The evidence-based topical therapies for management of minor burns in outpatient clinic

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The evidence-based topical therapies for management of minor burns in outpatient clinic

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Abstract

Burns are often seen in clinics or hospitals. Majority of burns are minor burns, which can be managed in outpatient setting with satisfactory result. The healing outcome depends on physician’s knowledge and competencies in burn pathogenesis and basic principles of burn care. Initial treatment of burns consists of emergency evaluation, assessment of depth and severity of burns and considerations for referral. The principles of minor wound therapy include cooling, cleansing, pain management, and topical therapy. Recently, many topical agents are available and indicated for first to second degree burn. Silver sulfadiazine (SSD) is the standard treatment; however, it has some limitations. Scientific evidences showed that topical antibiotics do not reduce the incidence of local infection, invasive infection, and mortality of infection. Burns heal faster with hydrogel dressings and some other dressings compared to SSD. There are insufficient evidences to support the use of aloe vera, honey, and negative pressure wound therapy in burns. Moist exposed burn ointment (MEBO®) has been demonstrated to have equal efficacy to SSD.

Keywords: burns, silver sulfadiazine, dressings, moist exposed burn ointment

Introduction

According to the World Health Organization, a burn is defined as an injury to the skin or other organic tissue which directly caused by heat or other causes, such as radiation, radioactivity, electricity, or chemicals.

Worldwide, it has been estimated that there are 195,000 of deaths due to burns every year and most cases occur in developing and under developed countries in South East Asia region. Adult women, parents and children have a higher risk for domestic burns, particularly in the kitchen; while in men, the risk involves accidents in the workplace. Burns has contributed to high morbidity rate in hospitals. Infection, self-esteem issue and disability due to burn have caused longer hospital stay and patients face stigma-related issue, and rejection from their social environment.

There were 303 patients who had intensive treatment at the Burns Unit in Dr. Cipto Mangunkusumo Hospital between January 2009 and December 2010 and most cases were caused by Liquefied Petroleum Gas or LPG (30.4%) followed by flames (25.7%) and hot liquids (19.1%) with a mortality rate of 34%. Nosocomial infection is the most common complication found at the Burns Unit in Dr. Cipto Mangunkusumo Hospital with three major types of pathogenic microorganisms including Klebsiela pneumonia (23%), Pseudomonas sp (20%) and MRSA strain of Staphylococcus aureus (14%).

In general, minor burn is defined as a burn that does not meet the criteria for referral to the Burn Unit and there are no adverse physical or social limitations to outpatient management. Over 95% of burn cases are minor burns, which can be managed well in outpatient...
units. The maximum healing outcomes are determined by physician’s knowledge in basic principles of burn care. Until now, there has been no data on morbidity and disability caused by minor burns either in the outpatient clinics of the Department of Plastic and Reconstructive Surgery or Department of Dermatology and Venereology at Dr. Cipto Mangunkusumo Hospital.

The Guideline for Specialist Education in Dermatology and Venereology at the Faculty of Medicine, Universitas Indonesia indicates that dermato-venereologists are expected to have knowledge and competencies in the management of first- and second-degree burn. Now a days there are various kinds of topical therapies indicated for the first- and second-degree burns and some of them have been investigated under clinical studies. This manuscript will discuss about the management of minor burns, particularly on the utilization of various kinds of topical therapies based on the most recent scientific evidences.

**Etiology and pathogenesis**

A burn injury occurs when some or all layers of skin are destroyed by physical energy delivered through a hot liquid, flame, contact with a hot surface, ultraviolet or infrared radiation, radioactivity, electricity and chemicals. Almost 70% cases of burns in children are scalds (due to hot beverages or hot baths). Hot liquids tend to cause first to second degree burns; while flames and contact with a hot surface may cause third to fourth degree burns.  

In electrical burn injury, the current runs from one point to another point (the entry and exit points). The higher the voltage entering the body, the greater it damage on tissues. Low-voltage electricity such as domestic electricity tends to cause minor burns; while high-voltage electricity (>1000 volt) may cause extensive tissue damage. Patients often lose their legs due to necrosis of soft tissues and bones. Rhabdomyolysis, renal failure and heart arrhythmia may also occur. Physical examination of electrical burn injury reveals erythematous serpiginous lesion on the skin with fading of the rash on the distal end. Burn injuries caused by explosion (flash injury) due to high-voltage current are usually superficial and injure exposed skin area such as face and hands.  

Burn injuries caused by chemicals can occur at work or home. There is a tendency of deep injuries and the length of contact time with chemicals is equal to the area of coagulation necrosis. Alkaline chemicals tend to have deeper penetration and cause more severe burn injuries than acid chemicals. An example of alkaline chemicals is liquid cement.  

Burn injuries due to ultraviolet/infrared radiation, either from the sun (sunburn) or artificial sources usually cause superficial injuries. Deeper injuries may occur when patients apply or ingest substances than can cause skin photosensitization. Burn injuries may also occur due to radiodiagnostics or radiotherapy procedures. Skin lesions caused by such procedures are categorized as radiodermatitis.

When the body has direct contact or near hot objects or radioactive liquids (beta particle), burn injuries may develop. Burns caused by beta particles are usually superficial and similar to sunburn, but it can be more severe depending on the length of contact time and radiation dose. A radiation dose of >2 Gy may cause acute radiation syndrome (ARS) involving central nervous, gastrointestinal, hematologic, dermatologic and cardiovascular systems. Initial symptoms include nausea and vomiting, head ache, fatigue, fever and purpuric lesion. Laboratory examination reveals low blood cell count or aplastic anemia.

The pathophysiology of burn injuries includes local and systemic responses. A relatively prolonged exposure to high temperature of more than 45°C causes protein denaturation and loss of cell membrane integrity. Local responses induced by tissue damage include release of inflammatory mediators such as histamine, serotonin, bradykinin, nitric oxide, reactive oxygen species, prostaglandin, thromboxane, tumor necrosis factor and interleukin. Histamine is considered as the most essential mediator at the beginning phase of burn injuries, which can increase microvascular permeability. Jackson (1947) described the local changes of burns into three zones (Figure 1.A).

1. **Zone of hyperemia**
   It is the outermost zone where there is increased tissue perfusion. The tissue here will recover unless there is severe sepsis or prolonged hypoperfusion.

2. **Zone of stasis**
   There is decreased tissue perfusion due to progressive thrombosis of blood vessels.
surrounding the zone. By increasing the tissue perfusion in this zone, some of tissue is salvageable and permanent damage can be prevented. Hypotension, infection and edema can convert the tissue in this zone into permanent loss.

3. Zone of coagulation
   It is the point of maximum damage. In this zone, there is irreversible tissue loss due to protein coagulation.

These three zones are three dimensional. Tissue loss in the zone of stasis will lead to deeper and wider wound. Necrotic tissue on skin surface as a result of burn injuries is called eschar. Systemic response occurs when the burn area reaches 30%. Releases of cytokines and inflammatory mediators by wound tissues, extensive loss of capillary integrity and accelerated trans-eschar fluid loss may cause cardiovascular, respiratory, metabolic and immunologic disorders. These responses are usually aggravated by bacterial growth surrounding the eschar as well as bacterial products. Infection that cannot be managed by local immunity will cause systemic infection. Clinical manifestations of systemic responses are characterized by fever, fluctuative hemodynamic status and increased body metabolism and muscle catabolism (Figure 1.B).

**Burn classification**

Burn injuries are clinically categorized based on the depth and surface area (Figure 2). The degree of burn consists of:

- **1st Degree**
  Tissue damage includes only the epidermis. Clinical manifestation involves erythematous, dry and painful lesions. Sometimes, the wound is deeper than it seems. Slough is a yellowish-white necrotic tissue that may be maintained until the seventh day. Healing usually occurs in 5-10 days.

- **2nd Degree (Superficial Dermal Burn)**
  Tissue damage in all of epidermal layers and part of the dermis (stratum papilare). The skin appears red and wet. There are also clear blisters (bullae) and when pressure is applied, it will blanch and is very painful. The wound should heal within 2 weeks and usually no scar will be developed; however, there is still a possibility of scarring or hypo- and hyperpigmentation lesion.

- **2nd Degree (Deep Dermal Burn)**
  Burn injury has reached the reticular layer of the dermis. The wound appears white and blanching is absent when pressure is applied. It usually does not heal within less than 3 weeks. It is often accompanied by scarring and contractures.

- **3rd Degree**
  The tissue damage has reached subcutaneous fatty layer. Clinically, the skin appears pale to dark brown, it has leathery appearance on palpation and the burns are not painful. It often needs skin grafting to heal and can cause contractures.

- **4th Degree**
  Total skin loss and it extends to muscles, tendons or bones.

The area of burn injury can be calculated using the Lund-Browder classification or the Rules of Nines. The Lund-Browder classification is more accurate for estimating surface area assessment of burn injury, particularly for children. However, for practical purpose, the Rule of Nines is reliable. (Figure 2).
Based on the classification on the severity and surface area affected by burns, the criteria for minor burn injury are:

1. 2nd degree of burn on <5% total body surface area in patients aged younger than 10 years or older than 50 years.
2. 2nd degree of burn on <10% total body surface area in patients with 10 to 50 years of age.
3. Burn injury does not affect face, hands, feet, perineum, genital or major joints.
4. Non-circumferential burn
5. Localized burn

Initial management of the burn injury

In general, initial management of the burn injury includes evaluations of A, B, C, D, E, F (Airway maintenance with cervical spine control, Breathing, Circulation with hemorrhage control, Disability of neurological status, Exposure with environmental control, Fluid resuscitation proportional to burn size) and providing anti-serum treatment of tetanus. It should then followed by an assessment of surface area affected by burns, which includes the area, degree of burn, the presence or absence of circumferential burn injury and high-risk signs of potential abuse to determine whether the patient needs a referral to the burns unit or only needs a good care in outpatient clinic. The criteria of burn injury for referral or outpatient care can be seen in table 1.

**Burn injury care**

Principles of burn injury care include ensuring adequate tissue perfusion by providing fluid and nutritional intake, optimal pain management and environmental management for optimal wound healing. The optimal wound environment to promote healing is one that can reduce bacterial contamination, lower the negative effects of inflammation and stimulate epithelialization. The principles are further described and applied through the following measures.

![Figure 2. Classification on the severity of the burns and surface area affected by burns.](image)

Classification on the severity of the burns is described schematically in the figure (a); clinical examples of 1st degree burn (b); 2nd degree (superficial dermal burn) (c); 2nd degree (deep dermal burn) (d); 3rd degree (e); Estimating surface area affected by burns using the Rules of nines (f); or Lund-Browder criteria (g).
Table 1. Criteria for outpatient care and referral on burn injury\textsuperscript{13,14}

<table>
<thead>
<tr>
<th>Outpatient Care</th>
<th>Refer to a Burn Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. No respiratory distress or indication for respiratory monitoring.</td>
<td>1. (2^{nd}) degree burns affecting (&gt;10%) total body surface area.</td>
</tr>
<tr>
<td>2. Burns area on (&lt;10%) total body surface area in adults and (5%) total body surface area in children; therefore, fluid resuscitation is not necessary.</td>
<td>2. Burns involving face, hands, feet genitalia, perineum and major joints.</td>
</tr>
<tr>
<td>3. Patient is able to drink well.</td>
<td>3. (3^{rd}) degree burn.</td>
</tr>
<tr>
<td>4. No burns involving face, ears, hands, feet, genitalia or major joints.</td>
<td>4. Burn injury caused by electricity, including lightning.</td>
</tr>
<tr>
<td>5. Patients and their families must have resources to execute the plan for outpatient care.</td>
<td>5. Burn injury caused by chemical.</td>
</tr>
<tr>
<td>6. An adult who provide care for a child patient must live under one roof with the patient.</td>
<td>6. Burns with associated inhalation injury.</td>
</tr>
<tr>
<td>7. The adult must be able to perform wound cleansing, wound inspection and wound dressing change.</td>
<td>7. Burns in patient with pre-existing medical condition that can complicate management, prolong recovery time or affect mortality.</td>
</tr>
<tr>
<td>8. The patient should have transportation support and access to the clinic for routine or emergency visits.</td>
<td>8. Every patient who had burn injury with concomitant trauma (such as multiple fracture), but the burn injury should have a higher risk than the trauma. When the concomitant trauma carries a higher risk, the patient must first be stabilized at the trauma center before being transferred to a burn unit.</td>
</tr>
<tr>
<td>9. There are no signs of abuse or neglect.</td>
<td>9. Burns in children at hospitals without qualified personnel or equipment for the care of children.</td>
</tr>
<tr>
<td>10. There is no (3^{rd}) degree burns that needs surgical correction.</td>
<td>10. Burn injury in patients who need special social, emotional or rehabilitative intervention.</td>
</tr>
<tr>
<td>11. No co-morbidity.</td>
<td></td>
</tr>
</tbody>
</table>

For acute burn injuries, the initial therapy is to cool the burn wound in order to stop the burning process with running tap water on the wound for 20 minutes. It can reduce the burn depth, stimulate re-epithelialization and improve the healing outcomes cosmetically. Ice should not be used as it will cause further injuries and hypothermia. The other immediate action is providing pain relief with adequate analgesics before cleansing and dressing the wound. Analgesics such as paracetamol and opioid can be given in keeping with the Visual Analog Scale (VAS) assessment.

After the pain has been controlled, wound cleansing is performed using 0.05%-2% chlorhexidine and the wound is then irrigated with normal saline (0.9%). Other method includes the use of water and baby soap. Wound cleansing using povidone iodine or other strong antiseptics is not recommended. The surface of the wound is cleaned by gentle scrubbing so that the wound should be free of slough, exudates, hematoma and creams. Debridement is carried out to eliminate non-vital tissue and to remove eschar. A blister (bullae) of less than 6 mm in size can be left intact; while large bullae with thin delicate wall should be treated with scrapping the roof of bullae. The procedure is very useful so that the dressing can have direct contact with the wound bed. Topical treatment is then applied according to the degree of wound.

Topical treatment is effective to fasten wound healing and prevent complications such as infection and scar. Burn injuries can have optimal healing in moist-not wet- condition. Moisture will stimulate re-epithelialization and prevent cell dehydration. The ideal wound healing can be achieved by applying topical agents or occlusive dressing to prevent fluid loss. Topical agents can reduce pain, stimulate healing, prevent infection and wound desiccation.\textsuperscript{6} In the \(1^{st}\) degree burns, there is actually no indication for topical treatment. The \(2^{nd}\) degree burns should be treated with topical antibiotics or occlusive dressing that can reduce pain, improve wound healing and keep the wound from drying.\textsuperscript{5, 6, 15}
Evidence-based topical treatment for minor burn injury

Topical treatment for burn injury has become interesting topics in many studies and discussion. Numerous randomized clinical trials (RCTs) have been reported regarding topical treatment for burn injuries. In recent years, the Cochrane Wound Group (CWG) has carried out a systematic review on those clinical trials. The following is a discussion on several types of topical treatment for burn injuries and the studies supporting its clinical application.

Topical antibiotics

So far, topical antibiotics for burn injuries are used with the aim of prophylaxis against secondary infection. Infection causes delayed wound healing, increased complication of scarring, and even invasive infection that may lead to death. Silver sulphadiazine (SSD) is a standard antibiotic for treatment of burn injuries. However, it has some limitation with relative contraindication for patients who are allergic to sulfa, pregnant and breast feeding women and neonates. Several topical antibiotics that have been commonly used for treatment of burn injuries and their characteristics are presented in table 2.5

The Cochrane Wound Group has established a systematic review and meta-analysis on 26 RCTs (n=1329) evaluating topical antibiotics for burn injuries up to January 2013. Topical antibiotics evaluated in those studies are in the form of ointments or dressings. Some studies that have met the inclusion criteria are categorized into several comparative groups (Group 1: neomycin, bacitracine, polymyxin B versus passive control; Group 2: SSD versus polymyxin B or bacitracin; Group 3: SSD versus dressings or skin substitutes; Group 4: SSD versus topical herbal product; Group 5: other antibiotics versus dressings or skin substitutes; Group 6: prophylactic antibiotics versus other treatment). The evaluation of outcome measures was categorized into completed primary outcomes (infection of burn injuries, invasive infection, infection that causes death and adverse effects) and completed secondary outcomes (the rate or speed of wound healing, antibiotic resistance, cause of death and length of hospital stay). In general, it has been found that there is insufficient scientific evidence to support the use of topical antibiotics to reduce the risk of infection for burn injuries, as well as to reduce invasive infections (pneumonia, bacteremia, sepsis or urinary tract infection) or mortality due to infection. Meta-analysis data of 11 RCTs (n=645) in subjects treated with SSD reveals that there is a statistically significant increased incidence of infection compared to those treated with dressings or skin substitutes (OR 1.87; 95% CI: 1.09-3.19). However, the clinical trials still had a high risk of bias since the review was not blinded. Based on the review, we did not find any evidence that topical antibiotics may affect the secondary outcomes. Time to complete wound healing could not be well identified or analyzed; therefore, the investigators found that it was difficult to determine whether the intervention of topical antibiotics actually has any effect on wound healing. Other findings reveal that subjects receiving SSD treatment had longer average length of hospital stay than those using dressings or skin substitutes (MD 2.11 days; 95% CI: 1.93-2.28 days).16

Dressings

There are several types of dressings available nowadays indicated for burn injuries. The selection of dressings needs to be adjusted with the wound condition to achieve the goal of wound care. The ideal dressings are those that can maintain optimal moisture, absorb exudates well, does not cause pain or are not traumatic during dressing changes, prevent altered tissue perfusion, offer protection against bacterial colonization and provide pressure effect so that the edema and scarring can be minimized. Some examples of common dressings for wound injuries can be seen in table 2.5

In November 2012, CWG conducted a systematic review on the effect of dressings on 1st and 2nd degree acute burn injuries. The dressings included in the study were hydrocolloid dressings, polyurethane film dressings, hydrogel dressings, silicon-coated nylon dressings, biosynthetic skin substitute dressings, antimicrobial silver-iodine dressings, fiber dressings, and wound pad dressings. The parameters of outcomes were divided into primary outcomes (time to complete wound healing and change in wound surface area) and secondary outcomes (number of dressings changes, cost, quality of pain during application and removal of dressings, patient satisfaction, quality of life, length of hospital stay, the needs of surgical intervention, the incidence of infection and adverse effects).17
Table 2. Some examples of common topical antibiotic preparation and dressings.\textsuperscript{5}

<table>
<thead>
<tr>
<th>Name</th>
<th>Type of therapy</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacitracin</td>
<td>Topical</td>
<td>Narrow antimicrobial coverage; inexpensive; painless; requires frequent dressing changes; can be used on face or near mucous membranes\textsuperscript{1}</td>
</tr>
<tr>
<td>Mafenide acetate</td>
<td>Topical</td>
<td>Broad-spectrum antimicrobial coverage; penetrates eschar; may delay healing or cause metabolic acidosis; used for deep burns\textsuperscript{1,2}</td>
</tr>
<tr>
<td>Mupirocin (Bactroban)</td>
<td>Topical</td>
<td>Good gram-positive antimicrobial coverage; expensive; painless; requires frequent dressing changes; can be used on face</td>
</tr>
<tr>
<td>SSD (Silvadene)</td>
<td>Topical</td>
<td>Broad-spectrum antimicrobial coverage; painless; requires frequent dressing changes; delays healing; stains tissue; used in deeper partial-thickness burns; relatively contraindicated in pregnant women; newborns; nursing mothers; and patients with glucose-6-phosphate dehydrogenase deficiency or sulfon allergy\textsuperscript{4}\textsuperscript{-6}\textsuperscript{,}10\textsuperscript{,}11</td>
</tr>
<tr>
<td>Aqueacel Ag</td>
<td>Absorptive dressing</td>
<td>Silver-impregnated; broad-spectrum antimicrobial coverage; decreases dressing changes; reduces pain; decreases use of pain medications; faster wound closure than with standard therapies\textsuperscript{12}; decreased total cost compared with SSD\textsuperscript{12}</td>
</tr>
<tr>
<td>Biobrane</td>
<td>Biocomposite dressing</td>
<td>Less pain and shorter time to healing than with SSD; expensive but lower total treatment cost compared with SSD\textsuperscript{13,14}; one study showed effectiveness in superficial burns, but high failure rates with mid-thickness deep burns\textsuperscript{14}</td>
</tr>
<tr>
<td>Hydrocolloids (Uroderm, UrgoL)</td>
<td>Absorptive dressing</td>
<td>Less pain and shorter time to wound closure than with SSD; good for weeping burns; malodorous; opaque\textsuperscript{15,16}</td>
</tr>
<tr>
<td>Impregnated nonadherent gauge (Kerlix)</td>
<td>Nonabsorbent dressing</td>
<td>No antimicrobial activity; messy; provides a nonadherent barrier over the burn for absorbent dressings; used for superficial burns\textsuperscript{17}</td>
</tr>
<tr>
<td>Silicone (Mepitel)</td>
<td>Nonabsorbent dressing</td>
<td>Expensive; painless; allows seepage of exudates to secondary bandage\textsuperscript{18}</td>
</tr>
<tr>
<td>Silver-impregnated dressing (Acticoat)</td>
<td>Nonabsorbent dressing</td>
<td>Delivers low concentrations of silver; broad-spectrum antimicrobial coverage; nonadherent; reduces pain; expensive\textsuperscript{12,18,19}</td>
</tr>
</tbody>
</table>

\textsuperscript{SSD} = silver sulfadiazine.

Information from references 1, 6, 10, 12, 24 through 31, and 33 through 36.

Overall, out of the reviewed 30 RCTs, the whole studies were low quality evidence-based studies since small studies with bad reporting and high risk of bias were included. However, it can be concluded from the systematic review that burn injuries treated with hydrogel dressings heal faster than the common therapy. The investigators also found evidences that burn injuries treated with silicon-coated dressings, biosynthetic skin substitute dressings and silver-impregnated dressings heal faster than those treated with SSD treatment. Nevertheless, there is insufficient strong evidence to determine the effect of hydrocolloid dressings and polyurethane dressings. There is inconsistent result on the rate or speed of wound healing using fiber dressings. No significant difference was found regarding shorter time to complete wound healing between the use of calcium alginate dressings and SSD. There was also no different on the time to complete wound healing between biosynthetic dressings and hydrocolloid dressings. For secondary outcomes, there is evidence that the dressings used for intervention can reduce the pain compared to the comparative dressings. The results were not statistically significant, but there were consistent reports except for antimicrobial dressings. The evidences on effective dressings to prevent secondary infection are limited since the measurement was inconsistent and the data reporting was poor. There was no significant difference on the incidence of infection between the interventional dressings and its comparative dressings. Interventional dressings seem to have better outcome regarding the number of dressings change. It can be explained as there is different protocol for each study. For example, a study using SSD and gauge needs dressing change every day; while for interventional dressings, the change can be adjusted according to the needs.\textsuperscript{17}
Negative pressure wound therapy

Negative pressure wound therapy (NPWT) is indicated for 2nd burn injuries. The instrument works with suction power, which can drain excessive fluid in burn injuries and increase blood perfusion to provide optimal oxygen and nutritional supply in burned area and a good wound healing takes place.18

In systematic review by CWG in May 2012, there is only one RCT that meet the inclusion criteria. The study has a high risk of bias. Limitations on scientific evidences on NPWT for burn injuries have made investigator in difficult position to make any conclusion. Further studies are necessary to identify whether NPWT is useful as an alternative treatment.18

Honey

Since ancient times, honey has been used by human for wound care. Honey is a thick sugar-saturated solution originated from nectar, which is produced by honey bees, Apis mellifera. Honey contains almost 30% glucose, 40% fructose, 5% sucrose and 20% water as well as other substances such as amino acids, vitamins, minerals and enzymes. Evidences from experimental animal studies and some clinical trials conclude that honey can accelerate wound healing.19

CWG performed a systematic review about the effect of honey on wound. Until June 2012, there were 12 studies evaluating the effect of honey on burn injuries. Most studies have a high risk of bias as they were not blinded. For acute 2nd burn injuries, honey shorten the time to complete wound healing compared to several conventional dressings (MD -4.48 days; 95% CI -4.28 to -5.09 days). In contrast, for 2nd – 3rd degree burn injuries, honey inhibit wound healings compared to early excision and skin graft (MD 13.6 days; 95% CI 10.02 – 17.18 days). There was no significant difference regarding the time to complete wound healing between the use of honey and SSD (MD 4.37 days; 95% CI -8.94 to 0.19 days). Considering that there are limitations of scientific evidences on the use of honey, the investigators suggest that the routine use of honey as topical treatment in health care services should be limited until further supporting scientific evidences are available.19

Aloe vera

Aloe vera is a cactus-like plant included in Lilacea family, which is easily grown in tropical area. It contains active substances such as vitamins (A, C, E, B12, folic acid and choline), enzymes (alkaline phosphatase, amylase, bradykinase, carboxypeptidase, catalase, cellulase, lipase and peroxidase), minerals (calcium, chromium, lead, selenium, magnesium, manganese, potassium, sodium and zinc), sugars (monosaccharide and polysaccharides), lignin, saponins, salicylic acid and amino acids. Salicylic acid in the aloe vera gel has anti-inflammatory effect, lignin can improve the ability of other substances to penetrate the skin; while saponins have a role as soap and antiseptics. Some experimental animal studies demonstrate that aloe vera can accelerate wound healing.20

Moist Exposed Burn Ointment (MEBO®)

MEBO® is a pure herbal formulation originated from China (China National Science and Technology Centre), which has received a patent in America since 1995 and now it is popular as an effective topical treatment for 2nd degree burn injuries. The ingredients of MEBO® herbal formulation are phellodendron amurense, scutellaria baicalensis, coptis chinensis, pheretima aspergillum, beeswax and sesame oil. The pharmacological effects are derived from β-sitosterol (isolated from Phellodendron amurense), flavonoids (particularly baicalin, which is isolated from Scutellaria baicalensis), alkaloids (especially berberine, which is isolated from Coptis chinensis) and vehiculum, which is a mixture of beeswax and sesame oil.21 The exact mechanism of action of MEBO® has not been confirmed. It is thought that the oil-based content has the most essential role in wound healing, i.e. for cooling the wound, maintaining moisture and reducing pain. Until now, no systematic review or meta-analysis has been carried out regarding MEBO®; however, there are some RCTs reports from some countries.
Ang ES et al. from the Singapore National Burn Center (SNBC) reported that Singapore has conducted the first RCT on MEBO®, which was published in 2000. The first study compared MEBO® and SSD for 2nd degree burn injury affecting face and it revealed no different results between MEBO® and SSD regarding the healing rates. The wound observation demonstrated that MEBO® developed less number of slough compared to SSD and therefore, the wound healing more easily occurred. The use of MEBO® is more practical and convenient since it does not need changing the dressings.23

The second study (n=115) was performed in patients with 2nd degree burn injury and affected wound area of less than 40% total body surface area. The subjects randomly received MEBO® treatment 6 times daily or SSD-dressings 2 times daily. Results of the study demonstrated faster wound healing in patients receiving MEBO® treatment than those with SSD-dressings; however, it was statistically not significant (median 17 days vs. 20 days, p=0.11). There was no significant difference regarding the incidence of infection between both groups. MEBO® compared to standard treatment has been demonstrated to be more effective for pain management in the first 5 days of care and it reduces hospital cost as many as 8%.22

The next RCT on MEBO® was reported by Hirtz et al. in 2008, which evaluated 40 patients with 2nd degree burn injuries. The study found that there was no significant difference between MEBO® and SSD regarding the time to complete wound healing, incidence of infection, pain and the development of scar or keloid. MEBO® has a better ability in reducing transepidermal water loss than SSD although it was statistically not significant. The investigators conclude that MEBO® can be an alternative topical treatment for burn injuries.21

Results of those three abovementioned studies show that MEBO® is as effective as SSD. This fact is supported by in vivo comparative study in experimental rats conducted by Jewo et al. in 2009, which revealed that there was no significant difference between MEBO® and SSSD in clinical and histological wound healing.23 The last two RCTs were conducted by Hindy in 2009 and Mabrouk et al. in 2012 who studied about the effectiveness of MEBO® for facial burns. Hindy performed a study in 60 subjects with 2nd degree superficial facial burn injuries who randomly received treatment of Aquacel® Ag, MEBO® and normal saline compresses. The study found equal results in quality of healing and patient satisfaction between the use of MEBO® and Aquacel® Ag. Subjects receiving MEBO® treatment felt minimal pain and pruritus as well as performed facial movement more easily compared to those with Aquacel® Ag. However, evaluation of the time to complete healing and the odor demonstrated that Aquacel® Ag was more superior compared to MEBO®. Treatment using normal saline compresses was considered as the least satisfying as it caused pain, pruritus and difficulty in facial movement as well as longer time to complete healing. We conclude that MEBO® is a good alternative treatment for facial burn injury as it has cooling effect, practical application, does not interfere movement and a good quality of healing.24

Mabrouk et al. conducted a comparative study between Aquacel® Ag and MEBO® in 40 subjects with 2nd degree of facial burn injuries. They found a significantly faster average time to complete healing by Aquacel® Ag compared to MEBO® (10.5 days vs. 12.4 days, p<0.05). However, in terms of dressing change, pain and convenience, MEBO® was considered to be better. The post-healing scar quality in those treated with Aquacel® Ag was better. There was no significant difference of treatment cost between both therapies.25

In 2013, the Burn Unit at Dr. Cipto Mangunkusumo Hospital reported a RCT comparing the use of MEBO® and honey for 2nd degree burn injuries. About 34 patients were randomly categorized into 2 groups, the MEBO® and honey group; they were then being evaluated for outcome assessment on healing rate, antibacterial effect, pain score and cost effectiveness. Results of the study found that the wound treated with MEBO® healed faster compared to those receiving honey (median of changes in wound epithelization rate 81.25% vs. 65%, p=0.002). MEBO® has been demonstrated can reduce pain compared to honey (median of VAS pain scale 3 vs. 4, p=0.038). Bacterial colonization in the first and second weeks of wound care showed that there was less bacterial colonization in subjects receiving MEBO® compared to those with honey (p<0.001). Total cost of care in MEBO® group was lower than the honey group.26
The various above mentioned studies showed that for 2nd degree burn injuries, MEBO® treatment has similar effectiveness with the standard SSD or Aquacel® Ag treatment and more superior than honey. However, for specific facial burn injuries, healing with Aquacel® Ag gives better results than MEBO® due to fast healing rate and good scar quality.

**Conclusion**

Topical treatment for burn injuries has essential role in healing process. Based on the available recent scientific evidences, the modern dressings (hydrogel, silicon-coated dressings, biosynthetic dressings and silver-impregnated dressings) give better results of wound healing compared to standard SSD treatment. No evidence supports that topical antibiotics can prevent secondary infection. Further advanced clinical studies are necessary to identify the effectiveness of NPWT treatment, honey and aloe vera treatment for burn injuries. MEBO® can be an alternative treatment in the management of minor burn injury.

**Table 3. Summary table of various evidence-based topical treatments for minor burn injury**

<table>
<thead>
<tr>
<th>Types of Topical Treatment</th>
<th>Severity of Burn Injury</th>
<th>Results of Treatment</th>
<th>Level of Evidence*</th>
<th>Recommendation*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Topical antibiotics</td>
<td>1st and 2nd degree</td>
<td>No evidence of reducing the incidence of infection in burns, invasive infection and mortality caused by infection.</td>
<td>1a</td>
<td>A</td>
</tr>
<tr>
<td>Silver sulfadiazine (SSD)</td>
<td></td>
<td>Increased incidence of infection compared to the use of dressings or skin substitutes.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Longer hospital length of stay for wound care compared to dressings or skin substitutes.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dressings: Hydrogel</td>
<td>1st and 2nd degree</td>
<td>There are evidences that burn injury heals faster than the usual treatment.</td>
<td>1a</td>
<td>B</td>
</tr>
<tr>
<td>Silicon-coated dressings, biosynthetic dressings and silver-impregnated dressings</td>
<td>1st and 2nd degree</td>
<td>There are evidences that burn injury heals faster than SSD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative Pressure Wound Therapy (NPWT)</td>
<td>2nd degree</td>
<td>No adequate evidence</td>
<td>1b</td>
<td>-</td>
</tr>
<tr>
<td>Honey</td>
<td>1st and 2nd degree, superficial</td>
<td>There are evidences that it reduces time to healing compared to conventional dressings</td>
<td>1b</td>
<td>B</td>
</tr>
<tr>
<td></td>
<td></td>
<td>There are evidences that the healing time is equal with SSD treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aloe Vera</td>
<td>1st and 2nd degree, superficial</td>
<td>There are evidences that aloe vera has the same wound healing effect with SSD</td>
<td>1b</td>
<td>B</td>
</tr>
<tr>
<td>Moist Exposed Burn Ointment (MEBO®)</td>
<td>1st and 2nd degree, superficial</td>
<td>There are evidences that it has equal effectiveness with SSD treatment</td>
<td>1b</td>
<td>A</td>
</tr>
</tbody>
</table>

References


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