc passing into and out of cells, and the body loses extra Zn through the wound fluids produced at the open burn wound areas[18]. Zn deficiency leads to abnormal leukocyte functions and slows recovery. From previous studies, the application of products containing Zn to burn wounds speeds recovery by increasing the chances of skin transplant success, minimizing graft loss, reducing the number of admission days, and reducing the incidence of infections[19,20].

Many previous studies have reported the results of using zinc oxide as a topical wound treatment. It helps with wound recovery and debridement, especially in the case of venous leg ulcers[21,24]. The use of a topical zinc agent for burn wounds seems to deliver superior healing outcomes to standard wound care[25]. Almost all of the topical zinc agents used in earlier studies were zinc oxide and 1%SSD. However, no previous study has assessed the results of utilizing 1%SSD cream containing Zn for wound and burn wound healing. Hence, the authors were interested in studying the effects of this medication on burn wounds.

Materials and Methods

The study was conducted as a double-blinded, randomized controlled trial with the approval of our institute's Ethics Committee (591/2559(EC3)) and clinical trial number TCTR20161 206004. The sample size (n = 28) was calculated using the complete healing days reported in a study by Wyatt et al[26]. The authors enrolled burn patients who were aged 18 to 65 years; had been diagnosed with superficial second-degree burn wounds at the torso, arms or legs; had a wound size of 20%TBSA or less; and had sought wound treatment within 24 hours post injury at the trauma emergency room of Siriraj Hospital. Excluded were patients who had underlying diseases that impaired their healing ability (such as diabetes mellitus, or liver or kidney failure), were immunocompromised hosts, or were pregnant. Patients with a history of allergy to silver, zinc, or sulfonamide were also excluded due to safety concerns.

After the patients were confirmed as meeting the study's inclusion criteria by the general surgical resident on call, they were randomized into 2 groups by a research assistant with the aid of a computer program. The patients' wounds were evaluated and measured by an experienced burn surgeon. The wounds were taken care of by observing the standard wound dressing protocol, as follows:

1) The wound was first cleaned with sterile normal saline solution to remove debris, foreign bodies, and excessive secretion. Bullae were peeled off to determine the type of wound and its actual size.

2) The appropriate cream for the group that the patient had previously been randomly assigned to (i.e., either the 1%SSD-with-Zn or standard 1%SSD cream) was applied. The containers and the appearance of the creams used by the two study groups looked identical (both were a thick, whitish cream). The patients, doctors, and nurses were not informed of the group to which the individual patients had been allocated.

3) The wound was covered with gauze and Gamgee padding.

4) Thirty minutes after the bandaging, the patients were evaluated for the presence of side effects or adverse effects (causalgia, allergies, or itching symptoms), and their pain score was measured using an 11-point numeric pain rating scale.

The patients were requested to clean the old cream remnants and apply new cream and clean dressings once daily. The patients were also required to attend the hospital for a wound dressing change and evaluation by a research nurse every 3 days until complete healing had taken place.

In addition, blood specimens were collected by venipuncture (5 ml of blood) in order to determine the serum zinc level on Days 0, 6, and 12 after the injury. Furthermore, a routine swab culture or if there was a clinically suspected infection a tissue culture was obtained from the wound base on Days 6 and 12.

Complete wound healing day was used as the primary outcome. The pain intensity, side effects or adverse events arising from the usage of the cream, Zn serum levels, wound swab culture results, and wound infection rates were studied as secondary outcome measures.

Statistical analysis

IBM SPSS Statistics for Windows, version 22.0 (IBM Corp., Armonk, NY, USA), was used for the data analyses. The image J program was used to calculate wound area. Demographic data that had a ratio scale were calculated as mean $\pm$ SD. The nominal scale, ordinal scale, and interval scale (such as sex and type of burn wound) were subsequently presented by frequency, amount, and percentage.

Information on the complete healing days, pain score levels, serum zinc levels, and the burn wound infection rates of both groups were compared using a two-tailed, unpaired, Student's t-test. The differences in the complete healing days were determined, compared to the 95% confidence interval (95% CI). Statistical significance was accepted when the *p*-value was less than 0.05. A Kaplan-Meier curve was utilized to compare the healing efficacies of the 1%SSD-with-Zn and standard 1%SSD cream.

Results

A total of 32 minor burns were enrolled and allocated into 2 groups using block randomization. Five patients were excluded from the data analysis (four were lost to follow-up, and one had an infection), leaving 27 patients (10 male, 17 female). The average ages in both groups are 31$\pm$14 year in 1%SSD-with-Zn group and 44$\pm$9.3 year in 2%SSD group. Their demographic data are detailed in Table 1. The 27-superficial second-degree of non-major burn patients were randomized into 2 groups: 13 were treated with 1%SSD-with-Zn, while the remaining 14 were administered the standard 1%SSD. The standard 1%SSD group showed about 3 days longer of complete healing day without statistic significance. The complete healing days of the 2 groups in subgroup analysis of wound area are presented in Table 2.

Table 1. Patient demographic information

Factors	All patients (n = 27)	1% silver sulfadiazine with zinc (n = 13)	1% silver sulfadiazine (n = 14)
1) Age (years) (mean ± SD)	37.9±13.5	31±14	44±9.3
2) Sex			
Male, n (%)	10 (37)	5 (38.5)	5 (35.7)
Female, n (%)	17 (63)	8 (61.5)	9 (64.2)
3) Time of injury (hours) (mean ± SD)	4.3±5.3	6±6.37	2.46±3.09
4) Underlying disease, n (%)	4 (14.8)		
- Hypertension, n (%)	2 (7.4)	0	2 (14.3)
- Asthma, n (%)	1 (3.7)	1 (7.7)	0
- Gout, n (%)	1 (3.7)	1 (7.7)	0
5) Site of injury			
- Neck, n (%)	2 (7.4)	1 (7.7)	1 (7.1)
- Trunk, n (%)	2 (7.4)	1 (7.7)	1 (7.1)
- Back, n (%)	1 (3.7)	1 (7.7)	0
- Upper extremities, n (%)	7 (25.9)	2 (15.4)	5 (35.7)
- Lower extremities, n (%)	15 (55.6)	8 (61.5)	7 (50.0)
6) Cause of injury			
- Flame, n (%)	4 (14.8)	1 (7.7)	3 (21.4)
- Scald, n (%)	13 (48.1)	7 (53.8)	6 (42.9)
- Contact with hot object, n (%)	9 (33.3)	4 (30.8)	5 (35.7)
- Chemical burn, n (%)	1 (3.7)	1 (7.7)	0
7) Percentage of total body surface area burned (%TBSA) (mean ± SD)	5±4.7	5±3.3	5±5.8
8) Area of wound (cm^2) (mean ± SD)	186±357.5	203±386	161±325

Table 2. Complete healing days of both formulae for different wound sizes

Wound size	Complete healing days (median ± SD, mean)		
	1% silver sulfadiazine with zinc	1% silver sulfadiazine	*p*-value
Area ≤10 cm^2 (n, 4)	6.5±0.5, 6.5	4.5±1.5, 4.5	0.333
Area >10 cm^2 to <100 cm^2 (n, 14)	11.5±3.3, 10.3	12±5.5, 14	0.294
Area ≥100 cm^2 (n, 9)	13.5±4.8, 15.5	15±9.81, 20.6	0.307

Table 3. Pain scores, adverse effect symptoms, and blood Zn levels at various time points of the healing days (days 0, 6, and 12 after burn injury) of both groups

Factors	1% silver sulfadiazine with zinc (n = 13)			1% silver sulfadiazine (n = 14)		
	Day 0	Day 6	Day 12	Day 0	Day 6	Day 12
1) Pain score (mean)	5.5	2	0	6	3	0
2) Adverse effects (percentage)						
Causalgia symptoms	78.6	23.1	0	76.9	41.7	0
Itching symptoms	0	0	0	0	8.3	0
3) Blood Zn level (mean)	0.084	0.117	0.079	0.079	0.073	0.018

Normal blood Zn level: 0.05 to 0.17 mg/dl (clinical pathology laboratory, Faculty of Medicine, Siriraj Hospital, Thailand)

Their pain scores, adverse effect symptoms, blood Zn levels, and wound swab culture results are listed in Tables 3 and 4. A comparison of the wound healing of the 2 groups is illustrated with a Kaplan-Meier curve in Figure 1.

Discussion

Just under a half of the minor burns in this study involved middle-aged housewives who had received a scalding burn from boiling water. Contact with a hot object represented

Table 4. Swab culture results from wound base for both groups at Days 6 and 12 after burn injury

Swab culture results	1% silver sulfadiazine with zinc (n = 13)	1% silver sulfadiazine (n = 14)
At day 6, n (%)		
No growth	7 (53.8)	9 (64.3)
S. aureus (MSSA)	2 (15.4)	3 (21.4)
Microbiota	1 (7.7)	0 (0)
Missing data (N/A)	3 (23.1)	2 (14.3)
At day 12, n (%)		
No growth	7 (53.8)	7 (50.0)
S. aureus (MSSA)	0 (0)	1 (7.1)
Microbiota	1 (7.7)	0 (0)
Serratia marcescen	0 (0)	1 (7.1)
Gram negative rod, non-fermentative	0 (0)	1 (7.1)
Missing data (N/A)	5 (38.5)	4 (28.6)

MSSA = methicilin-susceptible *S. aureus*

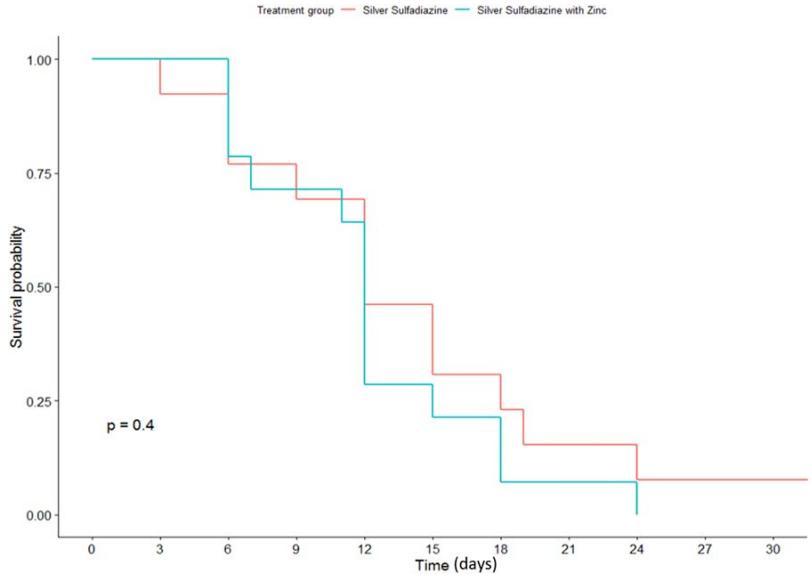

Figure 1. Kaplan-Meier curve comparison of complete healing days of standard formula (silver sulfadiazine) and Zn-containing formula (silver sulfadiazine with zinc).

the second most frequent type of minor burn in the study population (33%), and all of those incidents stemmed from accidental contact with a motorcycle exhaust pipe. In Bangkok, traffic congestion is one of the most serious problems faced by residents, and a strategy that is commonly employed to circumvent this hindrance is the use of a motorbike for personal transportation. Unfortunately, this has also contributed to evergrowing numbers of both traffic accidents involving motorbikes[27] and injuries related to motorbike usage, in particular, burns caused by contact with the hot exhaust pipes of bikes. A burn injury resulting from contact with an exhaust pipe typically happens in the lower extremities; in the present study, lower extremity injuries accounted for 55.6% of all injuries (Table 1). However, this finding is unlike those of other studies, which found that most of the burn population received their injuries from exposure to flames.

By definition, minor burns range in size from 1% to 20% TBSA, which was too wide a range for our analysis purposes. A subgroup analysis of the wound area size was therefore conducted in order to obtain more specific information. In terms of complete healing days, we found that, relative to the standard 1%SSD cream, the 1%SSD-with-Zn formula cream hastened the wound healing process by about 3 days for all wound area sizes. However, this positive finding for the experimental group was without statistical significance; this may have been because our study population was too small for the subgroup analysis to be

fully effective. An important consideration, however, is the current massive expenditure of public funds on wound healing. The difference of 3 complete healing days has the very real potential to translate into a substantially reduced demand for financial resources by the public health care system for the treatment of burn victims.

Although adding zinc to the 1%SSD cream increases its concentration and viscosity, no gross difference between it and the standard 1%SSD cream is apparent. On the other hand, the 1%SSD-with-Zn formula may cause more irritation to open wounds, which could present as symptoms like pain, causalgia, itching, or burning. However, Table 3 indicates that there were no differences in the pain scores or in the incidences of causalgia and itching symptoms of the patients in the 2 groups. This partly confirms the safety of the 1%SSD-with-Zn cream formula.

Zn is a trace element that plays an important role in tissue healing and the maintenance of the normal physiology of cell functions, especially proliferation. Humans obtain Zn primarily from the ingestion of food; however, Zn absorption via an open wound is another method of intaking Zn. A burn injury causes skin defects at the open wound. The application of a dressing agent like povidone iodine has been reported to increase iodine systemic absorption[28], which can lead to systemic complications from high levels of iodine in the body[29]. Williams et al reported finding rising levels of serum Zn in rats after the application of topical zinc oxide to an open wound over a 3-week period[30]. The present study found that, through zinc absorption via their open wounds, the patients using the 1%SSD-with-Zn cream increased their serum Zn levels from 0.084 mg/dl at day 0 to 0.117 mg/dl at day 6, and they maintained their baseline Zn level at day 12 (0.079 mg/dl). In contrast, the control group demonstrated a physiological trend towards markedly decreased Zn levels arising from the stress response (0.079 mg/dl at day 0, falling to 0.018 mg/dl at day 12).

In our series, a wound infection was diagnosed in 1 patient from the control group on day 3 after commencement of the 1%SSD treatment. The patient left the trial and was given standard treatment for an infection (a topical antiseptic wound dressing every day, combined with an oral antibiotic for 14 days). No wound infection incident was reported for the experimental group. The swab culture results from the wound base showed colonized microorganisms (Table 4).

A limitation of the present study was the small sample size of each wound-area-size subgroup. We plan to conduct a further study involving larger samples for each burn wound area size in order to establish the concentration of zinc in 1%SSD cream that is most effective in enhancing tissue healing in burn wounds.

Conclusion

Although the 1%SSD-with-Zn cream showed no statistical significance in burn wound healing compared with the standard formula, it did show a clinical trend towards treatment cost savings.

What is already known on this topic?

1% Silver Sulfadiazine cream is the common cream to apply for providing moisture and anti-septic properties in wound treatment especially in superficial burn wound.

What this study adds?

1% Silver Sulfadiazine with zinc formula trends to enhance wound healing in non-inferior efficacy in minor burn wound treatment when compare with standard formula.

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Potential conflicts of interest

The authors declare no conflicts of interest.

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การศึกษาเปรียบเทียบผลการรักษาของครีมซิลเวอร์ซัลฟาไดอาซีนความเข้มข้น 1 เปอร์เซนต์ที่มีและไม่มีการเพิ่มแร่สังกะสีเป็นส่วนประกอบในการหายของแผลไหม้

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ภูมิหลัง: ครีมซิลเวอร์ซัลฟาไดอาซีนความเข้มข้น 1 เปอร์เซนต์ถูกนำมาใช้เพื่อรักษาแผลไฟไหม้น้ำร้อนลวกความรุนแรงระดับที่ 1 และ 2 แบบตื้นอย่างแพร่หลาย เนื่องจากผลการรักษาที่ดีในต้นทุนราคาที่ต่ำ ส่วนแร่สังกะสีเป็นแร่ธาตุสำคัญในกระบวนการเจริญของเซลล์

วัตถุประสงค์: เพื่อศึกษาเปรียบเทียบผลการรักษาของครีมซิลเวอร์ซัลฟาไดอาซีนความเข้มข้น 1 เปอร์เซนต์สูตรที่มีและไม่มีการเพิ่มแร่สังกะสีในการหายของแผลไหม้

วัสดุและวิธีการ: การวิจัยแบบสุ่มมีกลุ่มควบคุมอำพรางสองฝ่าย (prospective randomized controlled trial, double blind study)

ผลการศึกษา: ผู้ป่วยแผลไหม้จำนวน 27 ราย ผู้ป่วยจำนวน 13 รายได้รับการสุ่มรักษาด้วยครีมซิลเวอร์ซัลฟาไดอาซีนความเข้มข้น 1 เปอร์เซนต์สูตรที่มีการเพิ่มแร่สังกะสี และ 14 รายสุ่มได้รับการรักษาด้วยครีมสูตรที่ไม่มีการเพิ่มแร่สังกะสีหรือสูตรมาตรฐาน พบว่ากลุ่มผู้ป่วยที่มีแผลไหม้ขนาดเล็กกว่า 100 ตารางเซนติเมตรที่ได้รับการรักษาด้วยครีมสูตรที่มีแร่สังกะสีแผลหายที่ 9 วันเทียบกับสูตรมาตรฐานแผลหายที่ 12 วัน (p-value = 0.193) กลุ่มผู้ป่วยที่มีแผลไหม้ขนาดตั้งแต่ 100 ตารางเซนติเมตรที่ได้รับการรักษาด้วยครีมสูตรที่มีแร่สังกะสีแผลหายที่ 12 วันเทียบกับสูตรมาตรฐานแผลหายที่ 15 วัน (p-value = 0.307) ผลการวิจัยรองไม่พบความแตกต่าง ระหว่างกลุ่มศึกษาและกลุ่มทดลองของระดับความปวดแผล การเกิดแผลติดเชื้อ ระดับของสังกะสีในเลือด และผลการเพาะเชื้อจากแผล

สรุป: การใช้ครีมซิลเวอร์ซัลฟาไดอาซีนความเข้มข้น 1 เปอร์เซนต์สูตรที่มีการเพิ่มแร่สังกะสีในการรักษาแผลไหม้ไม่พบความแตกต่างทางสถิติของวันที่แผลหาย แต่อาจมีความสำคัญทางคลินิกเนื่องจากสามารถลดจำนวนวันในการรักษาแผลซึ่งอาจนำไปสู่การลดต้นทุนในการรักษาผู้ป่วยได้