MEBO JOURNAL

Volume 1
Number 2
August 2020

Management of Wound Infection

MEBO JOURNAL

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Clinical Efficacy of Moist Exposed Burn Ointment Combined with Silver Dressing in Treating Infected Pressure Ulcers and Its Impact on Patients' Serum Inflammatory Markers

Huang Ying, Zeng Liang-Yu, He Xu-Liang

Affiliations: Department of Rehabilitation, General Surgery, Zhuzhou People's Hospital, Zhuzhou City, Hunan 412000, China

【**Abstract**】 **Objective** To assess the clinical efficacy of Moist Exposed Burn Ointment (MEBO) combined with antibacterial ionic silver dressing in treating infected pressure ulcers and its impact on patients' serum inflammatory markers. **Methods** 60 patients with infected stage Ⅲ pressure ulcers, admitted into Zhuzhou People's Hospital from July 2014 to May 2018, were randomly divided into study group (n=30) and control group (n=30) according to the random number table. Study group was treated with MEBO combined with ionic silver dressing, control group was treated with MEBO only. Changes of serum inflammatory markers and the clinical efficacy were assessed. **Results** After treatment, the levels of serum interleukin-6 (IL-6), interleukin-8 (IL-8), tumor necrosis factor-α (TNF-α) and hypersensitive C-reactive protein (hs-CRP) in both groups were gradually decreased, especially notable in the study group. After being treated for 7 and 14 days, the levels of serum IL-6, IL-8, TNF-α and hs-CRP were compared between two groups, difference was significant ($p<0.01$). After 6 weeks of treatment, in study group, healed (n=19), effective (n=9), ineffective (n=2), total effective rate was 93.33%; in control group, healed (n=15), effective (n=7), ineffective (n=8), total effective rate was 73.33%. Compare two groups, $p>0.05$. **Conclusion** Treating infected pressure ulcers with MEBO and ionic silver dressing could effectively inhibit the release of inflammatory markers and decrease the inflammatory response in pressure ulcers.

【**Key words**】 MEBO; Antibacterial ionic silver dressing; Pressure ulcer; Inflammatory markers; Clinical efficacy

Pressure ulcers are common in long term bedridden patients who suffer from cerebrovascular accidents, paraplegia and other diseases. Those patients are often malnourished and anaemic, which lead to wound infection in pressure ulcers, and followed by aggravated inflammatory response.[1,2] Situations like this are difficult to treat in clinical practice. Our study aims to find a better way to reduce inflammation and promote healing of pressure ulcers. In view of the fact that both Moist Exposed Burn Ointment (MEBO) and ionic silver dressing can effectively reduce the infection of pathogenic bacteria, so in this study, they were applied in combination to treat infected stage III pressure ulcers, and the result was compared with that of applying MEBO alone.

1. Clinical data

1.1 Baseline data

60 patients with infected stage III pressure ulcers were admitted to Zhuzhou People's Hospital from July 2014 to May 2018. They were randomly divided into study group (n=30) and control group (n=30) according to the random number table.

Study group: 14 males and 16 females, 56-90 years old (70.76 ± 11.47 years old), wound size (70.30 ± 14.46) cm^2, wounds on limbs (n=7), wounds on torso (n=23); control group: 13 males and 17 females, 58-89 years old (70.99 ± 10.63 years old), wound size (70.80 ± 15.11) cm^2, wounds on limbs (n=9), wounds on torso (n=21). Baseline data including gender, age, wound size and wound site of two groups are comparable (p>0.05) (Table 1). This study was approved by the Zhuzhou People's Hospital Ethics Committee, and all patients and their families signed informed consent documents.

Table 1: Comparison of baseline data

Group	Number of Cases	Gender (n)		Age (year, $\bar{X}$±S)	Wound Size (cm^2, $\bar{X}$±S)	Wound Sites (n)	
		Male	Female			Limbs	Torso
Study group	30	14	16	70.76±11.47	70.30±14.46	7	23
Control group	30	13	17	70.99±10.63	70.80±15.11	9	21
X^2 value		0.067		-	-	0.341	
t value		-		0.081	0.131	-	
p value		0.795		0.936	0.896	0.559	

Note: Gender, age, wound size and wound site were compared between two groups, p>0.05.

1.2 Inclusion criteria

(1) Meet the diagnostic criteria for stage III pressure ulcers established by National Pressure Ulcer Advisory Panel (NPUAP) in 2007; (2) complicated with infection; (3) complete the whole course of treatment with good compliance; (4) informed about this study and voluntarily signed informed consent.

1.3 Exclusion criteria

(1) Allergic to the pharmaceutical ingredients used in this study; (2) pressure ulcers due to vascular disease; (3) inflammation has been controlled; (4) has malignant tumors; (5) has mental illness and cannot comply with treatment.

2 Methods

2.1 Systemic treatment

Cephalosporin was given for a week; blood glucose and blood pressure levels were regulated;

nutritional supports were provided; and air mattress was used.

2.2 Wound treatment

Study group: after debridement, MEBO (ShanTou MEBO Pharmaceutical CO., LTD, China) was applied evenly on the wound surface at approximately 5mm thickness; and ionic silver dressing (Changsha Hairun Biological Technology Co., LTD) was covered on top; then sterile gauze was used to secure the dressing. Dressing was changed once a day until the wound was healed.

Control group: after debridement, MEBO (ShanTou MEBO Pharmaceutical CO., LTD, China) was applied evenly on the wound surface at approximately 5mm thickness; then sterile gauze was used to secure the dressing. Dressing was changed once a day until the wound was healed.

2.3 Assessment indicators and evaluation criteria

The level of serum interleukin-6 (IL-6), interleukin-8 (IL-8), tumor necrosis factor-α (TNF-α) and hypersensitive C-reactive protein (hs-CRP) were compared between two groups 1 day before treatment, and on day 7 and day 14 of treatment respectively. 5ml blood sample was obtained from median cubital vein and serum was obtained after centrifugation at 3000 rpm for 10 min, then stored at -80℃ for use. Enzyme-linked immunosorbent assay (ELISA) was used to measure the level of IL-6, IL-8 and the TNF-α in the serum in strict accordance with the kit instructions. Immunoturbidimetric assay was used to measure the serum level of hs-CRP.

After 6 weeks of treatment, clinical efficacy between two groups was compared. Healed: the wound is completely healed with well-grown epidermis; effective: the wound is red with well grown granulation tissue, and the wound size has been reduced by 25% or more; ineffective: large amount of wound exudate appears with poor granulation tissue growth, and the wound size has been reduced by less than 25%.[3] Total effective rate = (number of healed cases + number of effective cases) / total number of cases × 100%.

2.4 Statistical processing

SPSS 17.0 statistical software was used for data analysis. The measurement data was expressed as ($\bar{x}\pm s$), using *t* test or *t'* test; the count data was expressed as frequency or percentage, using chi-square test or rank sum test; $p<0.05$ is considered statistically significant.

3 Results

3.1 Comparison of serum level of IL-6, IL-8, TNF-α and hs-CRP.

The serum levels of IL-6, IL-8, TNF-α and hs-CRP were compared between two groups 1 day before treatment, and $p>0.05$ indicated that two groups were comparable. The serum levels of IL-6, IL-8, TNF-α and hs-CRP gradually decreased after treatment in both groups, especially notable in

the study group; they were compared again after 7 days and 14 days of treatment, and p<0.01 indicated that the difference was statistically significant (Table 2). It showed that MEBO combined with ionic silver dressing application could significantly reduce the serum levels of IL-6, IL-8, TNF-α, and hs-CRP in patients with pressure ulcers, and reduce inflammatory response in pressure ulcer wounds.

Table 2: Comparison of serum level of IL-6, IL-8, TNF-α and hs- CRP

Group	Number of Cases	IL-6 (ng/ml)			IL-8 (ng/ml)		
		1 Day before Treatment	Day 7 after Treatment	Day 14 after Treatment	1 Day before Treatment	Day 7 after Treatment	Day 14 after Treatment
Study group	30	78.44±6.84	31.80±5.24	19.58±3.54	125.32±14.91	43.03±6.61	32.67±7.18
Control group	30	77.74±8.10	45.43±11.16	37.84±5.60	122.14±16.91	61.62±6.50	46.47±7.70
X^2 value		0.362	-	-	0.773	10.983	7.179
t value		-	6.055	15.096	-	-	-
p value		0.719	0.000	0.000	0.443	0.000	0.000

Group	Number of Cases	TNF-α (ng/ml)			hs-CRP (ng/ml)		
		1 Day before Treatment	Day 7 after Treatment	Day 14 after Treatment	1 Day before Treatment	Day 7 after Treatment	Day 14 after Treatment
Study group	30	43.89±4.37	20.45±4.43	15.62±5.48	101.57±13.98	8.24±3.23	5.70±2.28
Control group	30	43.88±5.29	34.47±5.48	25.52±7.28	101.06±13.00	16.53±5.88	15.32±2.991
X^2 value		0.008	10.897	5.951	0.146	-	14.253
t value		-	-	-	-	6.768	-
p value		0.994	0.000	0.000	0.884	0.000	0.000

Note: Compare serum level of IL-6, IL-8, TNF-α and hs-CRP 1 day before treatment, p>0.05. Compare after 7 days and 14 days of treatment, p <0.01

3.2 Comparison of clinical efficacy

After 6 weeks of treatment, in the study group: healed (n=19), 9 effective (n=9), ineffective (n=2), the total effective rate was 93.33%; in the control group: healed (n=15), effective (n=7), ineffective (n=8,) the total effective rate was 73.33%. Compare two groups, p>0.05. (Table 3).

Table 3: Comparison of clinical efficacy

Group	Number of Cases	Healed	Effective	Ineffective	Total Effective Rate
Study group	30	19	9	2	93.33
Control group	30	15	7	8	73.33
Mann-Whitney *U* value	361.000				
Z value	-1.476				
p value	0.140				

4 Discussion

Research showed that with growing aging population, the incidence of cerebrovascular and other diseases continues to rise, and the number of long-term bedridden patients with pressure ulcers also increases yearly. Those patients with poor physical function often have wound infection, so that wound inflammatory response could be aggravated and wound healing could be affected. In this study, MEBO and ionic silver dressing were applied in combination to treat patients with infected stage III pressure ulcers, and the outcomes were compared with those that used MEBO alone.

After 7 days and 14 days of treatment, the serum level of IL-6, IL-8, TNF-α, and hs-CRP of patients in study group were significantly decreased comparing to control group, $p<0.01$. Combining MEBO and ionic silver dressing could effectively reduce the levels of serum inflammatory markers and reduce the inflammatory response in pressure ulcers. The possible mechanism of action is as follows.

Once infection presents in pressure ulcers, the serum levels of the inflammatory markers such as IL-6, IL-8, TNF-α, and hs-CRP could increase significantly, and the constituent of MEBO such as baicalin and berberine could alter the environment that bacteria live in, inhibit their activity and toxicity, prevent wound infections, therefore effectively reduce inflammation of the wound[4,5]; The main component of the ionic silver dressing, carboxymethylcellulose sodium, could isolate the wound from the external contamination, prevent infection aggravation.[6] Ionic silver has a strong and long-lasting bactericidal effect, which could effectively decrease inflammatory response caused by pathogens such as bacteria and fungus.[7]

The research conducted by Qianli Tang showed inflammatory cell infiltration reduced significantly with application of MEBO.[8,9] The research conducted by Yama Ba showed the wound inflammatory markers reduced with the application of ionic silver dressing. In our study, the outcome demonstrated that after the treatment of MEBO combined with sliver dressing, serum levels of IL-6, IL-8, TNF-α, and hs-CRP in infected pressure ulcer patients decreased notably. This

result is consistent with the research outcomes led by Qianli Tang, and Yama Ba.[10-12]

In summary, applying MEBO and ionic silver dressing in combination can effectively inhibit the release of inflammatory markers and reduce inflammatory response level in pressure ulcers. It is worth noting that after 6 weeks of treatment, the total effective rate of study group and control group was 93.33% and 73.33% ($p>0.05$), indicating that the difference between two groups was not statistically significant. This result, which is not consistent with the changes in inflammatory markers, might be due to small sample of this study. Further research is needed.

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Regenerative Medicine for Preventing and Controlling Burn Wound Infection

Zheng Yu-hong, Chen Yong-chong, Wang Zhi-ying, Hou Peng-fei, Chen Hong-quan, Wang Jin, Jiang A-li

Affiliations: Kaifeng Airforce Branch Hospital of Burns, Wounds and Ulcers, Kaifeng City, Henan 475002, China (Zheng Yuhong, Wang Zhi-ying, Hou Peng-fei, Chen Hong-quan, Wang Jin, Jiang A-li); Department of Burns, Wounds and Surface Ulcers, Nanyan Hospital, Beijing 100076, China (Chen Yong-chong)

【**Abstract**】**Objective** To compare the clinical efficacy of Moist Exposed Therapy/Moist Exposed Burn Ointment (MEBT/MEBO) and conventional burn treatment (silver sulfadiazine with or without skin-grafting) on preventing and controlling burn wound infection. **Methods** 60 patients with extensive severe burns were enrolled in this study and randomly divided into treatment group (MEBO group, n=30) and control group (conventional group, n=30). After admission, they were given corresponding systemic treatment and wound management according to MEBT and conventional burn treatment principles. Average days of antibiotics administration, the rate of second-time antibiotics administration, the invasive infection rate, and the healing time of wounds with various depths as well as the rate of skin grafting were compared between the two groups. **Results** After treatment, all wounds healed in both groups, and results were compared between treatment group and control group: average wound healing time (34.9±8.6 d vs. 39.4±9.1 d), average days of antibiotics administration (7.5 d vs. 15.5 d), second-time antibiotics administration (13.3% vs. 30.0%), invasive infection rate (13.3% vs. 66.7%), and rate of skin grafting (10% vs. 66.7%). All results were tested via t test or χ^2 test, and all outcomes showed significant difference ($p< 0.05$). **Conclusion** MEBT could effectively prevent and control wound infection, reduce use of antibiotics, promote wound healing and reduce skin grafting rate in extensive severe burn patients.

【**Key words**】Burns; Infection; MEBT/MEBO; Skin grafting; Silver sulfadiazine

Burns are common in daily life. Epidemiological statistics showed the incidence of burns is about 2%, among whom 5% need hospitalization.[1] At present, it is still difficult to treat extensive burns. Infection of burn wounds, systemic inflammatory response syndrome (SIRS) and sepsis are still the main causes of death for burn patients. It is reported, from 1966 to 1975, over 50% burn patients with 60%-80% TBSA in the United States died of sepsis caused by bacteria infection.[2] The prevention and control of burn wound infection has always been a concern in clinical practice. In order to seek an effective method to prevent and control burn wound infections, this randomized control trail with a total of 60 patients was initiated, aiming to assess the efficacy of Moist Exposed Burn Therapy (MEBT) and conventional treatment in treating extensive severe burns.

1. Materials and methods

1.1 Inclusion criteria

1) Agree to participate in this study and sign a consent form. 2) Agree to receive MEBT or conventional treatment (silver sulfadiazine with or without skin-grafting). 3) 1-80 years old. 4) Extensive deep burns,[3] that is 30%-49% TBSA, or 11%-19% TBSA of III degree burns, or 6%-9% TBSA of deep III degree burns.

1.2 Exclusion criteria

1) Disagree to participate in this study. 2) Fail to follow the treatment procedure, treatment efficacy is unable to be evaluated, or incomplete baseline data. 3) Give up treatment and voluntarily quit the study. 4) Age<1 year or >80 years old. 5) Total burn area <30% or >49% TBSA, III degree burn<11% or >19% TBSA, deep III degree burn <6% or >9% TBSA. 6) Electrical burn, phosphorus burn, hydrofluoric acid burn. 7) Complicated by severe inhalation injury, or severe combined injuries. 8) Forced to stop the treatment due to severe adverse reactions during treatment. 9) With severe underlying diseases, such as diabetes, hypertension, malignant tumor, etc.

1.3 Criteria for dropout

Patients who withdraw from the study at any time for any reason, are considered dropouts.

1.4 Clinical outcomes

1) Invasive infection rate. 2) Mean time of antibiotics administration. 3) Rate of second-time administration of antibiotics. 4) Mean healing time. 5) Rate of surgical skin-grafting.

1.5 Statistical analysis

Count data was expressed as mean ± standard deviation (x±s). The mean of both groups were compared via u-test; frequency in both groups were analyzed by χ^2, and evaluated with the threshold of a=0.05. $p<0.05$ stands for statistical significance, $p<0.01$ stands for high statistical significance.

1.6 Baseline data

From January 2006 to June 2011, 60 patients with extensive and deep burn admitted to our hospital met the inclusion criteria, and they were randomly divided into treatment group (MEBO, n=30) and control group (silver sulfadiazine, n=30). Treatment group: 21 males and 9 females, 15 months to 74 years old (mean age: 36.1±22.5 years old); cause of injury: hydrothermal burn (n=21), flame burn (n=5), steam burn (n=2), electrical burn (n=2); total burn area: 30%-49% TBSA (mean: 39.2%±15.7% TBSA).

Control group: 20 males and 10 females, 19 months to 72 years old (mean age: 23.8±21.4 years old); cause of injury: hydrothermal burn (n=19), flame burn (n=3), sulfuric acid burn (n=2), hot stove cinder burn (n=1), steam burn (n=2), electrical burn (n=1), hot lime burn (n=1), molten iron burn (n=1); total burn area: 32%- 49% TBSA (mean: 38.4%±15.9% TBSA). (Table 1)

Table 1 Comparison of injuries

Group	n	Age (year)	Burn surface area (%)	Superficial II degree (%, n)	Deep II degree (%, n)	III degree (%, n)
Treatment group	30	36.1±22.5	39.2±15.7	19.2±9.8 (6)	28.1±11.2 (24)	18.9±10.8 (12)
Control group	30	23.8±21.4	38.4±15.9	18.6±8.6 (8)	28.3±10.5 (26)	19.2±9.6 (16)

Note: There is no significant difference in terms of the severity of the wounds.

2. Methods

2.1 Systemic treatment

After admission, both groups were given IV fluid resuscitation in shock phase according to the conventional treatment method of burn shock resuscitation,[4] and IV antibiotics and nutritional supports.

2.2 Wound treatment

Treatment group: Moist Exposed Burn Ointment (MEBO) was applied, as soon as the patients were admitted. With a spatula or sterile gloves, apply MEBO evenly on wounds at 1mm thickness, wounds were covered with MEBO and kept moist to prevent dryness and maceration during entire treatment. MEBO was applied roughly every 4 hours after gently clearing the exudate and liquefied products with sterile gauze. For deep II degree and III degree burn, “ploughing knife” or scalpel was used to cut skin open to relieve tension of wound; as for larger area burn, Humby knife was used to thin the necrotic eschar, thus to relieve local tension, restore local blood circulation, improve exudate drainage and ointment absorption. For deep III degree burn, if “skin islands” did not appear on wounds with 4-6 weeks’ treatment, autologous micro-skin grafting was adopted to close the wounds.

Control group: After debridement and disinfection, silver sulfadiazine suspension was applied on the wounds and dried, 3 times a day; or silver sulfadiazine cream was applied and bandaged daily, and continuously treated with multi-functional device of burn treatment. For deep II degree and III degree burn, escharectomy and surgical skin grafting were performed after shock phase.

3. Results

After treatment, all the wounds healed and the clinical outcomes were compared between treatment group and control group: mean healing time: 34.9±8.6 d vs. 39.4±9.1 d; mean

administration time of antibiotics: 7.6 d vs. 15.9 d; second-time antibiotics administration: 13.3% vs. 30.0%; invasive infection rate: 13.3% vs. 66.7%; rate of skin grafting: 10.0% vs. 66.7%. After u-test, the mean wound healing time in both groups presented statistical significance, $p<0.05$. The comparison of second-time antibiotics administration, invasive infection rate, and rate of skin grafting in both groups presented high statistical significance, $p<0.01$. (Table 2, 3).

Table 2 Comparison of antibiotics administration and invasive wound infection

Group	n	Mean time of antibiotics administration (d)	Second-time administration of antibiotics (n, %)	Invasive infection rate (n, %)
Treatment group	30	7.6±5.6	4 (13.3%)※	4 (13.3%)★
Control group	30	15.9±5.8	9 (30.0%)※	7 (23.3%)★

Note: the antibiotics administration was tested, $u=4.0695>2.58$, $p<0.01$; ★invasive infection rate, $u= 3.6627 > 2.58$, $p< 0.01$.

Table 3 Comparison of mean healing time of wounds with different depths and rate of skin grafting (x±s)

Group	n	Superficial II degree (d)	Deep II degree (d)	III degree (d)	Mean healing time of wounds (d)	Rate of skin grafting (n, %)
Treatment group	30	7.1±2.4	16.8 ±2.5	32.2 ±6.5	34.9± 8.6△	3 (10.0%)▲
Control group	30	12.8±2.2	24.6±2.1	48.2 ±6.3	39.4 ±9.1△	20 (66.7%)▲

Note: the mean healing time of wounds was tested, $u = 2.0179 > 1.96$, $p< 0.05$. ▲Rate of skin grafting, $u=6.1067 > 2.58$, $p< 0.01$.

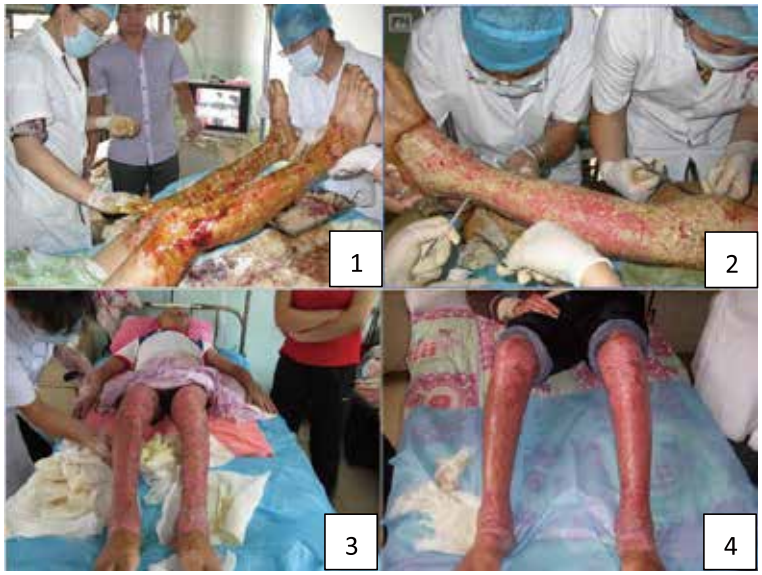
4. Patient case

4.1 Case 1

A 60-year-old male with multiple wounds was admitted 1 hour after flame burn. Examination on admission: conscious with facial expression of pain, T 36.8℃, P 90 bpm, R 24 bpm, BP 100/60 mmHg. Cardiopulmonary auscultation was normal. Wounds were noted on bilateral upper and lower limbs. Wounds on upper limbs and thighs were partially dark reddish-brown and partially waxy white, smooth, rough, painless and with a dull sensation; wounds on both lower legs and feet were yellow-brownish, rough, leathery, contracted and painless. Cold distal extremities and poor blood circulation.

Diagnosis on admission: extensive severe burn (total burn area 49% TBSA, deep II degree 20% TBSA, III degree superficial type 15% TBSA, III degree deep type 14% TBSA).

Treatment process: MEBO was applied and dressing was changed in accordance with the standard procedure to keep the wound moist. Tension relieving and eschar excision techniques were applied to eschar of deep burn wounds, and necrotic tissue was gradually eliminated without the damage of viable tissues. β-lactam and aminoglycoside antibiotics were given intravenously for 7 days, no infection was developed during treatment. Most necrotic tissue had been removed after 21 days and wounds (deep II degree, superficial III degree) on both upper limbs and thighs healed in 28-35 days. Autologous micro-skin grafting were performed in deep III degree burn granulation tissue on both lower legs, and wounds healed after 2 weeks with good skin elasticity. At half year follow-up, skin restored elasticity, and patient regained the ability to perform the activities of daily living with no dysfunctions. Details of treatment are shown in figure 1-4.



Progression of deep III degree burn wound on both lower legs during treatment

Figure 1: Day 1; **Figure 2:** Day 30; **Figure 3:** Day 53; **Figure 4:** Day 109 days (without notable hypertrophic scar)

4.2 Case 2

A 35-year-old male was admitted 23 hours after hot water scald at multiple body sites. The patient was crushed under a car and scalded by boiling water from the water tank. He was treated in another hospital with topical use of silver sulfadiazine without satisfactory outcome, and transferred to our hospital for further treatment.

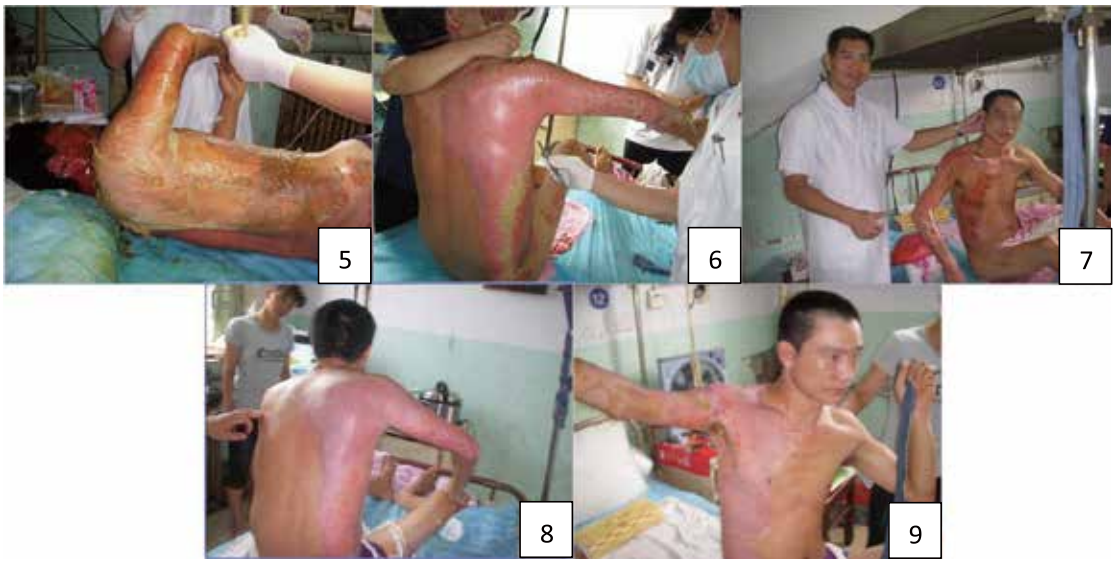
Examination on admission: patient was conscious, but lethargic with facial expression of pain. Results for cardiac, pulmonary and abdominal examinations were normal. Wounds were noted on face, neck, trunk, and right upper and lower limbs. Wounds on trunk and right upper limb were rough, leathery, painless and with dull sensation, with peeling skin on top and pale wound base. Wounds on head, face, neck and right lower limb were painful, on which scattered blisters of

different sizes were noted.

Blood test: WBCs: 17.0x10^9/L, Lymphocyte (%): 15.1%, Hemoglobin: 134g/L, Hematokrit: 0.368L/L; Plasma protein test: total protein: 5.6g/dL, Albumin: 2.87g/dL, Globulin: 2.73g/dL.

Diagnosis on admission: 1) extensive severe burn (total burn area: 38% TBSA, superficial II degree 15% TBSA, deep II degree 18% TBSA, III degree superficial type 5% TBSA); 2) hypoalbuminemia.

Treatment process: With a "ploughing knife", tension relieving was performed immediately after admission to promote liquefaction and removal of necrotic tissue. MEBO was applied and MEBO impregnated gauze was used to cover on top, with dressing change 2-3 times a day to keep the wound within a moist environment for better epidermal growth； intravenous administration was given to adjust metabolic balance. IV Mezlocillin (BID) was administered for a week to prevent infection. Superficial II degree, deep II degree and III degree superficial type burns healed respectively after 7 days, 23 days, and 30 days. Patient was discharged after 32 days with no dysfunctions. At follow-up after 6 months, a few soft flaky scars were found under the axilla. Treatment details are shown in figure 5-9.



Progression of the wound during treatment

Figure 5: Day 1; **Figure 6:** Day 23 ; **Figure 7:** 23 days; **Figure 8:** 30 days; **Figure 9:** 30 days

5. Discussion

5.1 The development and status quo of burn surgical treatment

From the late 1940s to the 1980s, invented by Dr. Joseph E. Murray, winner of Nobel Prize in Physiology or Medicine in 1990, escharotomy and skin grafting were adopted by professionals to treat burns. This technique, along with the application of Integra (artificial skin) and cultured

epidermal autograft,[5] had achieved remarkable progress in closing burn wounds and saving lives, also made treating extensive severe burns possible. In terms of preventing and controlling infection, it is to combine systemic antibiotics administration with topical disinfectant and antibiotics application (silver sulfadiazine, iodine tincture, etc.) to dry wounds and protect eschar, later achieve the purpose of preventing and controlling infection by escharotomy and skin grafting. But this technique could cause second injury to wounds and bacterial resistance. In addition, disinfectants and silver sulfadiazine might dehydrate wound, lead to vascular embolism, deepen burn wounds, prolong wounds liquefaction time and treatment course.[6]

5.2 Establishment and development of burn regenerative medicine

In 1962, Georges D. Winter put forward the idea of moist wound healing. His study proved that if wounds could heal under moist microenvironment, survival rate of epithelium could be increased.[7] Qingyue Zheng,[8] et al. suggested that keeping wounds moist could promote granulation tissue growth, and wounds could heal faster in a moist environment than in a dry environment.[9] MEBT/MEBO was invented by Dr. Rongxiang Xu from late 1970s to 1980s to treat burns and it realized in situ burn skin regeneration.

5.3 Mechanisms of MEBT/MEBO in preventing and controlling burn wound infection

1) Persistent drainage of exudate on wound, and management of necrotic tissues.

As dressing is changed every 4-6 hours, with autolytic debridement, liquefied products of necrotic tissues and exudate is removed timely, therefore, keeping the wound clean. Tension relieving technique or eschar excision was applied to III degree burns, which could remove necrotic tissues in time without damaging viable tissues and reduce the incidence of sepsis.

2) Bacteriostatic effect of MEBO.

Study conducted by Yang J-F[10] showed that MEBO could change the morphology of bacteria, decrease bacteria growth and reproduction, reduce bacteria toxicity, decrease the incidence of drug resistance and reduce antibiotics dosage needed.

3) Energy provided by lipid components

Quite a good amount of lipid components contained in MEBO could be the energy sources for skin regeneration, especially the synthesis of cell membranes, helps to benefit dying cells, assist in skin stem cells proliferation, boost immune cells to fight infections, and rebuild skin barrier to resist the invasion of microorganisms.

4) Anti-inflammatory effect of β-sitosterol

After absorbed into blood, β-sitosterol contained in MEBO showed an anti-inflammatory effect similar to glucocorticoids, which could reduce the incidence of systemic inflammatory response

syndrome and improve the overall nonspecific immune response, thereby helping to control burn wound infections.

5) Systemic antibiotics administration[11]

It is not generally required systemic antibiotics administration for burns with total burn area < 30% TBSA, but it's required for burns with total burn area >30% TBSA (children >10% TBSA) to prevent infection. The principle of using antibiotics is to choose antibiotics of high efficiency and low toxicity and use in short course. The first preventive administration of antibiotics should be less than 7 days, which could effectively reduce antibiotics' toxicity and side effects and limit the emergence of antibiotics resistant bacteria.

6. Conclusion

In this study, it is demonstrated that MEBT/MEBO could prevent and control infections, promote wounds healing, reduce antibiotics administration, skin grafting and scar formation, psychological suffering and economic burden for patients, and achieve good clinical efficacy. The study also indicates that applying tension relieving technique and eschar excision to II or III degree burns, along with application of MEBO, and autologous micro-skin grafting if needed, could assist in skin regeneration and achieve satisfactory clinical outcomes.

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DOI: 10.3748/wjg.v20.i24.7988

World J Gastroenterol 2014 June 28; 20(24): 7988-7992
ISSN 1007-9327 (print) ISSN 2219-2840 (online)

CASE REPORT

Necrotizing fasciitis secondary to enterocutaneous fistula: Three case reports

Guo-Li Gu, Lin Wang, Xue-Ming Wei, Ming Li, Jie Zhang

Guo-Li Gu, Xue-Ming Wei, Department of General Surgery, Air Force General Hospital, Chinese PLA, Beijing 100142, China
Lin Wang, Ming Li, Jie Zhang, Department of Colorectal Surgery, Key laboratory of Carcinogenesis and Translational Research (Ministry of Education), Peking University Cancer Hospital and Institute, Beijing 100142, China
Author contributions: Gu GL and Zhang J contributed equally to this work; Gu GL, Wei XM and Zhang J designed the research; Gu GL, Zhang J, Li M and Wei XM performed the research and wrote the paper; Gu GL and Wang L revised the manuscript.
Supported by General Projects of the Chinese PLA "Twelfth Five-Year" Logistics Research Subject, No. CKJ11J020
Correspondence to: Jie Zhang, Professor, Department of Colorectal Surgery, Key laboratory of Carcinogenesis and Translational Research (Ministry of Education), Peking University Cancer Hospital and Institute, Fucheng Road 52, Haidian Str, Beijing 100142, China. hero1822@163.com
Telephone: +86-10-88196085 Fax: +86-10-88196085
Received: March 13, 2014 Revised: April 15, 2014
Accepted: April 28, 2014
Published online: June 28, 2014

Key words: Necrotizing fasciitis; Enterocutaneous fistula; Diagnosis; Treatment

Core tip: Necrotizing fasciitis (NF) caused by enterocutaneous fistula may have more rapid progress and more severe consequences because of multiple bacterial infection and corrosion by digestive juices. Treating with three cases of NF secondary to enterocutaneous fistula, indicated that it was vital to heal NF by eliminating anaerobic conditions of infection, bypassing or draining digestive juice from fistula, and changing dressings with moist burn medical technology.

Gu GL, Wang L, Wei XM, Li M, Zhang J. Necrotizing fasciitis secondary to enterocutaneous fistula: Three case reports. *World J Gastroenterol* 2014; 20(24): 7988-7992 Available from: URL: http://www.wjgnet.com/1007-9327/full/v20/i24/7988.htm DOI: http://dx.doi.org/10.3748/wjg.v20.i24.7988

Abstract

Necrotizing fasciitis (NF) is an uncommon, rapidly progressive, and potentially fatal infection of the superficial fascia and subcutaneous tissue. NF caused by an enterocutaneous fistula has special clinical characters compared with other types of NF. NF caused by enterocutaneous fistula may have more rapid progress and more severe consequences because of multiple germs infection and corrosion by digestive juices. We treated three cases of NF caused by postoperative enterocutaneous fistula since Jan 2007. We followed empirically the principle of eliminating anaerobic conditions of infection, bypassing or draining digestive juice from the fistula and changing dressings with moist exposed burn therapy impregnated with zinc/silver acetate. These three cases were eventually cured by debridement, antibiotics and wound management.

INTRODUCTION

Necrotizing fasciitis (NF) is an uncommon, rapidly progressive, and potentially fatal infection of the superficial fascia and subcutaneous tissue[1]. NF caused by an enterocutaneous fistula has special clinical characters compared with other types of NF[2]. We treated successfully three cases of NF caused by postoperative enterocutaneous fistula since January 2007. From these three cases, we learned it was vital to heal NF by eliminating anaerobic conditions of infection, bypassing or draining digestive juice from fistula and changing dressings with moist exposed burn therapy.

CASE REPORT

Case 1

A 72-year-old male patient was hospitalized with severe infection of the abdominal wall. He had undergone distal

gastrectomy and duodenal drainage for a gastric ulcer with pyloric obstruction in another hospital 46 d previously. The first sign of NF was that bile and intestinal juice continuously flowed out around the drainage tube since postoperative day 4. He then presented continued high fever (39 ℃ or more), and inflamed soft-tissue area of the abdominal wall ranged from the right costal margin to the symphysis pubis. After treatment with antibiotics, drainage and dressing changes for about 1 mo, his temperature returned to normal. However, a great deal of pus continuously oozed from the short incisions of the inflamed area. He had a history of chronic bronchitis for about 10 years.

On physical examination, the inflamed area of the right abdominal wall was about 22 cm × 14 cm in size, and yellow-green pus with a bad smell pooled under skin. A CT scan confirmed a duodenal fistula with digestive juice leakage. His white blood cell (WBC) count was 15.2×10^9/L.

He was immediately treated by abdominal debridement and fistula drainage as soon as the diagnosis of NF was made (Figure 1A). Liquefactive necrosis was found with wide extension in the subcutaneous fascia tissue of the abdominal wall during surgical exploration. *Escherichia coli* (*E. coli*) and *Pseudomonas aeruginosa* (*P. aeruginosa*) were detected from pus culture with high sensitivity to Imipenem, Amikacin and Ceftazidime. After debridement of the necrotic tissue, fistula drainage, wet compress with Amikacin and moist exposed burn ointment for about 1 mo, the fistula gradually healed with cicatrization, and the purulent masses decreased. He then underwent self-skin split graft (Figure 1B). The skin grafts survived and ultimately inosculated (Figure 1C). The wound then gradually healed (Figure 1D).

Case 2

A 46-year-old male patient complained of swelling and pain in his right buttock and hip for about five months, with obvious aggravation and a high fever for 1 wk. He had a history of total colectomy and ileorectal anastomosis for familial adenomatous polyposis 8 years ago.

Physical examination revealed a swollen area with fluctuation and crepitus in the right buttock was about 20cm in diameter. His temperature was 39.2 ℃, and his WBC count was 32.2×10^9/L. CT scans showed that the soft tissue of the right buttock was filled with hydrops and pneumatosis (Figure 2A). Barium enema examination revealed a fistula connected to anastomosis within the soft tissue of right buttock (Figure 2B).

After being diagnosed as NF with abscess, he successively underwent radical debridement, drainage (Figure 2C) and ileostomy. Subcutaneous fascia tissue of his right buttock showed significant liquefactive necrosis, necrotic tissue and about 1000 mL yellow pus with stench were debrided (Figure 2D). *Enterococcus faecalis* (*E. faecalis*) and *P. aeruginosa* were detected from the pus culture with high sensitivity to gentamycin. After lavage with 3% oxydol, the wound was packed with gentamycin saline gauze and moist exposed burn ointment for about 1 mo. The purulent exudates disappeared and the drainage tubes were removed. The wound gradually healed well.

Case 3

A 67-year-old male patient underwent abdominoperineal resection for rectal cancer. He presented with a fever of 38.9 ℃ since postoperative 6th day, and a painful, swollen parastomal abdominal wall that ranged from the left costal margin to the symphysis pubis. Physical examination revealed an inflamed area of parastomal abdominal wall that was about 12 cm × 15 cm in size (Figure 3A). His WBC count was 19.0×10^9/L. A CT scan confirmed that a parastomal fistula had formed and the soft tissues of the parastomal abdominal wall were inhomogeneous in density.

After being diagnosed as NF of the abdominal wall caused by a parastomal fistula, he immediately was treated with debridement and drainage of the fistula (Figure 3B). Liquefactive necrosis was found widely in the subcutaneous fascia tissue of the parastomal abdominal wall during surgical exploration. Necrotic tissue and about 300 mL bloody, stinking pus were debrided. *E. coli* and *Enterobacter cloacae* were detected from the pus culture with high sensitivity to Imipenem, Amikacin and Ceftazidime. After washing the wound with 0.9% saline solution, we employed wet compresses with silver ion dressings and applied moist exposed burn ointment for 45 d (Figure 3C); the wound finally healed well (Figure 3D).

DISCUSSION

NF caused by an enterocutaneous fistula has special clinical characters compared with other types of NF. Intestinal contents containing a large amount of bacteria and various digestive enzymes are brought into truncal subcutaneous fascia tissue along the fistula[3]. Thus the inflammation and necrosis of truncal fascia tissue not only occurs from multiple bacterial infections, but also from corrosion by digestive juices and enzymes. For this reason, the inflammation of NF caused by an enterocutaneous fistula may have more rapid progress and greater severity.

Aggressive surgical debridement with antibiotic therapy would profoundly affect outcome of NF. For NF caused by an enterocutaneous fistula, the purpose of debridement is not only the removal of necrotic tissue, but also clearing away the anaerobic environment in which anaerobic bacteria survive. Even facultative anaerobic bacteria, which are commonly found in NF, are suppressed in an aerobic environment[4]. Drainage or bypass of the fistula is vital to cure NF caused by an enterocutaneous fistula, otherwise the intestinal contents along fistula would continuously contaminate the wound and prevent wound healing.

Skin grafting is an efficient method to accelerate wound healing[5]. However, the grafted skin finds it very difficult to survive in the wound of NF. We suggest that skin grafting should only be performed when the granu-

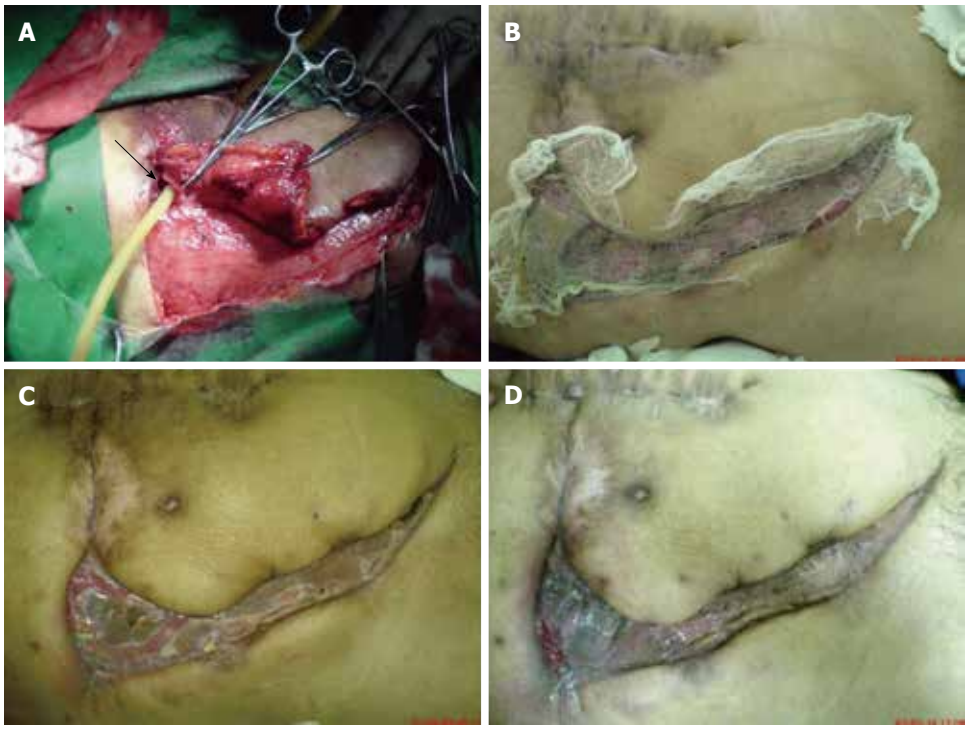

Figure 1 Debridement and drainage of fistula (arrow) (A); fistula healed and skin graft on wound (B); skin graft survived and grew (C); and the wound gradually healed (D).

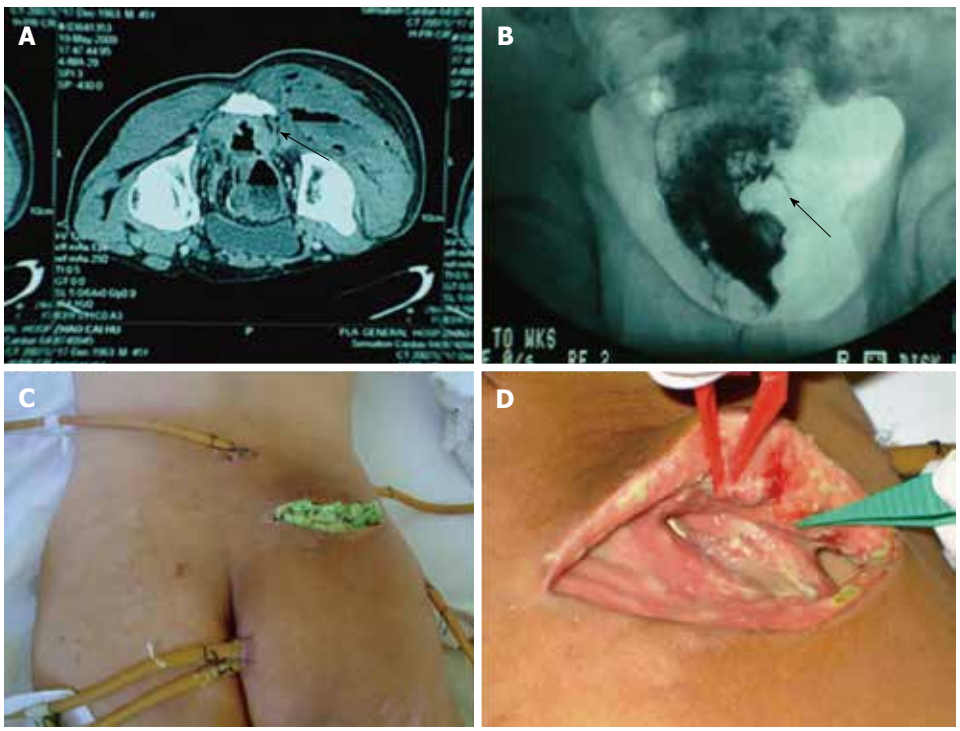

Figure 2 Computed tomography scan showing that the infection of the right hip had close relationship with rectum (arrow) (A); barium enema examination showed the fistula toward the right hip (arrow) (B); and placement of incisions and drainage tubes (C); and debridement and dressing change (D).

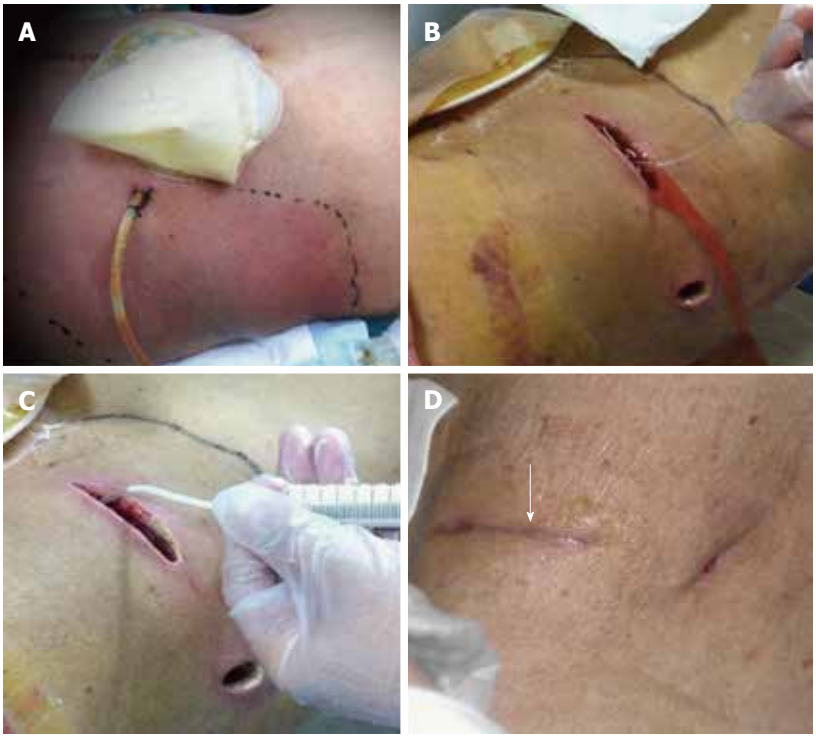

Figure 3 Inflamed area of the abdominal wall and parastomal fistula (supine position) (A); rinsing the wound with saline solution (right lateral position) (B); and infusing the wound with moist exposed burn ointment (syringe) (C); and the wound finally healed well (arrow) (D).

lated tissue grows better and the wound is clean without purulent secretion. Moist exposed burn therapy and moist exposed burn ointment are better than traditional dressings[6], because keeping the wound moist can prevent shrinkage of the incision. The main components of moist exposed burn ointment are zinc acetate and silver acetate. Silver and zinc ions have strong bacteriostatic functions toward *E. faecalis*, *P. aeruginosa*, *Staphylococcus aureus* and *Klebsiella*. Moreover, as an activating agent of biological enzymes, zinc ions can accelerate the synthesis of protein and nucleic acid to promote wound healing[7].

ACKNOWLEDGMENTS

We obtained consent for publication in print and electronically from the patients of these cases reports when they were hospitalized again for postoperative check-up.

COMMENTS

Case characteristics

Necrotizing fasciitis (NF) perhaps is the most severe form of soft tissue infection primarily involving the superficial fascia.

Clinical diagnosis

Early findings in NF are tenderness to palpation (extending beyond the apparent area of skin involvement), swelling, erythema, and warmth to palpation. The intermediate findings are marked by serous-filled blisters or bullae formation along with skin fluctuation and induration. The late findings are hemorrhagic bullae, skin anesthesia, crepitus, and skin necrosis with dusky discoloration progressing to gangrene.

Differential diagnosis

It is critical to promptly differentiate a case of NF from cellulitis or abscesses in the clinic.

Laboratory diagnosis

Three most commonly cultured organisms in NF were *Staphylococcus aureus*, group A *Streptococcus*, and *Escherichia coli*.

Imaging diagnosis

Findings of NF found on computed tomography (CT) are fat stranding, along with fluid and gas collections that dissect along fascial planes. Additionally, fascial thickening and non-enhancing fascia on contrast CT suggest fascial necrosis.

Pathological diagnosis

The skin findings of NF are induration and advancing erythema, followed by the development of overlying blisters and skin necrosis.

Treatment

NF is a clinical diagnosis where only emergent surgical debridement and appropriate antibiotic treatment can prevent progression and death.

Term explanation

NF is an uncommon, rapidly progressive, and potentially fatal infection of the superficial fascia and subcutaneous tissue.

Experiences and lessons

It was vital for healing NF to eliminate anaerobic conditions of infection, bypass or drain digestive juice from fistula and change the dressing with moist exposed burn therapy.

Peer review

The three cases reports were generally clearly presented in the manuscript. The manuscript is very well written. NF is an uncommon, rapidly progressive, and potentially fatal infection of the superficial fascia and subcutaneous tissue. NF caused by an enterocutaneous fistula has special clinical characters compared with other types of NF. The authors treated successfully three cases of NF caused by postoperative enterocutaneous fistula, and found it was vital for healing NF to eliminate anaerobic conditions of infection, bypass or drain digestive juice from fistula and change the dressing with moist exposed burn therapy.

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P- Reviewers: Coughlin S, Orbell JH **S- Editor**: Qi Y
L- Editor: Stewart G **E- Editor**: Zhang DN

Treating Pediatric Residual Burn Wound Complicated with MRSA with Moist Exposed Burn Ointment Impregnated Gauze

Xiao Yi-min

Affiliations: Burn Department, Chinese Medicine Hospital of Jinghai County, Tianjin 301600, China

【**Abstract**】**Objective** This study aims to evaluate the clinical efficacy of Moist Exposed Burn Ointment (MEBO) in the treatment of pediatric residual burn wounds complicated with Methicillin-Resistant Staphylococcus aureus (MRSA). **Methods** This retrospective study enrolled pediatric cases from Jan 2011 to Jan 2013 utilising MEBO impregnated gauze for residual burn wounds complicated with MRSA in Chinese Medicine Hospital of Jinghai County, Tianjin, and analyzed the duration of wound healing, analgesic and antipruritic effects, infection control and prognosis. **Results** All wound infections were effectively controlled 7-10 days after the application of MEBO impregnated gauze, and fully healed in 20 days. Analgesic and antipruritic effects were significant. **Conclusion** MEBO could effectively treat residual burn wounds complicated with multiple antibiotic resistant bacteria infection, and accelerate wound healing.

【**Key words**】 MEBO; MRSA; Infection; Pediatric; Burn; Residual wound

Burn is one of the common injuries that happen to children. Among all types of burns, scalding is on top of the list, accounting for 87.6% of the pediatric burn incidence.[1] Pediatric cases are commonly associated with deep II degree burns or III degree burns because of the vulnerability of children's stratum corneum and the thinness of their skins. Wounds could be aggravated by infection if they are not treated appropriately. Furthermore, they could develop into residual wounds that could be difficult to heal even with comprehensive treatment. In conventional treatment, topical antibiotics are widely used, which could easily lead to the emergence of antibiotic resistant bacteria, rendering it rather difficult to find effective antibiotics, especially for wounds complicated with MRSA. The later stage treatment of infected burn wound manifests as a tough part of the treatment.[2] The author has carried out a series of pediatric treatments with encouraging results using MEBO impregnated gauze for residual burn wounds complicated with MRSA. The report is detailed as follows.

1. General information

From Jan 2011 to Jan 2013, 26 children suffering from residual burn wounds complicated with MRSA were admitted to Chinese Medicine Hospital of Jinghai County, Tianjin. Gender: male (n=18), female (n=8). Age: 9 months to 5 years. Hot liquid scald (n=22), flame burns (n=4). Diameters of the wounds varied from 2 cm to 10 cm. Wound bases were uneven, remaining

necrotic tissues hadn't fallen off, granulation tissue edemas were noticed with pus on top. Bacterial culture test showed MRSA positive.

On admission, all the wounds were swollen, the epidermis had fallen off partially or completely, wound bases were pale or brown with a decreased sensitivity to pain. 1% to 10% TBSA. Deep II degree burn (n=14), III degree burn (n=12). Children with larger TBSA were given fluid resuscitation, anti-infection treatment, and nutritional support, etc. After eschar excision and tension-relieving procedure, SD-Ag impregnated gauze was applied on wounds daily, which was further secured with sterile gauze. 14 to 30 days later, some wounds were healed, while the others were seen to have shed off most of the necrotic tissues, appearing to be covered with pus, accompanied by pain and itch. The change to use Gentamicin or Chloramphenicol impregnated gauze had an unstable effect as pus did clear but then reappeared very quickly. Also antibiotics impregnated gauze is easy to get dry, so it could cause much pain to the patients when dressings are being changed.

2. Method of treatment

2.1 Systemic treatment

Considering the fact that MRSA is multi-antibiotics resistant and children's organs are immature, IV antibiotics were stopped. In later phase of a burn recovery, children are often in a state of negative nitrogen balance, so comprehensive treatment was given to reinforce systemic nutritional support and vitamins supplement, and maintain electrolyte balance.

2.2 Local treatment

Clean wound with 1.5‰ to 2.0‰ Chlorhexidine for the first time, use a sterile gauze to dry; apply MEBO impregnated gauze to the wound, cover with 8-12 layers of sterile gauze, change dressing with MEBO gauze QD or BID until healed. Before dressing change, do not use sterile solution and disinfectant to clean wound, but use sterile gauze to absorb exudate on wound.

3. Results

All the wounds started to produce fewer mucoid exudate after 2 days. Rough necrotic tissues started to shed off. 3-5 days later, "skin islands" started to emerge, and new tissues started to form along the peri-wound. 7-10 days later, MRSA and other pathogenic bacteria have been tested negative from bacterial culture.

All the wounds were healed, making the healing rate 100%. Healing time: 7-20 days, with a mean of 15.5 d ± 2.9 d; no pain or itch associating with dressing change was noted; healed skin turned out smooth, elastic with good integrity. Follow-ups on children who had recovered for more than 6 months showed that hypertrophic scar were hardly noticeable with no dysfunction.

Case report: male, 2.5 years old, admitted to Emergency at 18:00, Oct 2nd 2012, 1 hour after being scalded on the left calf. Admission examination: scald on left calf, swollen wound, absence of epidermis, pale and rough wound base, insensitive to pain. IV antibiotics were given and SD-Ag impregnated gauze was applied to the wound. After 2 weeks most of the necrotic tissues have fallen off and white slough that's difficult to remove appeared on the wound. Bacterial culture test of wound exudate showed MRSA positive. IV antibiotics were stopped, MEBO gauze (QD) was used on wound; wound healed after 12 days. Treatment process is illustrated in the figures below.

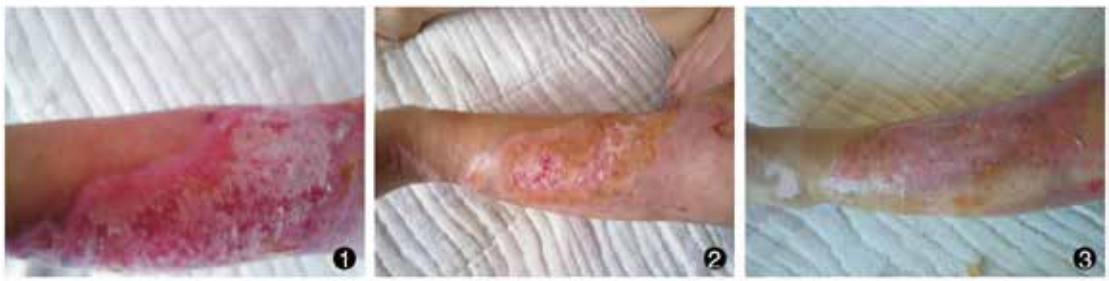

Figure 1: White slough on the wound before using MEBO;
Figure 2: New skin formed on peri-wound 1 week after using MEBO;
Figure 3: Wound healed 12 days after using MEBO

4. Discussion

Deep burns in pediatric cases could develop into residual wound in later phases, which could be difficult to heal even after comprehensive treatment. These wounds are prone to be broken, causing tremendous pain to the children. The main reason why residual wounds are hard to heal is that micro-circulation is impacted locally at the wound in addition to local infection.[3] Bacteria that proliferate on a large scale produce multiple metabolites, which undermines the growth of the epidermis. The conventional method of using SD-Ag impregnated gauze in a prolonged timeframe induces antibiotics resistant bacteria to emerge on the wound, especially multiple antibiotics resistant MRSA. The introduction of sensitive antibiotics at high concentration could easily lead to the emergence of new types of antibiotics resistant bacteria. As a result, not only the infection would be difficult to control, but also the search for new sensitive antibiotics could be problematic. Additionally, wounds might be enlarged and aggravated since SD-Ag along with antibiotics is not as helpful in tissue repair as it is in infection control.

MEBO's anti-infection property is demonstrated in four dimensions. 1) The lipophilic content of MEBO and the necrotic tissues go through a series of biochemical reactions, comprising hydrolysis, enzymolysis, rancidification, saponification, esterification. The necrotic tissues are liquefied and removed from wound without injuring any remaining viable tissue.[4] The removal of bacteria, toxins and metabolites will benefit the cleaning of the wound and prevent the aggravation

of wound infection or recurrent infections. 2) Its active constituents can induce bacteria into mutations, which will inhibit bacteria to proliferate and decrease their pathogenicity. 3) MEBO boost the innate immunity, making the resistance against infection better both systemically and locally.[5] 4) Gauze is beneficial to the removal of exudate, contributing to infection control.

MEBO stimulates the growth of epidermis by introducing constituents to improve micro-circulation and improve immunity of the cells in the wound. By providing a moist environment, MEBO promotes the growth of the remaining epidermal cells, to accelerate healing of the wound. In the meantime, Potential Regenerative Cells in the remaining tissue are activated to become epidermal stem cells to accelerate the repair of skin.[6]

MEBO has shown significant analgesic effects. It provides a physiologically moist environment to protect nerve endings from being exposed in the air. Contracted arrector pili muscles are relaxed so that pain is reduced.[7] As active constituents, β-sitosterol has anti-inflammatory, analgesic, bacteriostatic property, and Baicalin can antagonize adrenalin and noradrenaline.[8] These are the reasons why MEBO provides good analgesic effects. Given that the wounds are insensitive of pain and itch, most of the children could be compliant during the treatment.

MEBO could minimize scar formation. Its active constituents inhibit hyper-proliferation of the fibroblast, prevent excessive synthesis and accumulation of collagen so as to minimize the contracture scar formation caused by myofibroblast contraction,[9] ensuring that the newly formed tissues are soft and smooth .

In conclusion, MEBO provides an effective approach to treat residual burn wounds complicated with MRSA in pediatric cases. Moreover, its ability to control the infection of multiple resistant bacteria makes the wound heal faster with convincing results. It's also noticed that MEBO might be more effective when applied immediately after burn happens, and a much lower level of pain is reported in these cases. Also, secondary infections could be prevented without any risk of resistant bacteria growth, leaving patients no scars or only mild scars.

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Moist Exposed Burn Ointment in the Treatment of Wound with Antibiotic-Resistant Bacteria Infection

Liu Zi-qiang

Affiliation: The 2nd Affiliated Hospital of Chengdu Medical College, Nuclear Industry 416 Hospital, Chengdu City, Sichuan 610051, China.

【**Abstract**】 **Objective** To evaluate the clinical efficacy of Moist Exposed Burn Ointment (MEBO) in treating wounds with antibiotic-resistant bacteria infection. **Methods** A patient with wound infection caused by steel bar penetrating trauma, was treated with IV antibiotics and local application of hydrogen peroxide and iodophor. After 1 week, wound was not improved, bacterial culture of wound exudate showed antibiotic-resistant bacteria positive. Local treatment was then changed to MEBO dressing. **Results** Wound exudate decreased 2 days after applying MEBO, wound size gradually reduced with continuous MEBO standard treatment, and wound healed after 23 days. **Conclusion** MEBO demonstrated clinical efficacy in treating wound with antibiotic-resistant bacteria infection and alleviating pain during dressing change.

【**Key words**】MEBO; Antibiotic-resistant bacteria; Infection; Efficacy

1. Case data

A 23 years old male patient was admitted to our hospital for purulent exudate on wound 11 days after surgery: exploration and debridement for steel bar penetrating trauma on left shoulder, tear repair of left pectoralis major and pectoralis minor, and foreign body removal. Patient fell from a high place and penetrated by a steel bar on left shoulder 11 days ago, and was operated and treated in another hospital. After surgeries, purulent exudate appeared on wound, and he was transferred to our hospital for further treatment. Examination on admission: an approximate 11cm long sutured wound (sutures removed) was seen from left shoulder to left axilla, and drainage strips were used in two 1-2 cm long wound dehiscence sites, with odor-free exudate on it. A 2 cm deep sinus tract was noted in left axilla (Figure 1); peri-wound was mild swollen, skin temperature was normal; shoulder movement was limited due to pain, sensation at distal end was normal.

2. Treatment methods

After admission, hydrogen peroxide and povidone iodine solution were applied on wound, and wound exudate was taken for bacterial culture test and drug sensitivity test. IV cephalosporin antibiotic was given then changed to clindamycin after bacterial culture and drug sensitivity test results came back. After 1 week, the wound dehiscence gradually enlarged, and exudate was not reduced (Figure 2). Bacterial culture and drug sensitivity test were repeated again, results showed

that the pathogenic bacteria was resistant to clindamycin, so IV antibiotics was stopped, and changed to apply MEBO on wound, once per day.

3. Results

After IV antibiotics and local application of hydrogen peroxide and povidone iodine solution for 1 week, wound dehiscence gradually enlarged, and the pathogenic bacteria changed from Staphylococcus epidermidis to Staphylococcus haemolyticus, and further developed resistance to clindamycin. 2 days after changing to apply MEBO on wound, exudate decreased (Figure 3); with continuous application with MEBO, wound size gradually reduced, and sinus tract gradually became less deeper; after 23 days, sinus tract closed and wound healed (Figure 4-7). The bacterial culture test of wound exudate, during MEBO treatment, showed that pathogenic bacteria has non-hereditarily mutated from Staphylococcus haemolyticus to Staphylococcus warneri, and their reproduction rate was decreased and amount was reduced.

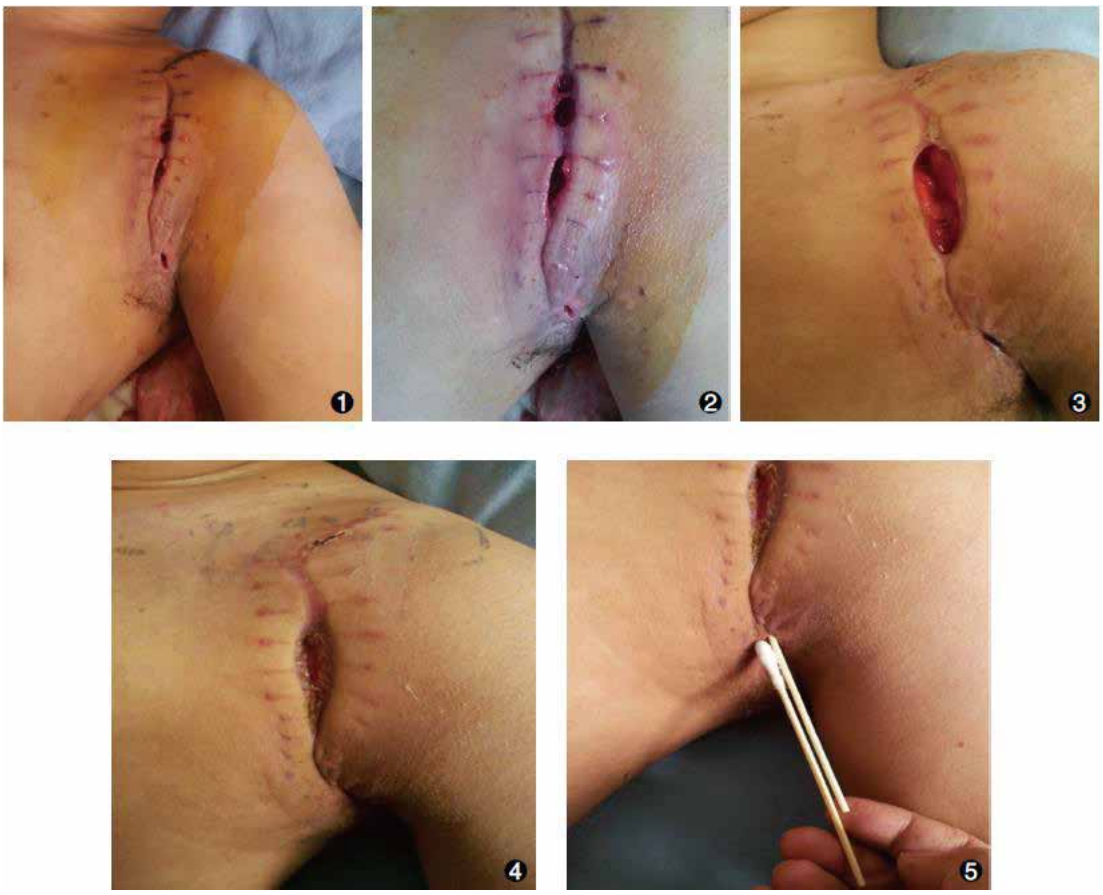


Figure 1: On admission **Figure 2:** Wound dehiscence sites enlarged after using hydrogen peroxide and povidone iodine solution for 1 week **Figure 3:** Exudate reduced after applying MEBO for 2 days **Figure 4:** Wound size reduced after 7 days **Figure 5:** Sinus tract became less deeper after 8 days **Figure 6:** 18 days after applying MEBO **Figure 7:** Sinus tract closed and wound healed after 23 days

4. Discussion

It is difficult to manage infected wounds, especially wounds with antibiotic-resistant bacteria infection in clinical practice. At present, hydrogen peroxide and povidone iodine solution, or VSD dressing are normally used, followed by skin grafting. However, hydrogen peroxide and povidone iodine solution may stimulate nerve endings of wounds, cause much pain to patients. In this study, hydrogen peroxide and povidone iodine solution were applied for 1 week, and wound dehiscence gradually enlarged, pathogenic bacteria changed from Staphylococcus epidermidis to Staphylococcus haemolyticus and developed resistance to clindamycin, which increased treatment difficulties.

Risk factors of infection mainly include the amount of bacteria, bacterial toxicity and patient's health status. In this case, after stopping IV antibiotics, and changing local treatment from hydrogen peroxide and povidone iodine solution to MEBO, wound size gradually reduced and finally healed, with much less pain during dressing change. Active constituent in MEBO, such as β -sitosterol and berberine could inhibit the reproduction of bacteria, reduce its amount and decrease the production of endotoxin.[1-2] Fatty acids, amino acids, polysaccharides and other nutrients in MEBO[3] could improve the non-specific immunity of wound to promote wound healing. In addition, MEBO could form a transparent protein membrane on the wound surface, so as to protect nerve endings from external stimulation, and reduce pain during dressing change.[4]

In summary, MEBO demonstrated satisfactory clinical efficacy in treating wounds with antibiotic-resistant bacteria infection in this case. Whether MEBO is an ideal choice in the management of such infected wounds remains to be further studied.

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Nasal Alar Infection and Necrosis Treated by Moist Exposed Burn Therapy: A Case Report

Zhang Yong, Ye Jing, Min Zhen-xing
Affiliation: Surgery Department of Beijing Xuanwu TCM Hospital, Beijing 100050, China

【**Abstract**】 **Objective** To evaluate the clinical efficacy of Moist Exposed Burn Therapy/Moist Exposed Burn Ointment (MEBT/ MEBO) in treating nasal alar infection and necrosis caused by hyaluronic acid injection. **Methods** A Patient with nasal alar infection and necrosis caused by hyaluronic acid injection was admitted to Surgical Department of Beijing Xuanwu TCM Hospital in August 2017, and treated with MEBT/ MEBO and IV infusion of etimicin sulfate. **Results** The patient was discharged after the treatment with MEBT/ MEBO for 10 days, the wound was basically healed with no noticeable scar and abnormal pigmentation. **Conclusion** MEBT/MEBO could effectively treat nasal alar infection and necrosis caused by hyaluronic acid injection, control wound infection and promote wound healing.

【**Key words**】 MEBT/ MEBO; Hyaluronic acid; Injection and filling; Infection; Necrosis; Efficacy

Along with continuous improvement of living standards, people tend to pay more attention to their external images. Therefore, since hyaluronic acid-based fillers were approved by National Medical Product Administration for cosmetic use in 2008, they have been widely used to reduce wrinkles, reshape nose and chin, lift cheek and plump up lip. Because they are relatively safe and effective with less adverse reactions and are simple to operate, they have become popular dermal fillers.[1] In pursuit of temporary interests, some lawbreakers take risks in using hyaluronic acid improperly or using hyaluronic acid which does not meet regulatory standard, thereby causing damage to people's appearance. A case of nasal alar infection and necrosis caused by injection of hyaluronic acid in the nasolabial fold is now reported as follows.

1. Reported case

A 30-year-old female patient was admitted for pus on her right side of nose. She received hyaluronic acid injection in the right nasolabial fold 3 days ago, and her right nasal ala had been covered with pus for 1 day. 3 days before hospital admission, patient received hyaluronic acid injection on her right nasolabial fold from an unlicensed doctor, without being informed of any specific detail of the hyaluronic acid filler. The right nasal ala was painful and swollen; dark purple floral pattern changes were noted on the right nasal ala 2 days before admission (Figure 1). Patient received another injection at the same site again with no specific details and it was considered that it might be hyaluronidase, a few pus-filled bumps appeared on the front right nasal

ala 1 day before admission (Figure 2). Without treatment, the number of pus-filled bumps gradually increased, and some areas were blackened and broken down. Patient came to our hospital to seek further treatment. The patient was in good health, and denied a history of liver and kidney disease, diabetes, and coagulation disorder. Examination on admission: right nasal ala was red and swollen, with a large amount of yellow and white pus. Some areas were black and broken, with dry blood on top (Figure 3). Clinical diagnosis: right nasal alar infection and necrosis.

After admission, IV etimicin sulfate was given once a day for 3 days. The affected area was evenly applied with Moist Exposed Burn Ointment (MEBO) (ShanTou MEBO Pharmaceutical CO., LTD, China) after debridement, and covered with MEBO impregnated gauze. Dressing was changed 3 times a day (Figure 4-5); At day 3, the purulent exudate was notably reduced. MEBO was applied on wound with no other secondary dressings at 5 times a day (Figures 6-8); On day 10, the affected area basically healed with no noticeable hypertrophic scar and abnormal pigmentation, and the patient was discharged (Figure 9).

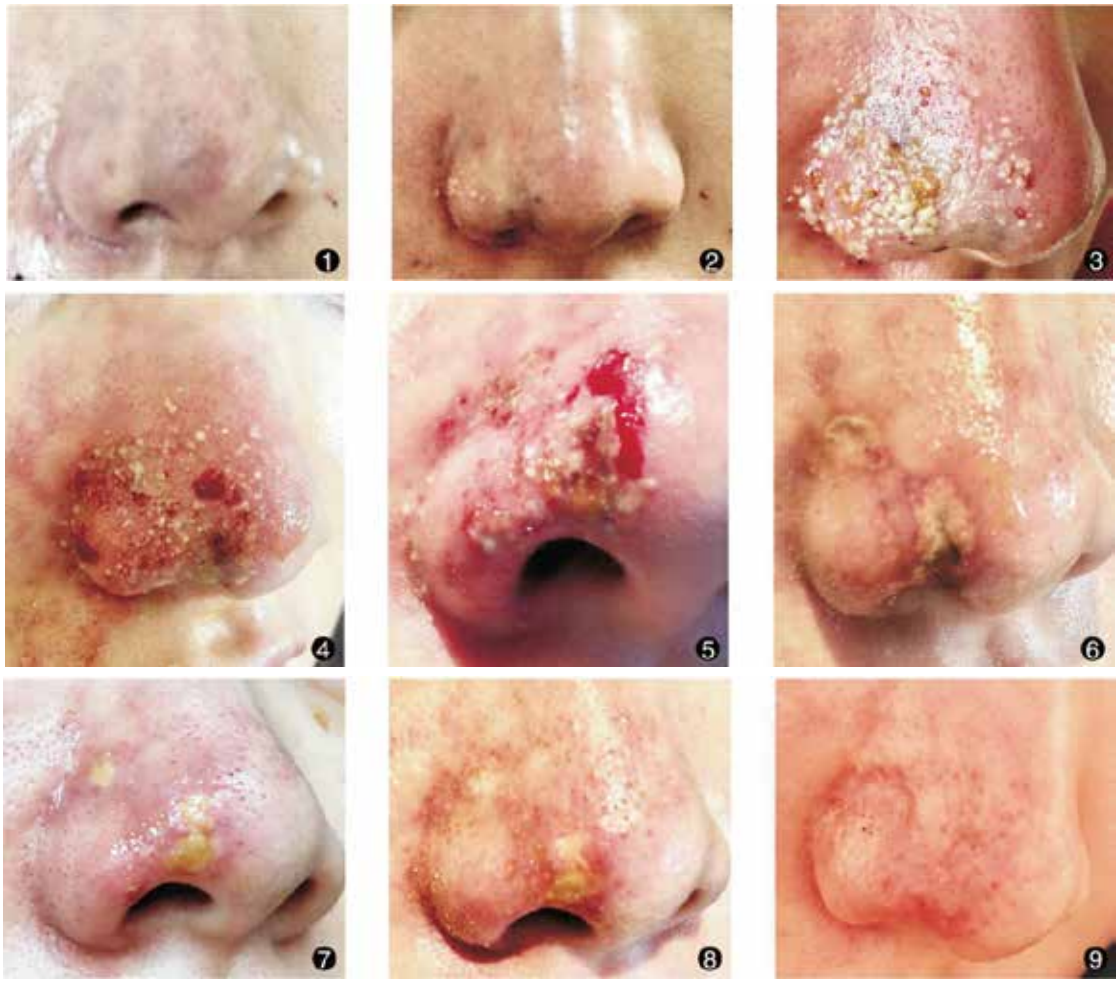

Figure 1: 2 days after hyaluronic acid injection **Figure 2：** After hyaluronidase injection (suspected, not confirmed) **Figure 3:** On admission **Figure 4-8:** During treatment with MEBO **Figure 9:** Day 10 of treatment with MEBO

2. Discussion

Hyaluronic acid is an acidic mucopolysaccharides with strong water retaining capacity. It keeps skin hydrated, eyes moist, and joints elastic. About 50% of hyaluronic acid in human body exists in skin, and the hyaluronic acid in dermis provides space for collagen and elastin fibers. It is an important extracellular matrix that maintains the stability and elasticity of skin, and is closely related to human aging.[2] Therefore, hyaluronic acid injection is commonly used in cosmetic and plastic industry to achieve the purpose of wrinkle removal and reshaping.

Studies have shown that the deepening of the nasolabial fold is one of the most common signs of facial aging, and hyaluronic acid injection into nasolabial fold could promote facial rejuvenation. However, since blood vessels in nasolabial fold are superficial, inadvertent injection of hyaluronic acid into the blood vessels could cause local vascular embolism, leading to local tissue necrosis which is difficult to treat.

In this reported case, after injection of hyaluronic acid, pus-filled bumps and blackened necrosis gradually appeared on patient's nose. It might be caused by injecting hyaluronic acid into blood vessels. Because regenerative medical technology has been widely used to treat wounds and ulcers, MEBO was applied to treat this patient. On day 10 of treatment, patient's wound basically healed. The mechanisms might be that wound reacts with the active ingredients contained in MEBO in a moist environment, and undergoes a series of biochemical reactions, which leads to an alteration of the environment that bacteria lives in; bacteria activity and toxicity could be inhibited; and wound infections could be prevented effectively.[3]

In summary, treating nasal alar infection and necrosis caused by hyaluronic acid injection with MEBO could effectively control infection and promote healing. It is worth noting that plastic surgeons should be proficient in the anatomy of skin to avoid injecting hyaluronic acid into the blood vessels and resulting in tissue necrosis.[4,5] Hyaluronidase is an enzyme that hydrolyzes hyaluronic acid. Once complications occur after hyaluronic acid injection, immediate diagnosis and treatment should be performed to prevent further thrombosis and tissue necrosis.[6] Once necrosis happens, applying MEBO in time could avoid wound deepening and hypertrophic scar formation. Since improper injection of hyaluronic acid or using substandard hyaluronic acid fillers could cause damage to healthy skin, public awareness should be increased, and people should choose organizations and clinics for cosmetic purposes carefully and wisely.

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Response to COVID-19 Pandemic: Study about COVID Toe Syndrome


Aristidis Veves, MD, ScD

Rongxiang Xu, MD, Professor of Surgery, Harvard Medical School

Director, Rongxiang Xu, MD, Center for Regenerative Therapeutics at BIDMC

Response to Covid-19 pandemic: Study about the Covid toe syndrome

Covid-19 main presenting symptoms are fever, dry cough, dyspnea, fatigue, anorexia, ageusia and anosmia. However, in a smaller portion of patients, skin symptoms in the form of erythematous lesions, dengue-like petechiae and urticaria and chickenpox-like vesicles have been described. In a recent study that included 277 patients, skin manifestations with skin manifestation, acral lesions were observed in more than half of the patients. More severe cases include the presence of toe cyanosis, bulla and dry gangrene. The frequency of this condition and its clinical characteristics are currently not well understood.

Main presenting symptoms of COVID-19 are fever, dry cough, dyspnea, fatigue, anorexia, ageusia and anosmia. However, in a smaller portion of patients, skin symptoms in the form of erythematous lesions, dengue-like petechiae, urticaria, and chickenpox-like vesicles have been described.

In a recent study that enrolled 277 patients, acral lesions, toe cyanosis, bulla and dry gangrene were found associated with COVID-19 patients. The frequency, pathophysiology and clinical characteristics of this condition are currently not well understood. Furthermore, it is not known whether conditions that cause lower extremity problems, such as diabetes mellitus or peripheral vascular disease are also risk factors in the development of this syndrome. The most appropriate hypothesis is that it is related to endothelialitis. Recent reports from lung biopsies have indicated that patients who died from COVID-19 associated or influenza associated respiratory failure also experienced severe endothelial injury and intussusceptive angiogenesis.

In order to further evaluate COVID toe syndrome, a multicenter study will be conducted with the primary objective to evaluate the frequency, clinical features and clinical course of COVID toe syndrome. The secondary objective is to describe cases treated with various modalities and collect preliminary data, including serum measurements of inflammatory cytokines and markers of endothelial function, and histopathological analysis of available tissues, which can lead to subsequent clinical trials.

This study will be carried out in approximately 6-8 clinical sites in the U.S., China and other countries. It will initially retrospectively identify cases of COVID toe in participating centers. At the same time, new patients will be prospectively enrolled. In addition, in selected centers, patients receiving care for COVID-related foot wounds will be followed for a maximum of 8 weeks or until complete healing occurs.

This study will be led by the Rongxiang Xu, MD, Center for Regenerative Therapeutics at Beth Israel Deaconess Medical Center, along with the Joslin-Beth Israel Deaconess Foot Center. The leading PI will be Dr. Aristidis Veves, Professor of Surgery, Harvard Medical School, Director of The Rongxiang Xu, MD, Center for Regenerative Therapeutics, Research Director of Joslin-Beth Israel Deaconess Foot Center.

The study is expected to be activated soon and will be conducted in collaboration with the National Rongxiang Xu Foundation.

International Academic Exchange—American Burn Association 52nd Annual Meeting

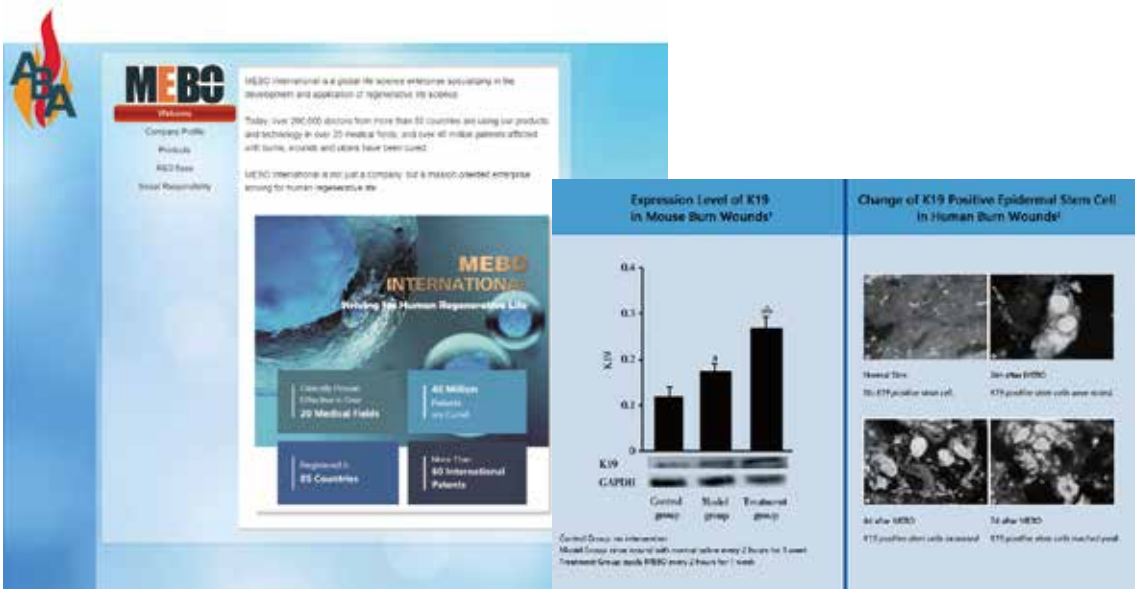
ABA virtual meeting hall

The 52nd annual meeting of American Burn Association (ABA) has kicked off recently online due to the prevalence of COVID-19 and will last until Aug 31st. Burn wound experts from all over the world will engage in academic discussions and exchanges. At the same time, more than 20 exhibitors will join virtually.

As an important academic institute in the realm of burn wound care, ABA was founded in 1967 with the initiative of promoting and supporting burn wound related studies and education as well as improving patients' living.

Education forums

The main contents of the meeting are showcased in 4 divisions: 1. the latest update of burn wound treatment, 2. the latest update in burn wound related domains, 3. posters, 4. exhibitors' booths.



Online booth of MEBO International

Upon its fourth participation in the ABA annual meeting, MEBO International introduces itself by briefing its history and mission, presenting its technology and focus areas. Attendees are encouraged to exchange ideas on regenerative medicine in the discussion.

MEBO International will reinforce the academic cooperation with ABA as a dedication to the global effort of burn wound care in the post-pandemic era when medical professionals are enthusiastic about studying and discussing burn wound care as ever.

Even though international academic meetings, seminars and symposiums have been widely impacted, International Society of Regenerative Medicine and Wound Repair (ISRMWR) will link global regenerative medical professionals to roll out online training sessions. Stay tuned for exciting academic events to come.

Student Action Fund: 38 Programs Rising Against COVID-19

PARTNER PERSPECTIVES

"I support CGI University because we share a belief in empowering our next generation of leaders. CGI U students work hard and creatively to tackle global challenges — including the current COVID-19 pandemic. By investing in their talent and unleashing their ideas we will create a better world, together."

— KEVIN XU, CHAIRMAN OF MEBO INTERNATIONAL

On Aug 7th 2020, Student Action Fund, a project fighting against COVID-19 driven by Clinton Global Initiative University and supported by Kevin Xu, Chairman of the Board of MEBO Group, has selected 38 remarkable programs worldwide from more than 10 thousand programs submitted from over 60 universities in 9 countries. After 4 months' collecting and evaluating, those who are selected will share a total of 100 thousand dollars as the seed funding for their commitments. These programs signify the pioneering endeavour to set up electronic medical record system in developing countries, provide medical resources to disabled children, extend health care services to minority communities.

Student Action Fund functions by the code that Clinton Global Initiative University has explicated, hatching 38 socially influential programs to tackle the emerging issues of public health, economic impact and social problems of COVID-19. The program encompasses the establishment of epidemic monitoring and response system, calling for social responsibility of enterprises and public awareness of health, as well as emphasizing the importance of proactive prevention, among other emergency reaction proposals. The prime goal is to provide immediate support to the front-line medical professionals and contributors in vital positions. Student Action Fund was announced in 2020 by US ex-president Bill Clinton in the virtual annual meeting of Clinton Global Initiative University.

In cooperation with GoFundMe, Clinton Global Initiative University has additionally launched a student fundraising program (Aug 10-28, 2020) to support student-led programs against COVID-19. Fundraising web pages will be set up for individual students to transfer donations directly to their accounts.

This initiative has approached more than 10 thousand alumni from more than 1100 universities in 160 countries. In all 50 states of the US, students from Clinton Global Initiative University have made more than 7000 "Action Promises", creating very constructive effects to their hometowns, university campuses and global communities.

Brilliant Action Fund Awardees

- Jonathan Dhanapala of University of Waterloo, Emre: Emre is an electronic medical record system built to support medical professionals in providing healthcare to displacement and refugee camps in Iraq.

- Melissa Diamond of Tsinghua University, A Global Voice for Autism COVID-19 Emergency Inclusion Fund: A Global Voice for Autism COVID-19 Emergency Inclusion Fund holistically equips caregivers of children with disabilities in refugee and conflict-affected communities to support their children's emergency and inclusive education needs in Jordan, Palestine, and Turkey.

- Vikrant Garg of University of Illinois Chicago, COVID Rapid Response Team Chicago (CRRTC): COVID Rapid Response Team Chicago mobilizes resources, skills, and time to provide critical life-sustaining services to marginalized communities in Chicago, IL during the COVID-19 crisis.

- Alekhya Majety of University of North Carolina at Chapel Hill, Quvi: Quvi directs UV-C light onto the interior and exterior of reusable water bottles to effectively neutralize any pathogens, or viruses such as COVID-19.

- Bincheng Mao of New York University, Equitable Health Care Access for Minorities: Equitable Health Care Access for Minorities mobilizes over 3,000 members of the East Coast Coalition for Tolerance to aid disadvantaged minorities with language barriers to seek medical attention in New York, NY, New Haven, CT, and Atlanta, GA.

- Zonia Moore of University of Pennsylvania, SANIPACK: a portable, battery-powered N95 mask sterilizer: SANIPACK is a N95 mask sterilizer that gives providers the confidence they need in reducing their risk of contracting COVID-19 and is appropriate for use in pop-up healthcare settings in Nigeria.

- Evelyn Wong of Harvard University, CovEducation: CovEd is a virtual platform that pairs underserved K-12 students with undergraduates/postgrads from higher education institutions across the U.S., providing them with 1-on-1 mentorship, web-based educational resources, and offline content.

- Sukhmeet Sachal of University of British Columbia, COVID-19 Response in Sikh Temples: The COVID-19 Response in Sikh Temples will implement public health interventions such as temperature checking and physical barriers in order to protect elderly patrons and the general public visiting Sikh Temples in British Columbia, Canada.

- Camir Ricketts of Cornell University, Project Access: Project Access is an extension program of the Minds Of Initiatives that will help schools in rural Jamaica gain access to internet-enabled devices and sponsored data plans so that students can engage in online courses in Jamaica.

Supportive Emergency Aids after the Explosion in Beirut

Around 18:10 (GMT + 3) on Aug 4th, there was a huge explosion happening at the Port of Beirut followed by a gigantic mushroom cloud, leaving at least 220 dead and more than 7000 injured as of now.

In response to this catastrophe, MEBO International has immediately activated emergency aid system evolved from its years' of participation in international aids. In collaboration with Julphar, MEBO International has started a program of emergency aid with joined efforts from Hammoud Hospital University Medical Center, Lebanese Hospital Geitaoui, American University of Beirut Medical Center, University of Balamand and relevant charity organizations.

The program will be focused on organizing a team of local medical professionals to heal the injured using regenerative technology, in addition to donating money and medicine (worth $100 k in total) to local hospitals and public service organizations for the sake of restoration.

As a concordant effect of United Nations Every Woman Every Child China Partnership Network (EWECCPN) Life Regenerative Action, Clinton Global Initiative, Belt and Road Initiative, more than 200, 000 clinical professionals of regenerative medicine from over 70 countries have been linked together to the platform that facilitates instant international aid and disaster rescue. It has played a crucial role in the emergence of fire, earthquake and explosion where lots of injured people need to be treated. These professionals are very important local supporters of this international aid system and have consistently contributed to the sustainable development of the world. The regenerative medicine has become critical in international aid.

On Dec 14th, 2018, EWECCPN Life Regenerative Action was launched in Lebanon to deliver trainings on regenerative medicine and domestic emergency aid technique, and for the cooperation with hospitals in public service programs with the goal of boosting local people's health. In collaboration with Hammoud Hospital University Medical Center, Life Regenerative Action has established local trainings on public health and medical care, such as "Women, Maternal & Child Wellness" and "Wound Care Management Updates" in the form of clinical practice, dramatically helping improve local people's health awareness and the quality of wound care.

As one of the most acknowledged approaches to treat wound, regenerative medicine has been practiced in Lebanon for more than 20 years, applied in the treatment of burn wound, acute wound, chronic wound, surgical wound, etc.

MEBO International will stand by Beirut against this challenge of medical crisis with decades of experience in regenerative medicine.

EWECCPN Life Regenerative Action launching ceremony in Lebanon in 2018