“A ONE YEAR RANDOMISED CONTROL TRIAL COMPARING THE EFFICACY OF TOPICAL SUCRALFATE VS SILVER SULFADIAZINE IN THE MANAGEMENT OF BURNS”

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ENDORSEMENT

This is to certify that the dissertation titled **"A ONE YEAR RANDOMISED CONTROL TRIAL COMPARING THE EFFICACY OF TOPICAL SUCRALFATE VS SILVER SULFADIAZINE IN THE MANAGEMENT OF BURNS"** is a bonafide research work done by **CANDIDATE REG NO. BH0114007**.

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LIST OF ABBREVIATIONS USED

°F	-	Degree Fahrenheit
^{0}C	-	Degree centigrade
aFGF	-	Acid fibroblast growth factor
AIDS	-	Acquired immune deficiency syndrome
bFGF	-	Basic fibroblast growth factor
BP	-	Blood pressure
DALYs	-	Disability-adjusted life-years
DBP	-	Diastolic blood pressure
DM	-	Diabetes mellitus
eGF	-	Epidermal growth factor
FGF	-	Fibroblast growth factor
FGFR	-	Fibroblast Growth Factor Receptor
g/dl	-	Grams per deciliter
gm	-	Grams
h	-	Hour
HIV	-	Human immunodeficiency virus
i.e.,	-	That is,
mg/dL	-	Milligrams per deciliter
mmHg	-	Millimeters of mercury
n	-	Total number
p	-	Probability
PDGF	-	Platelet-derived growth factor
SBP	-	Systolic blood pressure
SD	-	Standard deviation

SOS	-	Sucrose octasulfate
SSD	-	Silver sulfadiazine
TBSA	-	Total burn surface area
TGF-	-	Transforming growth factor
TGF-b	-	Transforming growth factor b
U.K.	-	United Kingdom
UL	-	Upper limb
uPAR	-	Urokinase-type plasminogen activator receptor
WHO	-	World Health Organization

ABSTRACT

Background and objectives

Many types of medications have been used for burn injuries. The present study was aimed to compare the efficacy of topical sucralfate with that of silver sulfadiazine, in the healing of second degree superficial burns.

Methodology

This one year randomized controlled trial was done in the Department of General Surgery, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi from January 2015 to December 2015. A total of 60 patients with <50% thermal superficial second degree burns were divided into two groups of 30 each as Group A (Topical sucralfate dressing) and Group B (Silver sulfadiazine dressing)

Results

Majority of patients were males in group A and group B (83.33% vs 16.67%; p=1.000). The mean age was comparable in group A and in group B (29.33±16.94 vs 29.87±16.83; p=0.903). Other characteristics including burn area, mean pulse rate, systolic BP, diastolic BP, respiratory rate, Temperature, personal history of tobacco consumption, Smoking, and Alcohol consumption, built (p>0.050) were comparable in group A and group B. However, all the patients in group A had burn injury in right upper limb (100.00%) compared to all the patients (100%) with burn injury on left upper limb in group B (p<0.001). In patients with group A, the day of granulation was less than 7 days among 50% of the patient While in group B, 56.67% of the patients had granulation between

15 to 20 days (p=0.149). The mean day of granulation was 8.11±3.92 days in group A compared to 8.93±3.29 days in group B (p=0.396). The wound culture on first, on seventh and 14th day (p>0.050) did not differ significantly in both the groups.

Conclusion and interpretation

Overall, topical sucralfate dressing is efficacious in terms of development of early granulation in the healing of second degree superficial burns.

Keywords

Topical sucralfate; Silver sulfadiazine; Second degree superficial burns;

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INTRODUCTION

Fire is considered as one of the five energy sources which are concerned with the living state. Man's march towards civilization started with his mastery and control over fire in the form of production or stoppage of fire. However, though man can produce this energy source, his control over stoppage of fire has not been as perfect. Because of this reason, we see man injuring himself with or by the fire.[1]

Burn injuries rank among the most severe types of injuries suffered by the human body with an attendant high mortality and morbidity rate.[2] Burn injury is a peculiar example of the harmful effects of external physical factors on health. The consequences of burns are protean and in most cases devastating for the patient. Burn injuries also have a great burden on society by consuming enormous health care resources.[3]

Non-fatal burn injuries are a leading cause of morbidity. Burns occur mainly in the home and workplace. Burns are preventable. In India, over 10,00,000 people are moderately or severely burnt every year. Nearly 173,000 Bangladeshi children are moderately or severely burnt every year. In Bangladesh, Colombia, Egypt and Pakistan, 17% of children with burns have a temporary disability and 18% have a permanent disability. Burns are the second most common injury in rural Nepal, accounting for 5% of disabilities. In 2008, over 410,000 burn injuries occurred in the United States of America, with approximately 40,000 requiring hospitalization.[4]

Burns represents an extremely stressful experience for both the burn victims as well as their families. An extensive burn profoundly affects the patients physique,

psyche, financial situation and family. Patients with extensive burns frequently die, and for those with lesser injury, recovery is slow and painful. In addition to their dramatic physical effects, burn injuries frequently cause deleterious psychological complications.[4]

Injury due to burns arising from unintentional incidents (accidents) and intentional incidents (suicide or homicide) is one of the leading causes of death and disability globally.[5]

Inflammation is vital to successful burn wound healing, and inflammatory mediators (cytokines, kinins, lipids, and so forth) provide immune signals to recruit leukocytes and macrophages that initiate the proliferative phase.[7] Wound re-epithelialization, or closure, in the proliferative phase via keratinocyte and fibroblast activation, or migration from dedifferentiated hair follicles and other epidermal analogs, is mediated by cytokines recruited in the inflammatory phase. While this indicates that inflammation is essential for wound healing, aberrant inflammatory pathways have also been linked to hypertrophic scarring, and anti-inflammatory treatments could potentially aggravate symptoms and delay wound healing.[8]

The most prevalent topical treatment for partial thickness burns is silver sulfadiazine 1% (SSD).[9] SSD is the topical agent of choice for severe burns and is used almost universally today in preference to compounds such as silver nitrate and mafenide acetate. SSD cream, in spite of being effective, causes some systemic side effects consisting of neutropenia, erythema multiforme, crystalluria and methemoglobinemia.[10-13]

Topical agents which are used only as antimicrobials include silver nitrate, sulfamylon and a combination of a sulfonamide and SSD. Sulfamylon has broad spectrum activities, but it is easily absorbed systemically and can lead to toxic complications. SSD has become the standard topical treatment for burn wounds.[10,13]

More recent studies have shown that the healing of partial thickness burns is delayed with the use of SSD[14,15], indicating the need for a better burn dressing.[13]

One of the potential burn dressings is sucralfate. Sucralfate is a basic aluminum complex of sucrose sulfate and a cytoprotective agent. The sporadic studies and case reports available in the literature are all consistent, indicating the favorable effect of topical sucralfate in wound repair and skin protection. Almost all studies have indicated the safe and effective behavior of this compound.[16-24] Sucralfate has also been shown to have antibacterial activity[25,26] and has been successfully studied in decreasing pain and improving healing after hemorrhoidectomy,[27] peristomal and perineal dermatoses, moist desquamation during radiotherapy, erosion and ulceration of the perineal area, vaginal ulceration, dystrophic epidermolysis bullosa, second and third degree burns, and in a pilot trial with nonhealing, full-thickness venous stasis ulcers refractory to 8 weeks of conventional therapy.[16-24]

Sulphated saccharides, primarily sucralfate, have previously been indicated for the treatment of gastric and duodenal ulcers. In radio-labeled form, sucralfate has also been used as a diagnostic agent for the imaging of gastrointestinal mucosa, since the substance binds selectively to ulcerated areas in the stomach and upper small intestine.

Although the evidence is not yet conclusive the clinical observations support the antiinflammatory effect and wound healing effect of sucralfate.[24,28] Further studies are needed to strengthen the existing evidence.

This prompted us to compare the efficacy of topical sucralfate with that of a control group using silver sulfadiazine, in the healing of second degree superficial thermal burns in terms of number of days required for healing or the appearance of healthy granulation tissue and to assess the effect of topical sucralfate on bacterial load.

OBJECTIVES

The objectives of this study were; to compare the efficacy of topical sucralfate with that of silver sulfadiazine, in the healing of second degree superficial burns in terms of:

Primary

Number of days required for healing or the appearance of healthy granulation tissue.

Secondary

To compare the antibacterial effect of sucralfate with that of silver sulfadiazine.

REVIEW OF LITERATURE

A burn is an injury to the skin or other tissue primarily caused by heat or due to radiation, radioactivity, electricity, friction or contact with chemicals. Thermal (heat) burns occur when some or all of the cells in the skin or other tissues are destroyed by hot liquids (scalds), hot solids (contact burns), or flames (flame burns).[4]

Ever since man discovered fire he has burnt himself either accidentally or intentionally. Burns are the oldest type of injuries that man suffers from and it is one of the important causes of mortality and morbidity. Burns afflicts all segments of the society. The rich and poor, men and women, children and adults fall victim to it.[29]

The pattern of causation of burn injuries has changed with the passage of time and varies from country to country. Countries where open domestic fires are customary (U.K., Africa, India) have deaths due to clothing catching fire. The increase in availability and use of inflammable liquids (Ex. Petrol, kerosene) has been followed by more burns from this cause, particularly in the working population age group (16 - 65 years).

In peacetime England, the types of burns severe enough to be admitted to hospital include those occurring in the home (domestic burns) which contribute about three fourth of the patients and industrial burns contribute about one quarter.

By far the most serious cause and the one which produces the most extensive burns and deaths is the catching fire of clothing from an open unguarded fire. This may be due to a coal or gas heater and the coal fire is still one of the commonest

causes in this type of injury. The three national habits, the drinking of tea or other hot fluids, the popularity of open unguarded fires and the wearing of flammable clothing all contribute to the large number of burns and scalds in India.

Children may put pieces of paper in an open fire and burn themselves. Infants may crawl into the fire. Children may fall into bowls of hot water or buckets of hot water may be knocked over. Cooking appliances can be dangerous and may cause gas explosions or set fire to clothing.

The method of suicide common in the eastern countries is by pouring kerosene over clothing and setting it ablaze.

Other causes include flammable liquids, electric burns, hot metal or ashes, gas ovens, burning houses, matches, candles etc.,

Industrial burns constitute to a quarter of the burns admitted to hospital and the causes include hot molten metal and materials, hot solid objects, explosions, flame, scalds, electric burns, chemical and friction burns.[30]

In the 19th century, the eminent French Surgeon Dupuytren (1836) who first described the degrees of depth of burns studied the numerous burns coming to the Hotel Dieu in Paris. He noted that the injuries were severe when clothes caught fire and that some of the most severe were associated with epilepsy.[30]

Later in the 20th century, the use of crinoline resulted in many deaths and disfigurement. The illustrated London news in 1864 reported that, Crinoline which slays our women as war slays our men, killed 3 or 4 victims in a week.[30]

Epidemiology

Understanding the epidemiological aspects and clinical details is helpful to find out the lacunae in burns' treatment and the need to improve the same.

Burns are a global public health problem, accounting for an estimated 265 000 deaths annually. The majority of these occur in low- and middle-income countries and almost half in the South-East Asia Region. In many high-income countries, burn death rates have been decreasing, and the rate of paediatric deaths from burns is currently over 7 times higher in low- and middle-income countries than in high-income countries. Non-fatal burns are a leading cause of morbidity, including prolonged hospitalization, disfigurement and disability, often with resulting stigma and rejection. Burns are among the leading causes of disability-adjusted life-years (DALYs) lost in low- and middle-income countries. In 2004, nearly 11 million people worldwide were burnt severely enough to require medical attention.[4]

WHO reports that, In India, over 1000000 people are moderately or severely burnt every year. Nearly 173000 Bangladeshi children are moderately or severely burnt every year. In Bangladesh, Colombia, Egypt and Pakistan, 17% of children with burns have a temporary disability and 18% have a permanent disability. Burns are the second most common injury in rural Nepal, accounting for 5% of disabilities. In 2008, over 410000 burn injuries occurred in the United States of America, with approximately 40000 requiring hospitalization.[4]

Acute thermal injuries requiring medical treatment affect nearly half a million Americans each year, and 3,400 deaths annually.[31] The survival rate for

admitted burn patients has improved consistently over the past four decades[32] and is currently a favorable 97 % for patients admitted to burn centers.[33] This can be largely attributed to national decreases in burn size, improvements in burn critical care, advancements in burn wound care and treatment that have been driven by research, as reflected in the dramatic increase in burn publications over the last several decades.[8] Since the first International Congress on Research in Burns over 50 years ago, progress has been made in a host of areas, and vital improvements in early resuscitation, infection management, wound excision and coverage, and fluid management have helped in the fight against burn mortality.[8,34,35]

Risk of burn injury

Gender

Females and males have broadly similar rates for burns according to the most recent data. This is in contrast to the usual injury pattern, where rates of injury due to various injury mechanisms tend to be higher in males than females. The higher risk for females is associated with open fire cooking, or inherently unsafe cookstoves, which can ignite loose clothing. Open flames used for heating and lighting also pose risks, and self-directed or interpersonal violence are also factors (although understudied).[4]

Age

Along with adult women, children are particularly vulnerable to burns. Burns are the 11th leading cause of death of children aged 1–9 years and are also the fifth most common cause of non-fatal childhood injuries. While a major risk is improper

adult supervision, a considerable number of burn injuries in children result from child abuse.[4]

Regional factors[4]

There are important regional differences in burn rates.

- Children under five in the African Region have almost three times the incidence of burn deaths than rest of the world.
- Boys under five years of age living in low- and middle-income countries of the Eastern Mediterranean Region are almost 6 times as likely to die from burns as boys living in the European Region.
- The incidence of burn injuries requiring medical care is nearly 20 times higher in the Western Pacific Region than in America.

Socioeconomic factors

People living in low- and middle-income countries are at higher risk for burns than people living in high-income countries. With all countries however, burn risk correlates with socioeconomic status.[4]

Other risk factors[4]

There are a number of other risk factors for burns, including:

- Occupations that increase exposure to fire;
- Poverty, overcrowding and lack of proper safety measures;

- Placement of young girls in household roles such as cooking and care of small children;
- Underlying medical conditions, including epilepsy, peripheral neuropathy, and physical and cognitive disabilities;
- Alcohol abuse and smoking;
- Easy access to chemicals used for assault (such as in acid attacks);
- Use of kerosene (paraffin) as a fuel source for non-electric domestic appliances;
- Inadequate safety measures for liquefied petroleum gas and electricity.

Burns occur mainly in the home and workplace. Community surveys in Bangladesh and Ethiopia show that 80–90% of burns occur at home. Children and women are usually burnt in domestic kitchens, from overturned receptacles containing hot liquids, flames, or from cookstove explosions. Men are most likely to be burnt in the workplace due to fire, scalds, chemical and electrical burns.

Prevention

Burns are preventable. High-income countries have made considerable progress in lowering rates of burn deaths, through a combination of prevention strategies and improvements in the care of people affected by burns. Most of these advances in prevention and care have been incompletely applied in low- and middle-income countries. Increased efforts to do so would likely lead to significant reductions in rates of burn-related death and disability.[4]

Prevention strategies should address the hazards for specific burn injuries, education for vulnerable populations and training of communities in first aid. An effective burn prevention plan should be multisectoral and include broad efforts to: improve awareness; develop and enforce effective policy; describe burden and identify risk factors; set research priorities with promotion of promising interventions; provide burn prevention programmes; strengthen burn care; strengthen capacities to carry out all of the above.[4]

Indian scenario

India, the second most populous country in the world with over 1-2 billion people has an estimated annual burn incidence of 6-7 million, based on data from major hospitals extrapolated to whole of the country. It is the second largest group of injuries after road accidents. Nearly 10% of these are life threatening and require hospitalization. Approximately 50% of those hospitalized succumb to their injuries. Nearly 1 to 1.5 lac people get crippled and require multiple surgeries and prolonged rehabilitation. Seventy percent of the burn victims are in most productive age group of 15 to 40 years and most of the patients belong to poor socioeconomic strata. All these figures are approximate figures as we have no national data on burns as it is not a notifiable disease and central registry is nonexistent. The burn scenario is grave not only due to the high incidence but is also compounded by absence of organized burn care at primary and secondary health care level. But there is a silver lining to this grim situation, that 90% of all burn injuries are preventable. However, absence of stringent law regarding environmental safety, substandard manufacturing of household electric and cooking equipments and general lack of safety consciousness fail to curb this preventable menace. The economic aspect of burns

also needs to be addressed. The prohibitive cost of treatment and rehabilitation and most victims being poor explain the gross shortage of specialized burn units in public sector and reluctance on the part of the private players to share the burden. Even in the capital city of Delhi, there are less than 200 beds for burn management to cater to the need of a population of over 14 million. The recent rise in the incidents of terrorist activities and manmade disasters, contributing to quantum jump in Burn Injury cases also calls for national preparedness to cope with the challenge of this Public Health Problem.[36]

Despite many medical advances, burns continue to remain a challenging problem due to the lack of infrastructure and trained professionals as well as the increased cost of treatment, all of which have an impact on the outcome. Previous epidemiological studies from different parts of India have revealed that burn cases are prevalent all over the country.[37] Most of these patients are poor and hence, seek healthcare from government hospitals. There is no information on the pattern of outcomes among burn patients in relation to clinical aspects in India.[38]

Anatomy and Skin Function

The skin's three anatomic layers (i.e., epidermis, dermis, and subcutaneous tissue) have functions that are lost after burn injuries. The epidermis is a barrier to bacteria and moisture loss. The dermis provides elasticity and protection from mechanical trauma, and it contains blood vessels that supply all skin layers. When the skin is damaged, epidermal cells regenerate from cells deep within the dermal appendages, which is why deep dermal injury causes significant scarring and permanent skin damage.[39]

Classification of burns

Burn depth and size are important factors in determining whether a burn can be classified as minor or major, and are crucial in dictating the initial steps of burn assessment and management.[39,40] Superficial burns can often be managed on an outpatient basis, whereas full-thickness burns must be evaluated by a specialist for possible excision and grafting. Determination of burn depth can be complicated by the conversion of lower degree burn to a higher degree burn within the first several days. Conversion occurs when the damage continues to spread and burn depth increases because of thermal injury that did not fully present on initial assessment; therefore, frequent evaluation and reassessment are necessary for all categories of burns.[39,41]

Minor Burn Classification Criteria

- Does not cross major joints
- Is not circumferential
- Isolated injury
- Does not involve face, hands, perineum, genitalia, or feet
- Partial-thickness burns on less than 5 percent of total body surface area in patients younger than 10 years or older than 50 years
- Partial-thickness burns on less than 10 percent of total body surface area in patients 10 to 50 years of age.[39-43]

Burn size is determined by estimating the percentage of the patient's body surface area sustaining partial-thickness and full-thickness burns.[44] First-degree burns are not incorporated into formal estimations of burn size. The Lund-Browder classification can be used for initial assessment of burn size in adults or children. The "rule of nines" diagram is helpful for rapid assessment of burn size, but this method is less accurate than the Lund-Browder classification, especially in children. The hand is often used to measure small burn areas; it correlates to 1 percent of total body surface area. Studies have shown that the adult hand is closer to 0.8 percent of total body surface area, and that a child's hand is about 1 percent.[45]

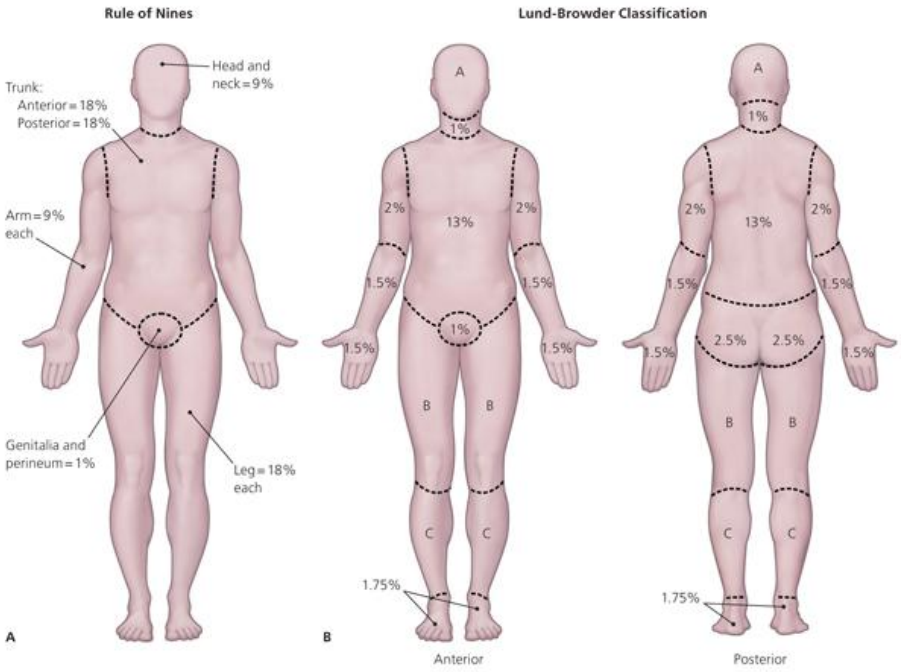


Figure 1. Diagrams to assess the extent of burns. (A) The "rule of nines" divides the body into areas of 9 or 18 percent of total body area. (B) The Lund-Browder classification is more accurate in estimating burn size, especially in children.[39,44]

Burns are classified as first-, second-, or third-degree, depending on how deep and severe they penetrate the skin's surface.[39]

First-degree (superficial) burns

First-degree burns involve only the epidermis; like a sunburn, they are erythematous, painful, and dry. They are most often the result of severe ultraviolet exposure or minor thermal injury. First-degree burns usually heal in five to 10 days.[40,46] Long-term tissue damage is rare and usually consists of an increase or decrease in the skin color.[39]

Second-degree (partial thickness) burns

Second-degree burns involve all of the epidermis and part of the underlying dermis. Superficial partial-thickness burns damage the upper layers of the papillary dermis; they are identified by clear blisters and weeping, wet, erythematous skin, and they blanch painfully when touched. These burns heal within two weeks and generally do not cause scarring; however, scarring and pigment changes are possible.[40,46]

Deep partial-thickness (deep second-degree) burns

Deep second-degree burns involve the deeper layers of the dermis (i.e., reticular dermis). They appear white and do not blanch. These burns do not heal in less than three weeks and often result in scarring and contractures.[39,40,46]

Full-thickness (third-degree) burns

Third-degree burns destroy all skin layers, including underlying subcutaneous fat. They are dark brown or tan and have a leathery feel with no sensitivity to touch. These wounds often require skin grafts, and can result in contractures.[39,40,46]

Fourth degree burns

Fourth degree burns also damage the underlying bones, muscles, and tendons. There is no sensation in the area since the nerve endings are destroyed.[47]

Pathophysiology of burn wounds

Thermal burns from dry sources (fire or flame) and wet sources (scalds) account for approximately 80 % of all reported burns[4,48] and can be classified based on the depth of burn.[4,49,50] In addition to local injury at the site of burn, severe thermal injury over a large area of the skin, roughly 20 % total body surface area (TBSA) or greater, results in acute systemic responses collectively known as burn shock.[4,51] Burn shock is characterized by increased capillary permeability, increased hydrostatic pressure across the microvasculature, protein and fluid movement from the intravascular space into the interstitial space, increased systemic vascular resistance, reduced cardiac output, and hypovolemia requiring fluid resuscitation.[52] The edema that forms in the interstitial space forms rapidly in the first 8 h following burn injury, and continues to form more slowly for at least 18 h. Volume requirements for resuscitation can be estimated by the total burn size and the patient's weight (or body surface area).[4] Additional factors influencing the management and outcome include the presence or absence of inhalation injury, the

extent of full-thickness burns, and the time since injury.[52] The actual fluid infusion rate is then titrated hourly, based on the adequacy of physiological responses, such as the urine output.[4]

Following successful resuscitation, patients with larger burns then enter a more prolonged period of catabolism, chronic inflammation, and lean body mass wasting, all of which may impair wound healing. Additionally, an increased susceptibility to infection due to altered immune status may lead to sepsis, further exacerbating systemic inflammation. The extent of inflammation and hypermetabolism is related to the extent and depth of burn, as deeper burns show higher levels of circulating cytokines and a greater hypermetabolic response. Similarly, the extent of burn is an efficient predictor of hospital length of stay and mortality.[4]

According to one model, the burn wound can be divided into three zones based on the severity of tissue destruction and alterations in blood flow. The central part of the wound, known as the zone of coagulation, is exposed to the greatest amount of heat and suffers maximum damage. Proteins denature above 41 °C (106 °F), so excessive heat at the site of injury results in extensive protein denaturation, degradation, and coagulation, leading to tissue necrosis. Around the central zone of coagulation is the zone of stasis, or zone of ischemia, which is characterized by decreased perfusion and is potentially salvageable tissue. In this zone, hypoxia and ischemia can lead to tissue necrosis within 48 h of injury in the absence of intervention. The mechanisms underlying apoptosis and necrosis in the ischemic zone remain poorly understood, but appear to involve immediate autophagy within the first 24 h following injury and delayed-onset apoptosis around

24 to 48 h postburn.[4] Other studies have shown apoptosis to be active as early as 30 min postburn[53] depending on the intensity of the burn injury.[54] Oxidative stress may play a role in the development of necrosis, as preclinical studies have demonstrated promising reductions in necrosis with systemic antioxidant administration.[55] At the outermost regions of the burn wound is the zone of hyperemia that receives increased blood flow via inflammatory vasodilation and is likely to recover, in the absence of infection or other injury.[56]

Total burn surface area (TBSA): Injured surface area refers to the extent of the burn expressed as a percent of body surface area. It reflects severity of injury, prognosis, fluid resuscitation requirements and type of treatment.

It is calculated by using the "Rule of Nine". According to this "rule", head and neck constitute 9% of TBSA, upper extremely is 9%, lower extremity 18%, anterior and posterior trunk 18% each and 1% of genitalia.

For small burns of irregular outline in adults the burn is compared to the dorsum of the patients hand which approximates 1% of TBS.[57]

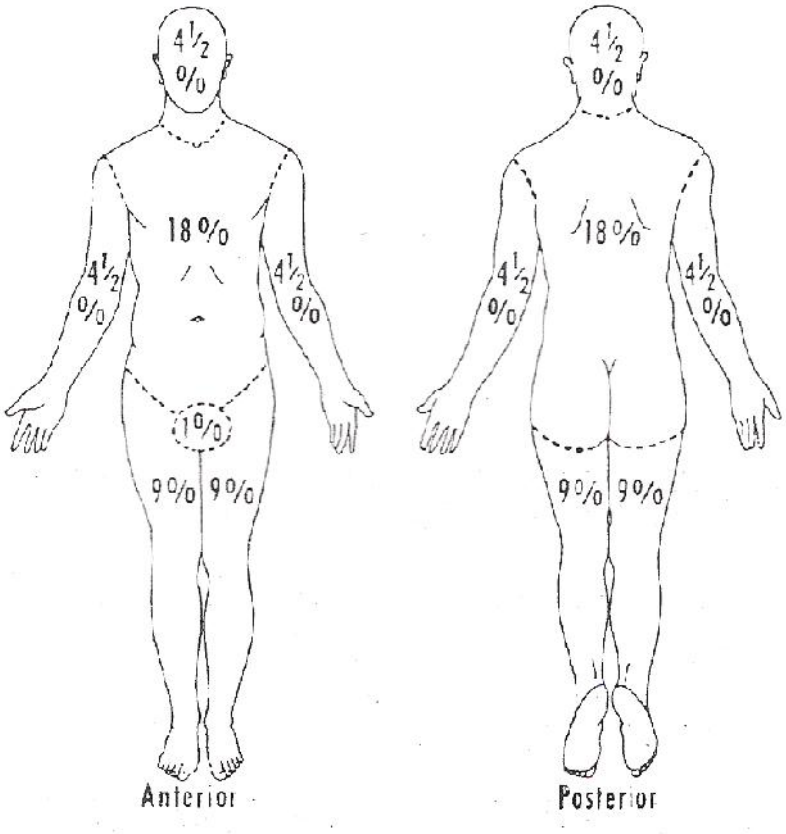


Figure 2. Rule of nines used to determine body surface area injured.[58]

In children the, size of the head is larger as compared to lower limbs. As the age advances, the proportion keeps changing till 12 years. At 12 years it reaches the adult level. The surface area of the head and neck and lower limbs in children is calculated as:

Percentage of TBSA of child's head and neck = 9 + (12 - Age)

Percentage of TBSA of child's lower limb = 41 – (12 - Age)

Although burns are different from other wounds in some respects, such as the degree of systemic inflammation, healing of all wounds is a dynamic process with overlapping phases.[59] The initial inflammatory phase brings neutrophils and monocytes to the site of injury via localized vasodilation and fluid extravasation,

thereby initiating an immune response that is later sustained by the recruitment of macrophages by chemokines. The inflammatory phase serves not only to prevent infection during healing, but also to degrade necrotic tissue and activate signals required for wound repair. Following, and overlapping with the inflammatory response, the proliferative phase is characterized by keratinocyte and fibroblast activation by cytokines and growth factors. In this phase, keratinocytes migrate over the wound to assist in closure and restoration of a vascular network, which is a vital step in the wound healing process. This network of communication between stromal, endothelial, and immune cells determines the course of healing, including closure and revascularization.[4]

Phases of wound healing[4,59]

Phase	Characteristics	Key players
Inflammatory	Vasodilation	Neutrophils
	Fluid extravasation	Monocytes
	Edema	Macrophages
Proliferative	Wound closure	Keratinocytes
	Revascularization	Fibroblasts
Remodeling	Wound maturation	Collagen
	Scarring	Elastin
		Fibroblasts/myofibroblasts

Overlapping with the proliferative phase, the final phase of healing involves remodeling the wound. During the remodeling phase, the wound scar matures as collagen and elastin are deposited and continuously reformed as fibroblasts become myofibroblasts. Myofibroblasts adopt a contractile phenotype, and thus are involved in wound contracture. The conversion from fibroblasts to myofibroblasts controls a delicate balance between contraction and re-epithelialization that, in part, determines the pliability of the repaired wound. In addition to fibroblast conversion, apoptosis

of keratinocytes and inflammatory cells are key steps in the termination of wound healing and the overall final appearance of the wound.[4]

Optimization of burn wound healing

Inflammation

Inflammation is vital to successful burn wound healing, and inflammatory mediators (cytokines, kinins, lipids, and so forth) provide immune signals to recruit leukocytes and macrophages that initiate the proliferative phase. Wound re-epithelialization, or closure, in the proliferative phase via keratinocyte and fibroblast activation, or migration from dedifferentiated hair follicles and other epidermal analogs, is mediated by cytokines recruited in the inflammatory phase. While this indicates that inflammation is essential for wound healing, aberrant inflammatory pathways have also been linked to hypertrophic scarring, and anti-inflammatory treatments could potentially aggravate symptoms and delay wound healing.[4]

Significant edema that is initiated by several factors including vasodilation, extravascular osmotic activity, and increased microvascular permeability often accompanies inflammation. Excessive or prolonged edema and inflammation exacerbate pain and impair wound healing. Interestingly, studies suggest that in the absence of infection, inflammation might not be required for tissue repair. Since inflammation can have both beneficial and detrimental effects on burn wound healing, the management becomes a clinical challenge needing therapeutic intervention only when inflammation and edema become excessive.[4]

Treatment of inflammation in large burns is difficult, as recently discussed in detail elsewhere.[60] Traditional anti-inflammatory treatments that focus on the

inhibition of prostaglandin synthesis, such as nonsteroidal anti-inflammatory drugs or glucocorticoids, impair wound healing. However, steroid administration has been shown to reduce inflammation, pain, and length of hospital stay in burn patients in several small studies. Early excision and grafting has become the gold standard for treatment of full and deep partial thickness burns, in part because early excision helps reduce the risk of infection and scarring. The timing of debridement coincides with the inflammatory phase of healing, as the burn eschar removed during excision is an inflammatory nidus and a rich medium for bacterial proliferation.[4]

Nontraditional anti-inflammatory treatments, such as opioids, have gained considerable attention but have yet to translate promising preclinical results into clinical practice for wound healing. While the majority of animal studies have demonstrated consistent anti-inflammatory effects of opioids on peripheral neurons, clinical studies have shown little to no effect on inflammation.[61] Furthermore, topical morphine delayed the early inflammatory phase and accelerated the later proliferative phase, which is supported by in vitro studies showing opioid stimulation of keratinocyte migration. Large-scale clinical trials evaluating opioid efficacy on wound healing have not yet been conducted.[4]

Infection

The skin functions as a barrier to the external environment to maintain fluid homeostasis and body temperature, while providing sensory information along with metabolic and immunological support. Damage to this barrier following a burn disrupts the innate immune system and increases susceptibility to bacterial infection. Burn wound infection was defined in a rat model with *Pseudomonas aeruginosa,* in

which the following progression was observed: burn wound colonization; invasion into subjacent tissue within 5 days; destruction of granulation tissue; visceral hematogenous lesions; and leukopenia, hypothermia, and death. Burn patients are at high risk for infection, especially drug-resistant infection, which often results in significantly longer hospital stays, delayed wound healing, higher costs, and higher mortality. Infection can lead to the development of a pronounced immune response, accompanied by sepsis or septic shock, which results in hypotension and impaired perfusion of end organs, including the skin – all processes that delay wound healing. Furthermore, the leading causes of death following a severe burn are sepsis and multiorgan failure, so prevention and management of infection is a primary concern in the treatment of burn patients. Early and accurate diagnosis of infection is difficult: C-reactive protein and the white blood cell count are most often used, since the diagnostic power of procalcitonin is questionable in burns.[4] Consensus definitions of sepsis and infection have recently been proposed that are more relevant to the burn population and are often used clinically but still require validation.[62]

The management of burn wound infections has been extensively reviewed elsewhere. Since the adoption of topical antibiotics, such as mafenide in the 1960s and silver sulfadiazine in the 1970s, and of early excision and grafting in the 1970s and thereafter, systemic infections and mortality have consistently decreased. However, Gram-positive and Gram-negative bacterial infections still remain one of the most common causes of mortality following burn injury. Bacterial cultures can aid in the selection of an appropriate antibiotic, especially in cases of bacterial drug resistance, but altered pharmacokinetic parameters in burn patients must be

considered and dosing should be adjusted accordingly to maximize antibiotic efficacy. Importantly, effective topical antimicrobials do not exist for invasive fungal infections, and fungal wound infections are associated with greater mortality rates in large burns (>30 % TBSA). Owing to high lethality, suspicion of an invasive burn wound infection mandates rapid diagnosis, often by histopathology, and excision or re-excision of the wound.[4]

Nutrition

Sustained hypermetabolism, hormone elevations, and muscle wasting following severe burn injury all contribute to the clinical outcome. Accordingly, reducing the impact of a hypermetabolic state and providing adequate nutrition are key factors that affect burn wound healing and recovery, as has been reviewed elsewhere. There is a difficult balance between the additional caloric needs to meet the demand from hypermetabolism and the consequences of nutrient overconsumption. Nutritional support following a burn injury is a complex issue. For example, early excision and aggressive feeding in children does not diminish energy expenditure but is associated with decreased muscle protein catabolism, a decreased rate of burn sepsis, and significantly lower bacterial counts from excised tissue [85]. In adults, early nutritional support is correlated with shorter stays, accelerated wound healing, and decreased risk of infection.[4]

Several nutritional factors must be considered. For example, excess carbohydrate consumption may lead to hyperglycemia that can exacerbate systemic inflammation and muscle degradation. Furthermore, excess fat consumption may exaggerate the immunosuppressed state; and since major burn injuries may also

result in immunosuppression, this exaggeration may increase the risk for infection and sepsis. Carbohydrate and fat intake must therefore be closely monitored in burn patients[4]. Guidelines for nutritional support of burn patients vary; consensus recommendations have been given by the American Burn Association and the American Society for Parenteral and Enteral Nutrition for carbohydrates, proteins, and fats.[63]

In addition to support with amino acids and vitamins, administration of insulin has been shown to decrease healing time by reducing protein catabolism and increasing skeletal muscle protein synthesis. More research is needed to optimize insulin delivery, as many recombinant growth factors, such as epidermal growth factor and transforming growth factor, are often cost prohibitive. Other anabolic agents, such as oxandrolone, have been shown to increase lean body mass recovery, decrease length of stay, and improve overall outcomes, including wound healing. Additionally, while conventional theory suggests that hemoglobin levels must be maintained above 10 g/dl to promote wound healing, preliminary evidence suggests that mild to moderate anemia has no effect on graft success if perfusion is maintained with proper circulatory volume [102]. The results of a multicenter, randomized, controlled trial (ClinicalTrials.gov NCT01079247) comparing blood transfusion with lower volumes (target hemoglobin of 7 to 8 g/dl) and conventional volumes (target hemoglobin >10 g/dl) for a large cohort of patients are expected soon and will allow for more definitive clinical guidelines on blood transfusion volumes.[4]

Resuscitation

Severe thermal injuries over a large area of the skin (>20 % TBSA) require fluid resuscitation for stabilization. Although volume guidelines and fluid compositions vary widely between centers, the goal of fluid resuscitation is to maintain organ perfusion with the least amount of fluid necessary.[52] Common traditional resuscitation formulas, such as the modified Brooke, and Parkland formulas, employ crystalloids such as lactated Ringer's that contain sodium, chloride, calcium, potassium, and lactate. During large-volume resuscitations, the addition of colloids (for example, albumin, fresh frozen plasma) as adjuncts has been successful in reducing the total volume.[52] Despite extensive research into resuscitation fluid compositions and volumes, little is known about the effect of resuscitation on wound healing. A recent meta-analysis showed a positive association between the number of grafting procedures and hypernatremia, suggesting that high serum sodium levels may inhibit graft take.[64] Additionally, it is recently shown that the rate of wound closure (healing rate) is significantly faster in patients who received lower 24-h fluid resuscitation volumes.[65] More work is needed to evaluate the effect of resuscitation on wound healing trajectories before clinical recommendations for preferred fluid compositions and volumes can be made.[4]

Wound coverage and grafting

Early excision and grafting has been the standard of care for decades. Most studies have shown that excision within 24 to 48 h after injury is associated with decreased blood loss, infection, length of hospital stay and mortality, and increased

graft take, although mortality reductions may only occur in patients without inhalation injury. Since one of the main challenges in treating acute thermal injuries is preventing infection, excising the eschar and covering the wound as early as possible are critical. The standard for rapid and permanent closure of full-thickness burns is a split-thickness skin graft from an uninjured donor site on the same patient (autograft). Such grafting provides sufficient coverage without risk of rejection, although meta-analyses have yet to determine the failure rate of split-thickness skin grafts in burn patients. Split-thickness skin grafts can be meshed with variable expansion ratios to increase the coverage area, but concerns remain over the effect that meshing has on range of motion and the graft site healing rate. On the other hand, donor sites are painful and impose their own wound-healing burden on the patient. Various dressings have been used to cover donor sites during healing, with variable results.[4]

Patients with more extensive burns often require temporary coverage with an allograft, xenograft, skin substitute, or dermal analog due to insufficient or unavailable donor sites. Allografts, or tissue taken from a living or deceased human donor, and xenografts, taken from a different species, promote re-epithelialization and prepare the wound bed for autograft, increasing the healing rate when compared with traditional dressings. A recent meta-analysis suggested that since allografts and xenografts appear to be equally effective, xenografts may be a superior choice for their increased safety and reduced price.[67] However, caution should be exercised in drawing broad conclusions from this meta-analysis because the cited studies lack standardization and critical details such as depth and size of burn, and many studies cited were merely anecdotal. A cadaver allograft is thus widely considered the best

material for temporary closure of excised wounds in patients with extensive, life-threatening burns and inadequate donor sites. The cadaver allograft is also the preferred material for protection of widely meshed autografts (3:1 or higher meshing ratios) during healing. In the latter setting, the allograft is applied over the meshed autograft in the manner of a sandwich.[4]

A variety of different skin substitutes and dermal analogs exist that can be broadly divided into those which replace the epidermis or replace the dermis. Epidermal substitutes are normally only a few cell layers thick and lack normal dermal components. Commercially available dermal substitutes include acellular matrices, commonly from human – for example, Alloderm (LifeCell, Bridgewater, NJ, USA) or GraftJacket (KCI, San Antonio, TX, USA) – or other sources (for example, Integra; Integra LifeSciences, Plainsboro, NJ, USA). Biobrane (Smith & Nephew, London, UK) is a semisynthetic, bilaminar material consisting of a nylon-mesh dermal analog (bonded with porcine collagen) and a silicone epidermal analog. Biobrane is used for temporary closure of superficial burns and donor sites. Products currently under development integrate the concept of dermal scaffolds that actively promote revascularization by incorporating stem cells and growth factors to recreate a favorable cellular microenvironment.[4]

Skin substitutes and coverage options[4]

Product name	Classification	Characteristics	Availability (company)
EpiDex	Autologous	Keratinocyte-based	No (Modex, Lausanne, Switzerland)
Alloderm	Acellular	Human origin Dermal matrix	Yes (LifeCell, Bridgewater, NJ, USA)
GraftJacket	Acellular	Human origin Tissue scaffold	Yes (KCI, San Antonio, TX, USA)
Integra	Acellular	Bovine/shark origin Bilayer matrix	Yes (Integra, Plainsboro, NJ, USA)
Biobrane	Acellular	Biocomposite dressing, nylon fibers in silicone with collagen	Yes (Smith & Nephew, London, UK)
Dermagraft	Cellular	Bioabsorbable polyglactin mesh scaffold with human fibroblasts (neonatal origin)	Yes (Organogenesis, Canton, MA, USA)
Epicel	Cellular	Keratinocyte-based cultured epidermal autograft	Yes (Genzyme, Cambridge, MA, USA)
Recell	Cellular	Autologous cell suspension of keratinocytes, fibroblasts, Langerhans cells and melanocytes	Yes (Avita, Northridge, CA, USA)

Numerous options exist for dressings. The selection of an appropriate dressing depends on several factors, including depth of burn, condition of the wound bed, wound location, desired moisture retention and drainage, frequency of dressing changes, and cost. While many factors must be considered in dressing selection, the goals in selecting the most appropriate dressing should include providing protection from contamination (bacterial or otherwise) and from physical damage, allowing gas exchange and moisture retention, and providing comfort to enhance functional

recovery. The traditional approach to burn wound care developed at the US Army Burn Center includes alternation of mafenide acetate cream in the morning and silver sulfadiazine cream in the evening, with gauze dressings used over the creams. More recently, silver-impregnated and other dressings have been introduced. Major classes of dressings include: alginate, for example Aquacel (ConvaTec, Bridgewater, NJ, USA), Comfeel (Coloplast, Minneapolis, MN, USA), or Sorbsan (Mylan, Morgantown, WV, USA); antimicrobial, for example Acticoat (Smith & Nephew, London, UK) or Silverlon (Argentum, Geneva, IL, USA); collagen, for example Fibracol (Johnson & Johnson, New Brunswick, NJ) or Puracol (Medline, Mundelein, IL, USA); hydrocolloid, for example Duoderm (ConvaTec, Bridgewater, NJ, USA), Granuflex (ConvaTec, Bridgewater, NJ, USA), or Tegaderm (3M, Maplewood, MN, USA); hydrogel, for example Dermagel (Maximilian Zenho & Co, Brussels, Belgium), SilvaSorb (Medline, Mundelein, IL, USA), or Skintegrity (Medline, Mundelein, IL, USA); and polyurethane foam, for example Allevyn (Smith & Nephew, London, UK) or Lyofoa (Molnycke, Gothenburg, Sweden). Notably, many of these dressings exhibit antimicrobial properties through silver impregnation, but recent studies suggest silver may delay wound healing and should not be routinely used on uninfected donor skin even though silver dressings may reduce wound pain. In patients with extensive or deep burns, antimicrobial efficacy should be the first priority in burn wound care.[4]

Alternatively, cell-based techniques for more permanent coverage have made progress. Research on cultured epithelial cells has made advancements, especially with respect to culture time. Culture-based options, such as Epicel (Genzyme, Cambridge, MA, USA), use a small biopsy of the patient's skin to provide

keratinocytes, which are expanded over 2 to 3 weeks (for Epicel, in the presence of proliferation-arrested murine fibroblasts) into a confluent epidermal autograft. Other options, such as ReCell (Avita, Northridge, CA, USA), take a small biopsy of the patient's skin and prepare a mixture of keratinocytes, melanocytes, and stem cells in a liquid formulation for spraying onto the excised burn wound during the same operation. These techniques may reduce the amount of donor skin needed for treatment of large burns, significantly reducing the healing time of both the donor and the burn sites, and increasing overall graft success and scar quality. More work is needed on cell-based coverage options before widespread implementation can be recommended.[4]

Initial Management of Burns

More than 95% of burn wounds can be successfully managed in the outpatient setting.[68] Excellent results can be achieved by primary care physicians with knowledge of basic concepts of burn care. Close monitoring and follow-up are important aspects of outpatient management because of the dynamic and fragile progression of burn injuries.[68] Goals of burn management include rapid healing, pain control, return of full function to the injured area, and good aesthetic results.[42]

All burns are considered trauma; therefore, the initial evaluation should include a primary survey, ensuring that body surface areas are covered after inspection because damage to the epidermis can result in temperature regulation problems. Because of the risk of airway edema and possible inhalation injury, burns to the face or neck should always prompt evaluation of the patient's airway, regardless of the burn size. The secondary survey should include a careful evaluation

of the burned area and consideration of abuse. The size, depth, and circumference of the burn should be evaluated. These initial evaluations will be used in decisions about inpatient versus outpatient management. A tetanus shot should be given to all patients with more than a first-degree burn.[39]

Immediate treatment of minor thermal burns with cool running water is controversial but often recommended. Animal studies have shown that exposing the burned area to cool running water for 20 minutes reduces the depth of injury, increases reepithelialization, and improves cosmetic outcomes; however, human studies are limited and show that the benefits last for only one hour. Although cool water is an acceptable home treatment for minor burns, ice water immersion is not because it can lead to further injury and hypothermia. Any materials that could cause further injury should be removed. Immediate attention should be given to pain control. Because burns can take weeks to heal, judicious use of narcotic analgesics is recommended. Adequate analgesia should be obtained before cleaning the wound or applying dressings.[39,67]

After evaluation and pain control, the wound must be cleaned. Scrubbing the wound with povidone/iodine solution (Betadine), chlorhexidine (Peridex), or other cleaning agents is not recommended.[67] Cleaning the wound with sterile water is generally adequate to remove debris. Management of blisters in patients with partial-thickness burns is controversial, but overwhelming evidence has shown that small blisters (less than 6 mm) should be left intact. Large blisters with thin walls should be debrided; they will likely rupture on their own, and it is beneficial from a pressure and infection standpoint to apply dressings directly to the wound bed.

Blisters that prevent proper movement of a joint or that are likely to rupture should be debrided.[39,69]

Topical burn care is the topic of many studies and discussions. Burn wounds heal best in moist not wet environments that promote reepithelialization and prevent cellular dehydration. This environment is best created by applying a topical agent or occlusive dressing to reduce fluid loss1 Topical agents provide pain control, promote healing, and prevent wound infection and desiccation.[39,43]

Commonly Used Topical Medications and Wound Membranes[39]

Name	Type of therapy	Characteristics
Bacitracin	Topical	Narrow antimicrobial coverage; inexpensive; painless; requires frequent dressing changes; can be used on face or near mucous membranes
Mafenide acetate (Sulfamylon)	Topical	Broad-spectrum antimicrobial coverage; penetrates eschar; may delay healing or cause metabolic acidosis; used for deep burns
Mupirocin (Bactroban)	Topical	Good gram-positive antimicrobial coverage; expensive; painless; requires frequent dressing changes; can be used on face
SSD (Silvadene)	Topical	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 sulfa allergy
Aquacel Ag	Absorptive dressing	Silver impregnated; broad-spectrum antimicrobial coverage; decreases dressing changes; reduces pain; decreases use of pain medications; faster wound closure than with standard therapies; decreased total cost compared with SSD
Biobrane	Biocomposite dressing	Less pain and shorter time to healing than with SSD; expensive but lower total treatment cost compared with SSD; one study showed effectiveness in superficial burns, but high failure rates with mid-dermal depth burns
Hydrocolloids (Duoderm, Urgotul)	Absorptive dressing	Less pain and shorter time to wound closure than with SSD; good for weeping burns; malodorous; opaque
Impregnated nonadherent gauze (Xeroform,	Nonabsorptive dressing	No antimicrobial activity; messy; provides a nonadherent barrier over the burn for absorptive dressings; used for superficial burns

Name	Type of therapy	Characteristics
Vaseline gauze)		
Silicone (Mepitel)	Nonabsorptive dressing	Expensive; painless; allows seepage of exudates to secondary bandage
Silver-impregnated dressing (Acticoat)	Nonabsorptive dressing	Delivers low concentrations of silver; broad-spectrum antimicrobial coverage; nonadherent; reduces pain; expensive

Superficial burns can be treated successfully with topical application of lotion, honey, aloe vera, or antibiotic ointment.[70] The lipid component of these treatments accelerates the repair of damaged skin and reduces drying. Although there are no medication requirements for patients with superficial burns, evidence has shown that topical nonsteroidal anti-inflammatory drugs and aloe vera reduce pain. Topical corticosteroids have not been shown to reduce the inflammatory reaction; therefore, they should not be used to treat superficial thermal burns or sunburns. Partial-thickness burns should be treated with a topical antimicrobial agent or an absorptive occlusive dressing to reduce pain, promote healing, and prevent wound desiccation. Topical silver sulfadiazine (Silvadene) is the standard antimicrobial treatment for partial-thickness burns; however, it is relatively contraindicated in patients with sulfa allergy, pregnant and lactating women, and newborns.[39,70]

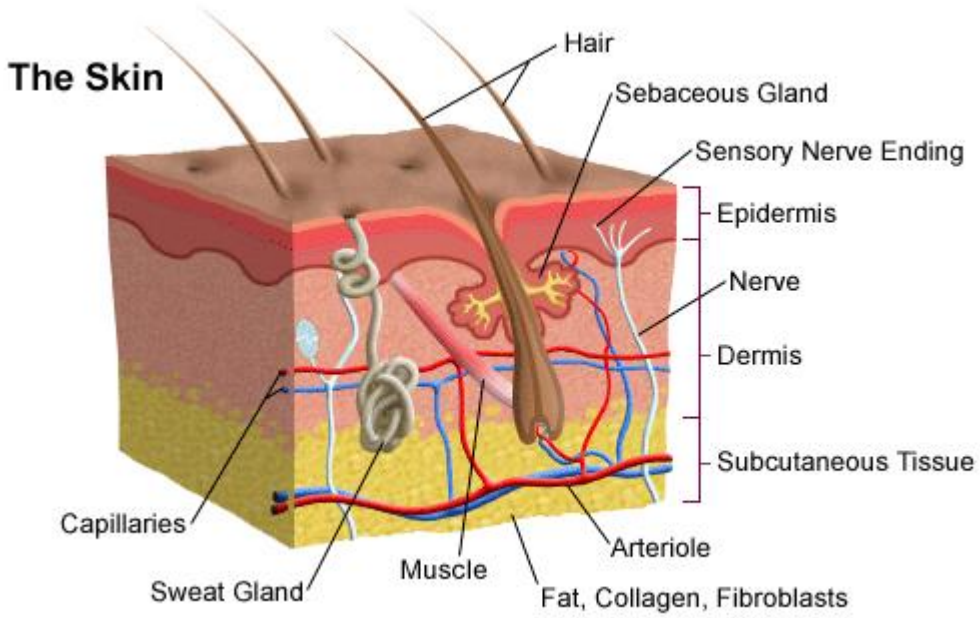
Numerous small studies have compared newer occlusive dressings with silver sulfadiazine. However, a 2008 Cochrane review found only minimal evidence to guide physicians because the included studies were flawed. The authors concluded that the use of newer occlusive dressings should be considered instead of silver sulfadiazine because they resulted in faster healing, decreased pain, fewer dressing changes, and improved patient satisfaction. Some newer occlusive

dressings are more cost-effective than silver sulfadiazine. Physicians must educate patients on the proper method for changing dressings at home.[39]

A systematic review showed that prophylactic systemic antibiotics administered in the hospital setting did not improve mortality; therefore, they generally are not recommended for burns.[39]

Treatment of second degree burns

Second-degree burns (also known as partial thickness burns) involve the epidermis and part of the dermis layer of skin.



The burn site appears red, blistered, and may be swollen and painful. In most cases, partial thickness second-degree burns are caused by the following:

- Scald injuries
- Flames

- Skin that briefly comes in contact with a hot object
- Sunburn
- Chemicals
- Electricity

The most common signs and symptoms of a partial thickness second-degree burn include Blisters, Deep redness, Burned area may appear wet and shiny, Skin that is painful to the touch and Burn may be white or discolored in an irregular pattern. The symptoms of a second-degree burn may resemble other conditions or medical problems. Superficial second-degree burns usually heal in about three weeks, as long as the wound is kept clean and protected. Deep second-degree burns may take longer than three weeks to heal. Specific treatment for a second-degree burn may be determined based on age, overall health, and medical history. extent of the burn, location of the burn, cause of the burn, tolerance for specific medications, procedures, or therapies. A second-degree burn that does not cover more than 10 percent of the skin's surface can usually be treated in an outpatient setting. Treatment depends on the severity of the burn and may include the Antibiotic ointments, Dressing changes one or two times a day depending on the severity of the burn, Daily cleaning of the wound to remove dead skin or ointment, Possibly systemic antibiotics, Wound cleaning and dressing changes may be painful. In these cases, an analgesic (pain reliever) may need to be given. In addition, any blisters that have formed should not be burst.[71]

Topical treatment

Silver sulfadiazine 1% (SSD)

Silver sulfadiazine (SSD) is the agent of choice for the outpatient management of minor or partial-thickness burns. The most prevalent topical treatment for partial thickness burns is silver sulfadiazine 1% (SSD). SSD is the topical agent of choice for severe burns and is used almost universally today in preference to compounds such as silver nitrate and mafenide acetate. SSD cream, in spite of being effective, causes some systemic side effects consisting of neutropenia, erythema multiforme, crystalluria and methemoglobinemia. Topical agents which are used only as antimicrobials include silver nitrate, sulfamylon and a combination of a sulfonamide and SSD. Sulfamylon has broad spectrum activities, but it is easily absorbed systemically and can lead to toxic complications. SSD has become the standard topical treatment for burn wounds. More recent studies have shown that the healing of partial thickness burns is delayed with the use of SSD, indicating the need for a better burn dressing. One of the potential burn dressings is sucralfate. Sucralfate is a basic aluminum complex of sucrose sulfate and a cytoprotective agent. The sporadic studies and case reports available in the literature are all consistent, indicating the favorable effect of topical sucralfate in wound repair and skin protection. Almost all studies have indicated the safe and effective behavior of this compound.[9]

Chung JY reported that, Published reports show, however, that other methods of outpatient burn management are superior. Indeed, it is difficult to find results of any trial in which SSD is the preferred treatment. The traditional idea that

SSD cream is the first-line treatment for minor burn wounds is archaic. Other methods are better and more cost effective. Evidence exists that the use of SSD may place patients at increased a risk of developing neutropenia, erythema multiforme, crystalluria, and methemoglobinemia.[72,73]

Earlier in 1984 Hoffmann S. opined that, silver sulfadiazine is an effective agent with low toxicity and few side effects. Deposition of silver in tissues, and absorption of sulfadiazine are both minimal. Present and future problems are represented by the emergence of resistant Gram negative bacilli, including Pseudomonas aeruginosa. The development of related metal sulfadiazines to be used against resistant bacteria is on an investigational stage, and clinical trials are few. Silver sulfadiazine may be used in a variety of other conditions than burns.[74]

In 1994 Fuller FW et al. reviewed the periodical literature relating to burn topical antibacterial agents as listed in the Cumulated Index Medicus from January 1, 1965, through November 30, 1992, as well as bound volumes and unpublished material reveals that the optimal dose and mode of deployment of 1% silver sulfadiazine cream in burn wound therapy have not been fully defined. Defining these should provide better control of sepsis in burn facilities. The effectiveness of a burn topical antibacterial agent depends in part upon the extent to which it is absorbed. The process of absorption of a burn topical antibacterial agent may be likened to that of an in vitro model in which the absorption of a test solute through an isolated preparation of the stratum corneum is determined in a diffusion cell. Some of the determinants are the concentration of the solute, the volume of the solvent, the duration of contact with the membrane, the binding tendency of the solute to the membrane, the integrity and wetness of the membrane, intrinsic factors

of the solute/membrane interaction (distribution and diffusion coefficients), and the adjuvant formulation. Three of these (solvent volume, duration of solute contact, and membrane wetness) are readily adjusted. As a possible preliminary to the more effective clinical use of 1% silver sulfadiazine, a study of these three factors and of the silver sulfadiazine concentration, should be carried out in a rat model with septic burns. Though control of burn wound bacteria remains of overriding importance, the absorption of silver through the burn wound treated with silver sulfadiazine, binding to normal tissues, is a source of rising concern and requires further investigation.[75]

Same authors in 2009 reported that, Silver sulfadiazine cream has an enviable safety record in burn treatment. However, it side effects, exemplified by allergic reactions to its sulfadiazine moiety, silver staining of the treated burn wound, hyperosmolality, methemoglobinemia, and hemolysis due to a congential lack of glucose-6-phospate dehydrogenase, may be missed or misinterpreted. Early post burn leukopenia, once thought to be a side effect of the use of silver sulfadiazine in burn wound therapy, is no longer regarded as such since it has been found to occur with the use of other burn topical agents. Its presence is no longer an indication to discontinue silver sulfadiazine burn wound therapy. Because these side effects are uncommon, any one physician or burn facility usually has limited experience in diagnosing and treating them.[76]

Sucralfate Cream

Sucralfate is a basic aluminium salt of sucrose octasulphate which was orally employed for prevention and treatment of several gastrointestinal diseases including gastroesophageal reflux, gastric and duodenal ulcer. Recent studies have employed

sucralfate as a topical drug for the healing of several types of epithelial wounds such as ulcers, inflammatory dermatitis, mucositis and burn wounds. Epithelial wound healing is a well orchestrated process involving hemostasis, inflammatory reaction, cell proliferation and tissue remodelling which leads to granulation tissue development and filling of the wound space. This report will review clinical evidences on the use of topical sucralfate for the management of epithelial lesions and deal with the current knowledge on the molecular mechanisms of action of this compound towards the epithelial wound healing process and will also discuss relevant patents.[77]

Sucralfate has also been shown to have antibacterial activity and has been successfully studied in decreasing pain and improving healing after hemorrhoidectomy,[9] peristomal and perineal dermatoses, moist desquamation during radiotherapy, erosion and ulceration of the perineal area, vaginal ulceration, dystrophic epidermolysis bullosa, second and third degree burns, and in a pilot trial with nonhealing, full-thickness venous stasis ulcers refractory to 8 weeks of conventional therapy.[24]

A clinical study by Banati A et al[23] in 2001 tested the efficacy of topical Sucralfate Cream in second and third degree burns. The study was carried out in two phases. The first phase comprised 60 patients, 30 of whom were treated with Sucralfate Cream while the other 30 were treated with other topical antimicrobial agents. Twenty-one of the patients in the study group had second-degree burns and nine patients' third degree burns. In the second phase, a double blind study was carried out on 25 patients where one area of burns was treated with Sucralfate Cream while another control area of the same patient was treated with a placebo

ointment, containing the excipients used during preparation of the Sucralfate Cream, without Sucralfate. In the first phase, it was seen that the period of epithelialisation of second degree burns in the study group treated with Sucralfate Cream was 18.8 days compared with 24.6 days with other topical agents. This difference is statistically significant with a P value of <0.00001. In the double blind study, also healing in the areas treated with Sucralfate was more rapid than those treated with bland placebo ointment. The difference in the two rates of healing was statistically significant with a P value of 0.00067. Histopathological studies were also carried out in 10 patients of phase I of the trial. Sucralfate Cream promotes rapid epithelialisation of second degree burns with minimal side effects and offers another topical agent in the burn care specialist's armamentarium.

Sucralfate is the aluminium hydroxide salt of the disaccharide sucrose octasulfate. It is considered a cytoprotective agent which was earlier employed to prevent or treat several gastrointestinal diseases such gastroesophageal reflux, gastritis, peptic ulcer, stress ulcer. Venous leg ulcers are an important medical issue which treatment requires a multidisciplinary approach. The main causes for chronic ulcers are considered pressure, venous and diabetic ulcers. Treatment options which rely on compression treatment, surgical intervention and medical treatment including the delivery of growth factors, require a deep knowledge of the ulcer pathogenesis.[77]

Tsakayannis et al.[79] first investigated, in a single blind fashion, the use of topical sucralfate ointment to cure non healing venous stasis ulcers in 9 patients not responding to 8 weeks of conventional therapy.[16-24] At the end of the study, 2 of 5 wounds in the sucralfate treated patients were completely healed, while the other 3

displayed a remarkable granulation tissue, neoangiogenesis and wound contraction. Conversely, wounds in the placebo patient group had no clinical improvement.

Recently a study investigated the efficacy of topical sucralfate on the healing of chronic venous leg ulcers in 50 patients by a double-blind, placebocontrolled randomized study. The study showed that the daily application of topical sucralfate (hydrophilic gel containing precipitated sucralfate at 25 g per 100 g gel) to non infected post-phlebitis/vascular ulcers, for a median time of 42 days, led to complete healing in 95.6% of patients, compared to only 10.9% of patients treated with placebo only.[24] A significant amelioration was obtained in the group treated with sucralfate with regard to local tissue inflammation, pain, burning and evolution of the granulation tissue.[24]

Morphological representative features of tissue specimens from patients affected by chronic venous ulcers after topical sucralfate treatment are depicted in. The wound area of a sucralfate treated patient shows reepithelialization. Topical sucralphate prepared as either a powder or an emollient (4 g% sucralfate in a eucerin-glycerin-water base) was also used to treat 15 patients with stomal or perineal skin ulceration after other agents had failed.[77]

Hayashi et al.[81] demonstrated complete healing in 13 patients. Conversely, one patient had partial healing while in the other patient it was necessary to threat with an additional therapy of an antifungal agent. The authors indicated that the recovery time was dependent on the severity and extent of skin ulceration and that topical application of sucralfate in the management of resistant peristomal and perineal excoriation is soothing, safe and effective.

Similarly, the effectiveness of topical sucralfate on patients with peristomal skin diseases was investigated.[17] The authors reported that in 8 out of 9 patients with faecal or urine erosions, the daily and topical application of sucralfate powder was associated with healing within 4 weeks. Conversely, there was a limited or no response to treatment in 9 patients with excoriated dermatitis (4 patients), pyoderma gangrenosum (3 patients) and traumatic ulceration after colostomy or ileostomy. It was concluded that sucralfate is an effective, safe treatment for peristomal erosions resulting from faecal or urine irritation.[17]

Likewise, the usefulness of topical sucralfate on peristomal and perineal excoriations was demonstrated.[82] Complete reepithelialization occurred in more than 90 percent of patients after 110 days of application of sucralfate prepared either as a powder or an emollient (in glycerol base).[82]

Markhan et al.[83] reported the effect of topical sucralfate 4% aqueous cream treatment on erosive dermatitis, which developed in the perineal area, buttocks and upper posterior thighs of a 42-year old woman with spina bifida and paraplegia, due to a previous ileal diversion and urostomy which have led to chronic urethral discharge and diarrhea. The authors showed that after application of the sucralfate cream 4 times daily, the erosion and ulceration healed and the dermatitis resolved within 2 months.

Recently, the potential role of sucralfate as a topical agent to treat intertrigo, a superficial inflammatory dermatitis involving juxtaposed skin surfaces to friction, heat, moisture and maceration was evaluated.[84]

A pilot study was designed in which were enrolled 8 patients with intertrigo. Sucralfate was applied twice daily to the affected skin region. The formulated agent contained 20% zinc oxide, 7% sucralfate, and 1% ketoconazole in an adsorption base. The investigators then posed a survey question in which they examined patient satisfaction after the use of topical sucralfate vs. patient' prior therapy. According to the authors, all patients stated improvement of their rash after treatment with the sucralfate preparation.[84]

The utility of the topical application of sucralfate on nonneoplastic vaginal ulceration was also reported. Three patients with vaginal ulceration were treated with vaginal douches of sucralfate 10% suspension twice daily. The authors reported that sucralfate treatment was successful in all three patients.[85]

The efficacy of the topical application of sucralfate on ulcer healing was reported by Alpsoy et al.[86] who topically applied sucralfate suspension for the treatment of oral and genital ulceration developing in patients with Behçet disease. Patients with oral ulceration were given 5 mL of sucralfate to use as an oral rinse for 1-2 minute before sleep, while in patients with genital ulceration, sucralfate solution was applied to external or intravaginal lesions using a cotton-tipped applicator or a vaginal douch, respectively. Sixteen and 14 patients with oral or genital ulceration, respectively, received sucralfate, while 14 and 13 showing matched diseases received only the placebo. Sucralfate topical treatment decreased significantly the frequency, healing time, and pain of oral ulceration and the healing time and pain of genital ulceration.

Lin et al.[87] by reviewing the topical or intralesional treatment for mucocutaneous lesions in Behçet disease, include sucralfate among the different drugs which are considered safe and useful for the treatment of mild to moderate mucocutaneous disease.

It has been suggested that the topical application of growth factors, which appear to be diminished in chronic as compared to acute wounds, would be beneficial for the healing process. On the other hand, some growth factors require long term wound contact before exerting their action. This long stay is counteracted by growth factor degradation as a result of protease activity.[88]

Szabo,[89] describing the multiple activity of sucralfate to affect gastric and duodenal ulcer healing and prevention, proposed the '1 x 1 x 1' mechanism of sucralfate action which encompasses: i) preservation of mucosal vascular integrity and of blood flow, ii) enhancement of bicarbonate and mucus secretion and finally iii) increase of binding of sucralfate to FGF and EGF which improves growth factors bioavailability and potentiates angiogenesis, granulation tissue, and epithelialization, which is regarded as the main phase of the epithelial wound healing.

Indeed, sucralfate has been demonstrated to interact with several growth factors which are involved in epithelial wound healing. Increased activity of FGF appears to have a pivotal role in the action of sucralfate. FGFs are a class of heparin binding proteins, mainly represented by basic FGF (bFGF) and acid FGF (aFGF) which stimulate mitogenic, chemotactic and angiogenic activity in several cellular types including epithelial, mesenchymal and neuronal cells. Because of their

mitogenic activity on endothelial cells, chondrocytes and fibroblast, FGFs play a key role through all healing phases.[77]

Folkman et al.[90] showed that sucralfate binds to bFGF with high affinity and protects it from acid degradation and inactivation. Later, it was demonstrated that the soluble potassium salt and the insoluble aluminum salt of sucrose octasulfate, equally to heparin, are able to bind in vitro to the aFGF and to stabilize aFGF against denaturation induced by thermal stimuli, urea and acidic pH. Thus sucralfate protects aFGF from degradation allowing it to maintain its angiogenic and mitogenic activity.[91]

Slomiany et al.[92] by investigating the susceptibility of several growth factors to degradation by H. pylori protease, demonstrated that PDGF and TGF- , but not EGF and bFGF, were susceptible to degradation by H. pylori protease and that sucralfate was capable of counteracting the effect of the bacterium. It was also indicated that SOS potentiates FGF signalling by promoting FGF-dependent FGFR (Fibroblast Growth Factor Receptor) activation and by imitating the dual role of heparin in increasing FGF-FGFR affinity and promoting receptor dimerization.[93]

Konturek et al.[94] demonstrated that ulcer healing by bFGF involves angiogenesis and cell proliferation, particularly at the ulcer border, and is increased by treatment with sucralfate.

Local application of both bFGF and sucralfate was demonstrated to be more effective than that of sucralfate or FGF alone to induce cell multiplication during early skin expansion and to facilitate the growth of neo-formed skin soft tissue.[95]

Moreover, it was demonstrated that the combined use of sucralfate and bFGF promotes endothelial cell proliferation around porous alloplastic implants in vitro.[96] By developing a non inflammatory model of angiogenesis in the rabbit cornea, it was indicated that the addition of sucralfate to bFGF determines a strong neovascular response with a low dose of bFGF that by itself is unable to elicit neovascularization.[97]

Louw et al.[98] showed a significant increase of TGF- at the ulcer size in patients with duodenal ulcer treated with sucralfate. TGF- induces proliferation of mucosal cells, gastroprotection, and vasodilatation as well healing of acute and chronic lesions. It was also demonstrated that sucralfate binds EGF in a pH-dependent manner and carries EGF to the ulcer making it available for a longer period of time. EGF exerts a trophic effect on gastroduodenal mucosa, protects it against injury, and accelerates ulcer healing by stimulating cell migration and proliferation. In addition, the important role of EGF in mediating the ulcerhealing action of the sucralfate was reported. The importance of the interaction between EGF and sucralfate in accelerating the wound healing was further corroborated by Itoh et al. who demonstrated that the combination of EGF and sucralfate significantly accelerated experimental gastric ulcer healing. The effect of sucralfate, on the expression of EGF and PDGF on gastric mucosal cell membranes, isolated from the stomach of rats treated with sucralfate, was investigated as well. It was proposed that sucralfate increases epithelial proliferation through the stimulation of gastric mucosal EGF and PDGF receptors. Moreover, improvement of duodenal mucosal turnover associated with increased levels of TGF- and epidermal growth factor receptor (EGF-R) in patients with duodenal ulcers after sucralfate treatment

was shown.[77] In addition, Liu et al.[99] showed that sucralfate protects cellular integrity from calcium imbalance by modulating the EGF-stimulated gastric mucosal calcium channel phosphorylation. Using an experimental rat model of cervicitis, it was reported that sucralfate promotes the healing of ulcerative cervicitis and reduces the healing time because of increased uPAR and EGFR expression.[100]

Sulphated saccharides, primarily sucralfate, have previously been indicated for the treatment of gastric and duodenal ulcers. In radio-labeled form, sucralfate has also been used as a diagnostic agent for the imaging of gastrointestinal mucosa, since the substance binds selectively to ulcerated areas in the stomach and upper small intestine.

Tumino G et al.[24] concluded that patients with chronic venous ulcers show improvement after the use of topical sucralfate.

Gupta PJ et al.[27] concluded that Topical sucralfate significantly reduces pain at Days 7 and 14 after hemorrhoidectomy and promotes faster wound healing compared with a placebo.

Banati A et al.[101] concluded that Sucralfate Cream promotes rapid epithelialisation of second degree burns with minimal side effects and offers another topical agent in the burn care specialist's armamentarium.

Markham T et al.[20] in a study demonstrate that Sucralfate has also been shown to have antibacterial activity. They have shown that sucralfate, structurally similar to heparin, has angiogenic properties. All 3 of these actions would account for its healing action in erosive dermatitis and Sucralfate ointment applied twice

daily for 8 weeks has also been shown to be effective in the treatment of chronic venous stasis ulcers. Sucralfate tablets softened with an aluminum hydroxide gel have been used successfully to treat decubitus ulcers. A 10% aqueous solution of sucralfate, given as a rectal enema or vaginal douche, was also successful in treating radiation-induced rectal and vaginal ulcers. More recently, a sucralfate suspension was used successfully in the treatment of oral and genital ulceration of Behçet disease. Topical 4% sucralfate in aqueous cream was effective in treating a patient with chronic irritant dermatitis when traditional barrier methods had failed.

Lentz SS et al.[21] concluded that Sucralfate vaginal douches should be considered for the treatment of non-neoplastic vaginal ulcerations, particularly when other therapy has failed.

Alpsoy E et al.[86] concluded that topical sucralfate suspension is an easy, safe, inexpensive, and effective treatment for oral and genital ulceration in patients with Behçet disease.

Andersen J et al.[102] in a study concluded that topical application of sucralfate powder does not appear to increase the rate of healing in secondary abdominal wounds after incision of a wound abscess.

More recently Beheshti A. et al.[9] in 2013 analyzed comparatively the effects of sucralfate and SSD on second degree burn wounds in rats. Forty-eight male rats were divided into three equal groups. A burn model was constituted on the back of all rats. The burned areas in the first, second and third groups were covered daily with sucralfate, SSD and cold cream (control), respectively. At the end of the 7th, 14th, 21st and 28th day, the rats were anesthetized and the burned skin tissue

samples were collected for histopathological examination. At the end of the study, the epidermis and horny layer was completely formed in the SSD and sucralfate group; however the appendix of skin was just formed in the sucralfate group. Also the percentage of wound healing was calculated at 76%, 91% and 100% respectively in the control, silver sulfadiazine and sucralfate groups. Study concluded that, Sucralfate is known to have multiple beneficial effects on wound healing. Using topical sucralfate accelerates the burn wound healing process in comparison with both the control and SSD groups and can be used as an adjunctive or alternative agent in the future.

Although the evidence is not yet conclusive the clinical evidence tends to support the antiinflammatory effect and wound healing effect of sucralfate.[24]

METHODOLOGY

This one year randomized controlled trial was conducted in the Department of General Surgery, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi from January 2015 to December 2015.

Study design

The study design was a randomized controlled trial.

Study period and duration

This study was conducted for the period of one year from January 2015 to December 2015.

Place

The present study was carried out in the Department of General Surgery, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi a tertiary care teaching hospital attached to Jawaharlal Nehru Medical College, Belagavi.

Source of Data

Patients who sustained from <50% thermal superficial second degree burns treated in the in the Department of General Surgery, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi were enrolled.

Sample size

A total of 60 patients divided into two groups of 30 each were studied.

Sampling procedure

For this study, 60 patients was considered as sample size based on the Thumb's Rule, that is, 30 in Group A (in this group patients were treated with Topical sucralfate dressing) and 30 in Group B (in this group patients were treated with Silver sulfadiazine dressing).

Selection criteria

Inclusion

- All patients with<50% thermal superficial second degree burns and scalds.

Exclusion

- Patients With >50% burns
- Patients with co-morbidities i.e DM, HIV/AIDS, Gross Anaemia (<5 gm% HB), Hypoproteinaemia (Total Protein <5mg/dl) and in a state of debility
- Electric Burns
- Corrosive Burns
- Inhaltional Burns

Ethical clearance

Prior to the commencement, the study was approved from the Ethical and Research Committee, Jawaharlal Nehru Medical College, Belagavi

Informed Consent

The patients fulfilling selection criteria were informed about the nature of study and a written informed consent was obtained (Annexure I).

Randomization

The patients with <50% thermal superficial second degree burns were randomized sequentially into two groups of 30 each as below;

- Group A: Patients in this group were treated with Topical sucralfate dressing.
- Group B: Patients in this group were treated with Silver sulfadiazine dressing.

Method of collection of data

Demographic data was recorded. All the patients included in the study were evaluated by a thorough history and physical examination and systemic examination. These findings were noted on a predesigned and pretested proforma (Annexure II).

Investigations

As a standard practice all the selected patients were subjected to the following investigations.

- Complete blood count, biochemical, serological tests, plasma proteins
- Random Blood Sugar
- Renal function tests
- Culture and sensitivity.

Procedure

The photographs of the ulcers before the dressing were taken. Also discharge was sent for culture and sensitivity before the dressings was applied.

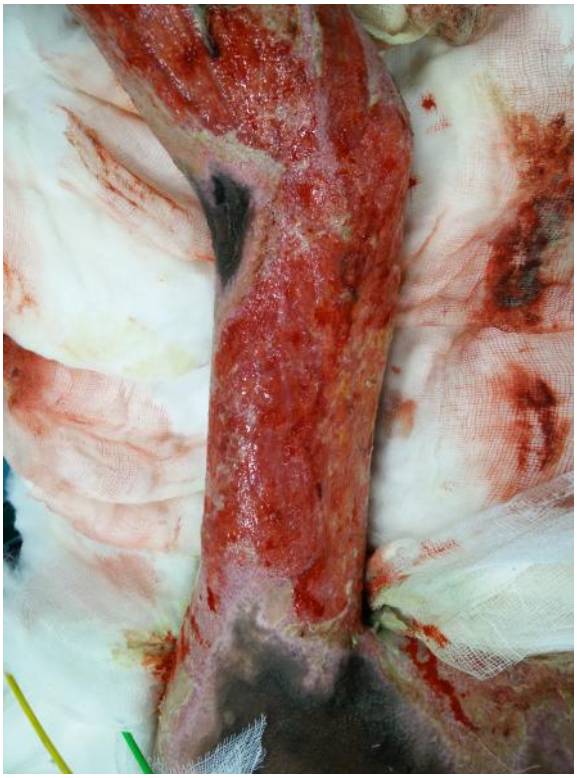
Intervention

Group A

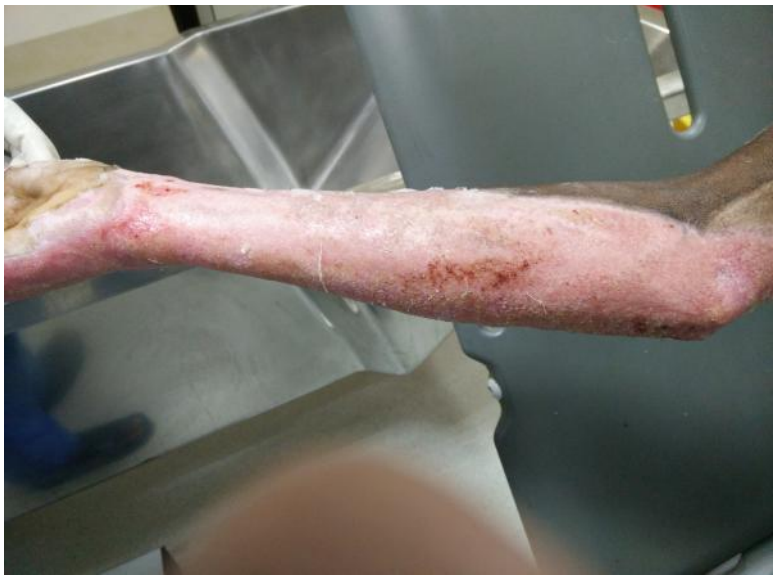
Patients in this group received topical sucralfate for wound dressing.

Group B

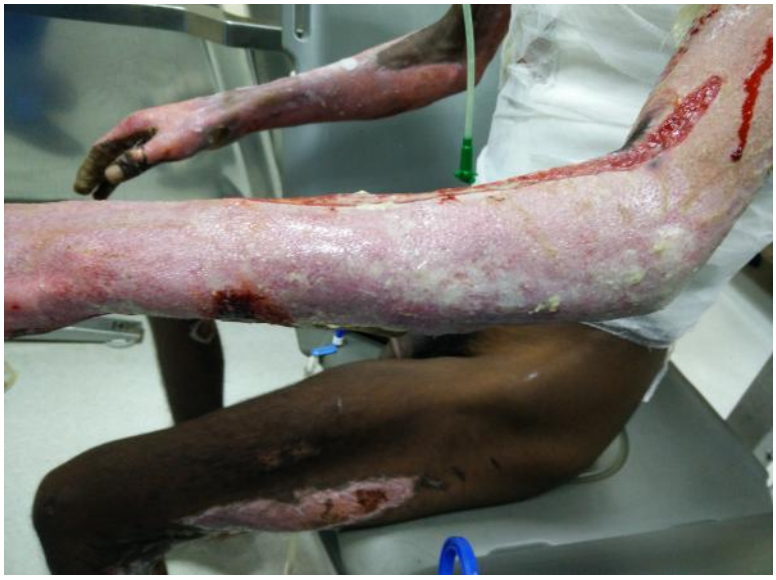
Patients in this group received dressing with silver sulfadiazine.



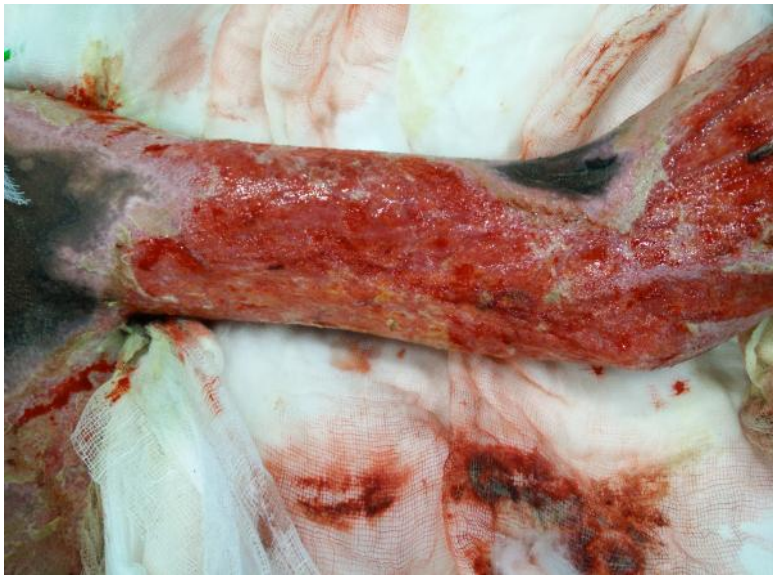
Photograph 1. Burns wound on Day 8 after Topical Sucralfate Dressing



Photograph 2. Burns wound on Day 12 after Silver Sulfadiazine dressing



Photograph 3. Burns wound on Day 12 after Silver Sulfadiazine dressing



Photograph 4. Burns wound on Day 8 after Topical Sucralfate Dressing

Outcome variables

Patients were evaluated for

- Number of days required for the healing or the appearance of healthy granulation tissue on the end point of the study that is, 21 days
- Rate of healing was compared on the end point of the study that is, 21 days

Statistical analysis

The data obtained was coded and entered in Microsoft Excel Spreadsheet (Annexure III). The data analysed using SPSS software version 20.0. The categorical data was expressed as rates, ratios and percentages and comparison was done using Fishers exact test and chi-square test. Continuous data was expressed as mean ± standard deviation and comparison was done using independent sample t test. A ‘p’ value of less than or equal to 0.050 was considered as statistically significant.

RESULTS

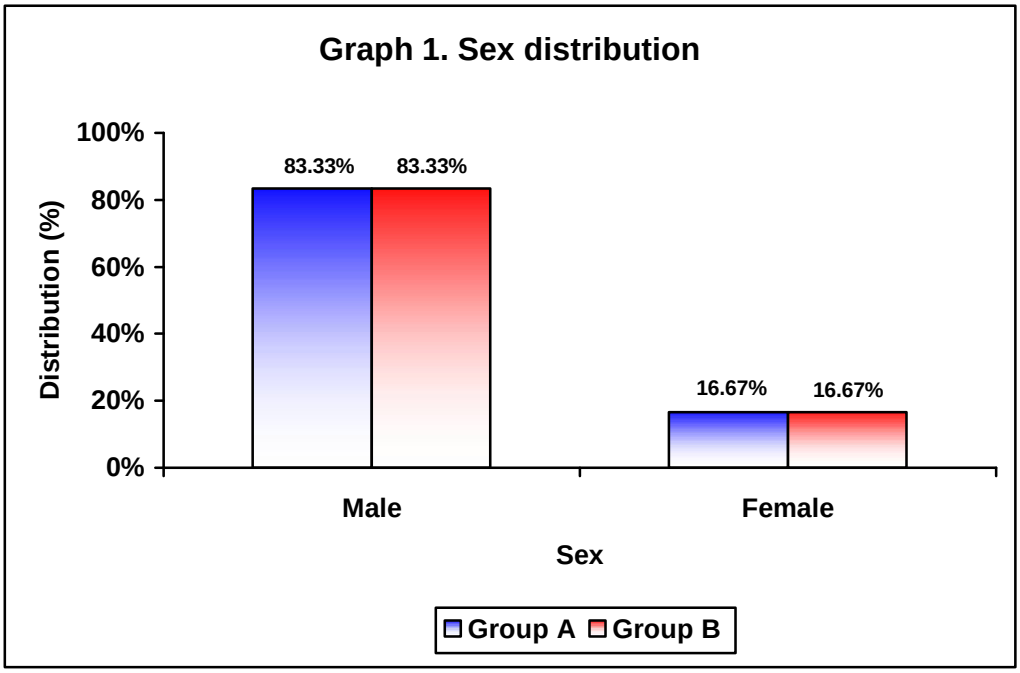
This one year randomized controlled trial was conducted in the Department of General Surgery, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi. A total of 60 patients who suffered from <50% thermal superficial second degree burns during the study period that is, from January 2015 to December 2015 were studied. These patients were divided into two groups of 30 each as Group A (in this group patients were treated with receiving Topical sucralfate dressing) and 30 in Group B (in this group patients were treated with Silver sulfadiazine dressing).

The data obtained was analysed and the final results and observations were interpreted as below.

Table 1. Sex distribution

Sex	Group A (n=30)		Group B (n=30)	
	Number	**Percentage**	**Number**	**Percentage**
Male	25	83.33	25	83.33
Female	5	16.67	5	16.67
Total	**30**	**100.00**	**30**	**100.00**

p = 1.000

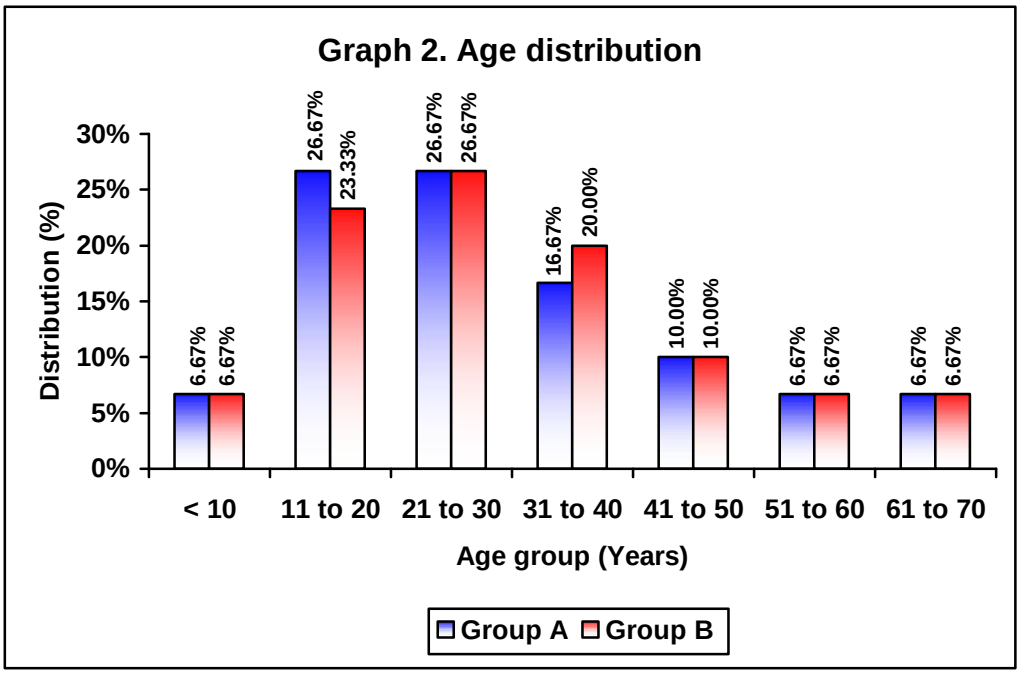


In the present study the majority of patients were males (83.33% vs 16.67%) in group A as well as group B (p=1.000).

Table 2. Age distribution

Age group (Years)	Group A (n=30)		Group B (n=30)	
	Number	Percentage	Number	Percentage
< 10	2	6.67	2	6.67
11 to 20	8	26.67	7	23.33
21 to 30	8	26.67	8	26.67
31 to 40	5	16.67	6	20.00
41 to 50	3	10.00	3	10.00
51 to 60	2	6.67	2	6.67
61 to 70	2	6.67	2	6.67
Total	**30**	**100.00**	**30**	**100.00**

p = 1.000



In this study there are equal number of patients in group A and group B in all age groups except 11 to 20 years and 31 to 40 years (p=1.000).

Table 3. Mean age

Variables	Group A (n=30)		Group B (n=30)		p value
	Mean	SD	Mean	SD	
Age (years)	29.33	16.94	29.87	16.83	0.903

In this study statistically, the mean age was comparable in group A and in group B (29.33± 16.94 vs 29.87±16.83; p=0.903).

Table 4. Burn area

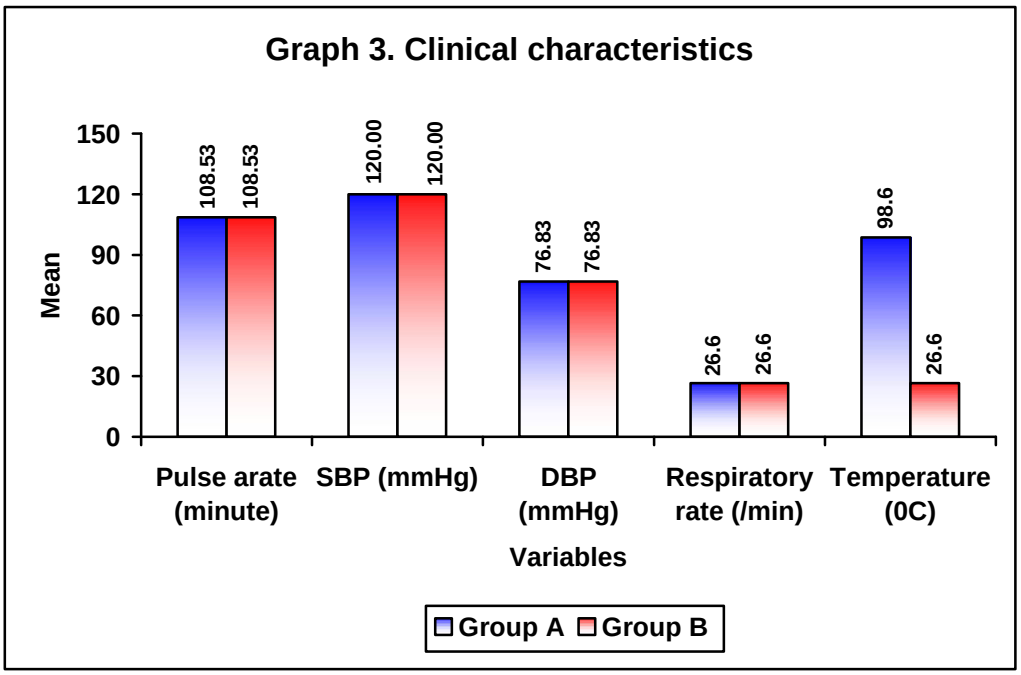
Percentage of burn area	Group A (n=30)		Group B (n=30)	
	Number	**Percentage**	**Number**	**Percentage**
10-15%	3	10.00	3	10.00
10-25%	1	3.33	1	3.33
11%-20%	1	3.33	1	3.33
12-15%	1	3.33	1	3.33
15-20%	2	6.67	2	6.67
18-23%	1	3.33	1	3.33
20-25%	1	3.33	1	3.33
21-26%	1	3.33	1	3.33
22-27%	2	6.67	2	6.67
25-30%	3	10.00	3	10.00
28-33%	1	3.33	1	3.33
30-35%	3	10.00	3	10.00
40-48%	1	3.33	1	3.33
42-45%	1	3.33	1	3.33
44-48%	1	3.33	1	3.33
45-50%	4	13.33	4	13.33
48-50%	3	10.00	3	10.00
Total	**30**	**100.00**	**30**	**100.00**

p = 1.000

The comparison of burn area in group A and group B is as shown in table. It was observed that distribution of patients according to burn area was comparable in group A and group B (p=1.000).

Table 5. Clinical characteristics

Variables	Group A (n=30)		Group B (n=30)		p value
	Mean	SD	Mean	SD	
Pulse rate (minute)	108.53	12.63	108.53	12.63	1.000
SBP (mmHg)	120.00	15.54	120.00	15.54	1.000
DBP (mmHg)	76.83	10.75	76.83	10.75	1.000
Respiratory rate (/min)	26.60	2.29	26.60	2.29	1.000
Temperature (^{0}C)	98.60	2.29	26.60	2.29	1.000

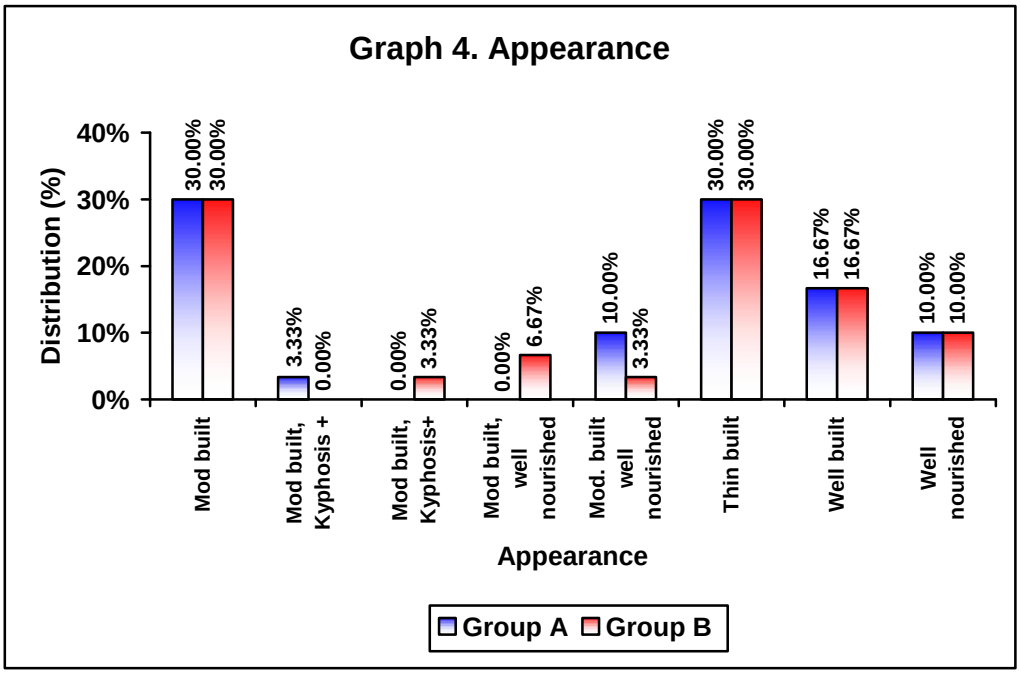


The comparison of clinical characteristics is as shown in table 5 and graph 3. It was observed that the mean pulse rate (p=1.000), systolic blood pressure (p=1.000), diastolic blood pressure (p=1.000) respiratory rate (p=1.000), and temperature (p=1.000) were comparable in group A and group B.

Table 6. Appearance

Appearance	Group A (n=30)		Group B (n=30)	
	Number	**Percentage**	**Number**	**Percentage**
Mod built	9	30.00	9	30.00
Mod built, kyphosis +	1	3.33	0	0.00
Mod built, kyphosis+	0	0.00	1	3.33
Mod. built, well nourished	0	0.00	2	6.67
Mod. built well nourished	3	10.00	1	3.33
Thin built	9	30.00	9	30.00
Well built	5	16.67	5	16.67
Well nourished	3	10.00	3	10.00
Total	**30**	**100.00**	**30**	**100.00**

p = 0.806

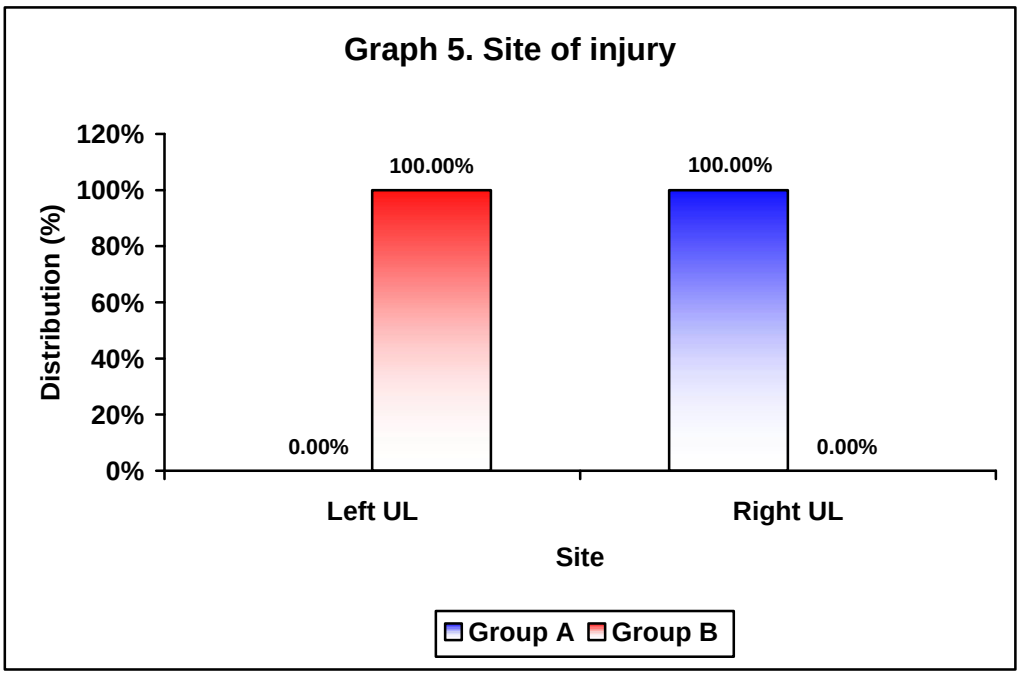


In the present study most of the patients were moderate and thin built in group A where as in group B most of the patients were moderately built (30.00%), (p= 0.806).

Table 7. Site of injury

Site	Group A (n=30)		Group B (n=30)	
	Number	**Percentage**	**Number**	**Percentage**
Left UL	0	0.00	30	100.00
Right UL	30	100.00	0	0.00
Total	**30**	**100.00**	**30**	**100.00**

p = <0.001

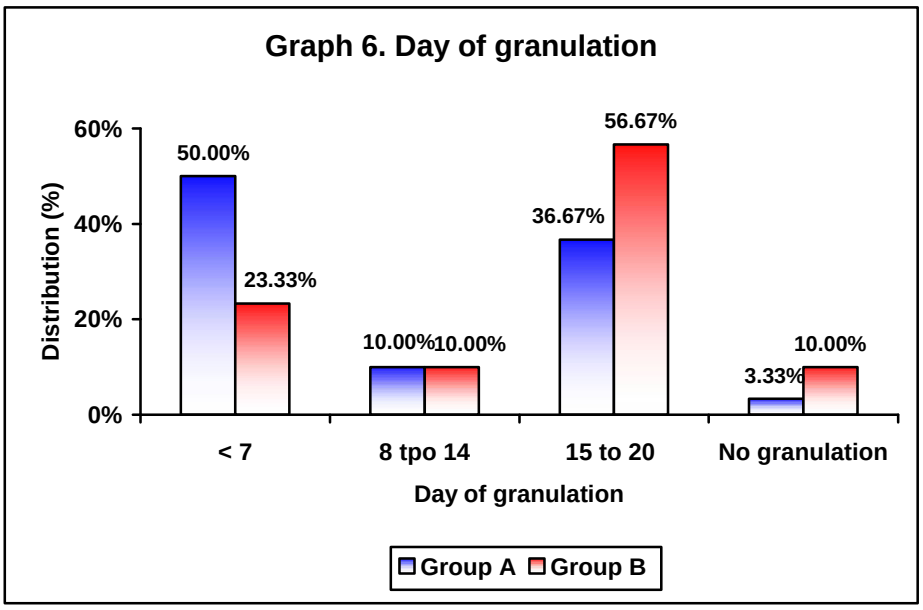


In the present study all the patients in group A had burn injury in right upper limb (100.00%) compare to left upper limb in group B. This difference was statistically significant (p <0.001).

Table 8. Day of granulation[#]

Day of granulation	Group A (n=30)		Group B (n=30)	
	Number	Percentage	Number	Percentage
< 7	15	50.00	7	23.33
8 to 14	3	10.00	3	10.00
15 to 20	11	36.67	17	56.67
No granulation	1	3.33	3	10.00
Total	**30**	**100.00**	**30**	**100.00**
Mean Day of granulation[*]	8.11	3.92	8.93	3.29

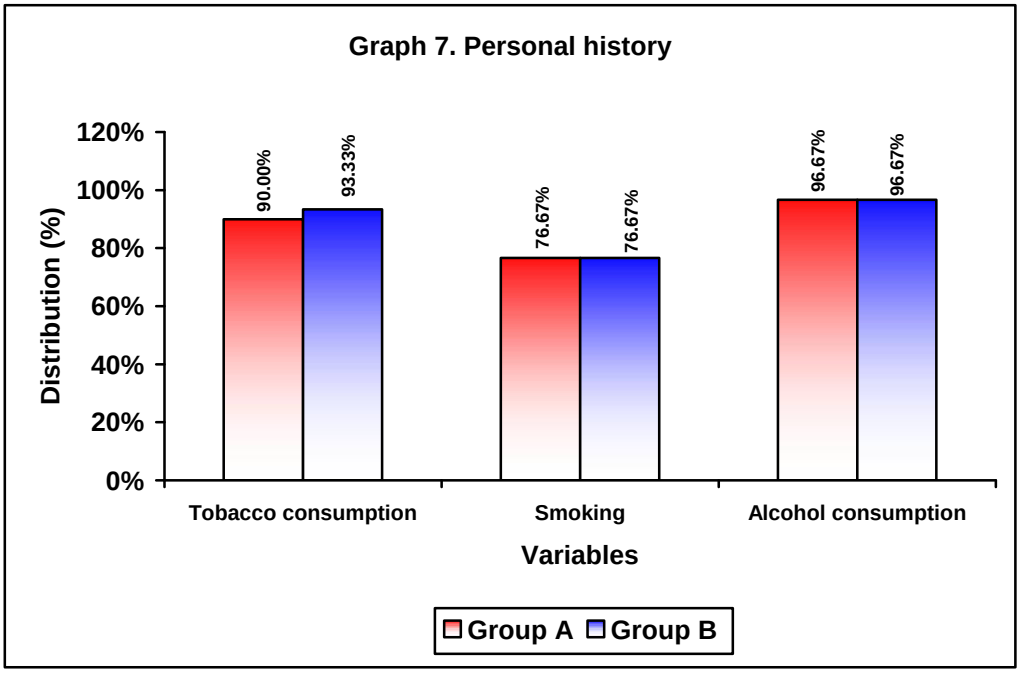
[#]p = 0.149; [*]p=0.396



In this study among 50% of the patients in group A, the day of granulation was less than 7 days. While in group B, 56.67% of the patients had granulation between 15 to 20 days (p=0.149). The mean day of granulation was 8.11± 3.92 days in group A compared to 8.93 ± 3.29 days in group B (p=0.396).

Table 9. Personal history

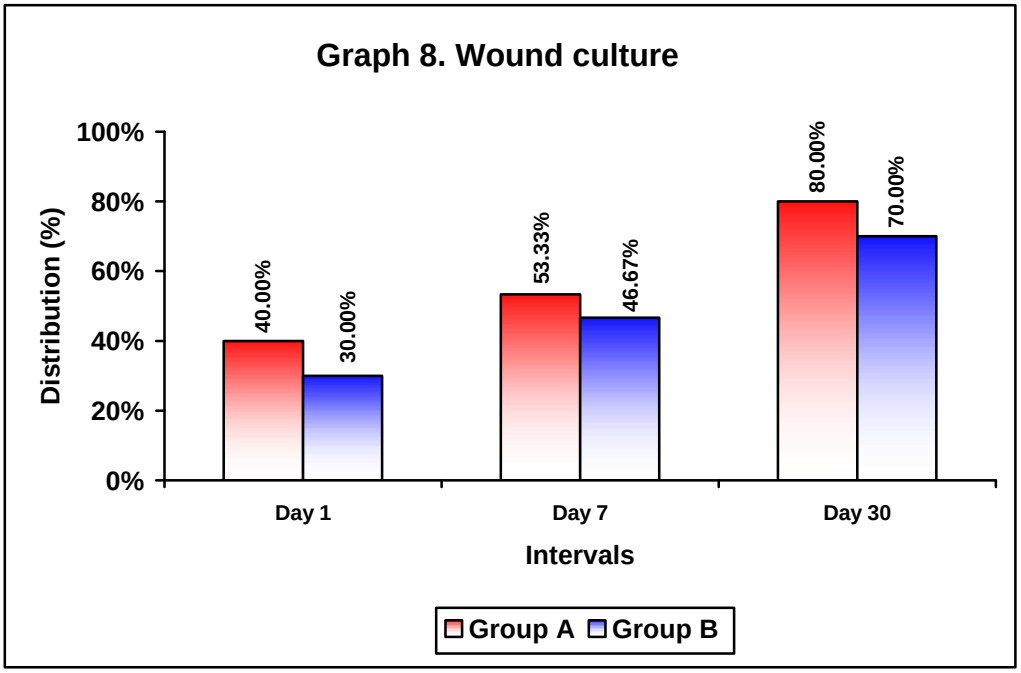
Variables	Findings	Group A (n=30)		Group B (n=30)		p value
		No	%	No	%	
Tobacco consumption	Present	27	90.00	28	93.33	0.500
	Absent	3	10.00	2	6.67	
	Total	**30**	**100.00**	**30**	**100.00**	
Smoking	Present	23	76.67	23	76.67	1.000
	Absent	7	23.33	7	23.33	
	Total	**30**	**100.00**	**30**	**100.00**	
Alcohol consumption	Present	29	96.67	29	96.67	0.754
	Absent	1	3.33	1	3.33	
	Total	**30**	**100.00**	**30**	**100.00**	



In the present study personal history of tobacco consumption (90.00% vs. 93.33%; p=0.500), Smoking (76.67% each; p=.1.000) and Alcohol consumption (96.67% each; p=0.754).

Table 10. Wound culture

Intervals	Findings	Group A (n=30)		Group B (n=30)		p value
		No	%	No	%	
Day 1	Positive	12	40.00	9	30.00	0.416
	Negative	18	60.00	21	70.00	
	Total	**30**	**100.00**	**30**	**100.00**	
Day 7	Positive	16	53.33	14	46.67	0.606
	Negative	14	46.67	16	53.33	
	Total	**30**	**100.00**	**30**	**100.00**	
Day 14	Positive	24	80.00	21	70.00	0.371
	Negative	6	20.00	9	30.00	
	Total	**30**	**100.00**	**30**	**100.00**	



In the present study wound culture on day 1(40.00% vs. 30.00%; p=0.416), on day 7 (53.33% vs. 46.67%; p= 0.606) and on day 14 (80.00% vs. 70.00%; p=.0.371).

DISCUSSION

Burns are one of the most widespread injuries all over the world. However, most burns are not severe and could be managed outside the hospital. Many types of medications have been used for burn injuries.[31]

Furthermore, different surface agents are used in burn injury treatments. The basic purpose of their use is to expedite the epithelial healing and to prevent the formation of a scar. The method in topical burn injury treatments depends on the depth of the injury and on the treatment targets. While growth hormones and cytokines considerably support the healing of burn wound, suppressor hormones adversely affect the healing. Therefore, growth hormones, cytokines, and also pharmacological agents that influence receptors of target tissue positively are used for effective treatment of wound healing.[103]

The most prevalent topical treatment for partial thickness burns is silver sulfadiazine 1% (SSD).[9] It is the topical agent of choice for severe burns and is used widely today in preference to compounds such as silver nitrate and mafenide acetate. SSD cream, in spite of being effective, causes some systemic side effects consisting of neutropenia, erythema multiforme, crystalluria and methemoglobinemia. Topical agents which are used only as antimicrobials include silver nitrate, sulfamylon and a combination of a sulfonamide and SSD. However, SSD has become the standard topical treatment for burn wounds.[9]

Recent studies have shown that the healing of partial thickness burns is delayed with the use of SSD,[14,15] indicating the need for a better burn dressing.

One of the potential burn dressings is sucralfate. Sucralfate is a basic aluminum complex of sucrose sulfate and a cytoprotective agent. The sporadic studies and case reports available in the literature are all consistent, indicating the favorable effect of topical sucralfate in wound repair and skin protection, and they have indicated the safe and effective behavior of this compound.[16-24] Sucralfate has also been shown to have antibacterial activity[25,26] and has been successfully studied in second and third degree burns, and in a pilot trial with nonhealing, full-thickness venous stasis ulcers refractory to 8 weeks of conventional therapy.[16-24]

The present study compares the efficacy of topical sucralfate with that of silver sulfadiazine, in the healing of second degree superficial burns in terms of number of days required for healing or the appearance of healthy granulation tissue and its antibacterial effect with that of silver sulfadiazine.

This one year randomized controlled trial was conducted in the Department of General Surgery, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi. A total of 60 patients who suffered from <50% thermal superficial second degree burns during the study period that is, from January 2015 to December 2015 were studied.

In the present study burn injuries were common among males as the majority of patients (83.33%) were males in group A as well as group B compared to 16.67% of the females. The sex distribution pattern in group A and group B was almost similar (p=1.000).

In this study the burn injuries were common in 21 to 30 years age group with 26.67% of the patients in group A and group B. The mean age in group A and in

group B was 29.33± 16.94 and 29.87±16.83 respectively suggesting that burn injuries are common in younger individuals, and the age distribution pattern (p=1.000) and mean age (p=0.903) were comparable in group A and group B. These findings show that, the demographic characteristics of the study population in group A and group B were similar.

With regard to characteristics of burn injury the burn area in patient in group A and group B was comparable with most of the patients (13.33%) with burn area between 45 to 50%. (p=1.000). On examination, the clinical characteristic that is, mean Pulse rate (p=1.000), systolic blood pressure (p=1.000), diastolic blood pressure (p=1.000) Respiratory rate (p=1.000), and Temperature (p=1.000) did not deferred significantly in patients in group A and group B (p>0.050). Most of the patients were moderate and thin built in group A whereas in group B most of the patients were moderately built (30.00%), (p= 0.806). Personal history of tobacco consumption (90.00% vs. 93.33%; p=0.500), Smoking (76.67% each; p=.1.000) and Alcohol consumption (96.67% each; p=0.754) were comparable in patients with group A and group B. These findings suggest that the clinical characteristics and burn injury profile of the study population in group A and group B was comparable.

Hence, the clinical and demographic characteristics of the study population in Group A and Group B were similar ruling out the possible bias in study results.

However, In this study all the patients in group A had burn injury in right upper limb (100.00%) while in group B, all the patients had burn injury on left upper limb (p <0.001).

In this study nearly half of the patients (50%) with group A had granulation within 7 days. While in group B, time for granulation took longer, among half of the patients (56.67%) it took 15 to 20 days. Furthermore, the mean day of granulation was 8.11± 3.92 days in group A compared to 8.93 ± 3.29 days in group B (p=0.396). These findings suggest that, topical sucralfate dressing results in early granulation compared to Silver sulfadiazine dressing. However this difference was statistically not significant (p=0.149).

In the present study wound culture on day one was comparable in group A and group B (40.00% vs. 30.00%; p=0.416). Similarly on day seven (53.33% vs. 46.67%; p= 0.606) and on day 14 (80.00% vs. 70.00%; p=.0.371) the wound culture was comparable in Group A and Group B.

Overall, the above observations postulate some benefit of using topical sucralfate dressing over silver sulfadiazine dressing in terms of early granulation in the healing of second degree superficial burns but no antimicrobial benfit. However we do not have similar previous studies to support these findings. Although the evidence is not strong the clinical observation in several other settings tends to support the beneficial effect of sucralfate.[24]

The role of topical use of sucralfate in the treatment of burn wounds was investigated by Banati et al.[23] The authors enrolled a group of 60 patients: 30 patients were treated with sucralfate cream and 30 with other topical agents like silver sulfadiazine or povidone iodine. They showed that sucralfate was able to increase the rate of epithelialization and earlier appearance of healthy granulation tissue in second and third degree burns, respectively.[23] The results of the present

study are in agreement with the observations reported by Banati et al despite of methodological differences

Behesti A. et al.[9] compared the effects of sucralfate and SSD on second degree burn wounds in rats and concluded that, sucralfate is known to have multiple beneficial effects on wound healing, topical sucralfate accelerates the burn wound healing process in comparison with both the control and SSD groups and can be used as an adjunctive or alternative agent in the future.

Sucralfate is used in peptic ulcer, because of its ability to enhance the protective function of the "mucus-bicarbonate", to increase the production and hydrophobicity of mucus gel and to bind bile acids. Besides, sucralfate has been shown to accelerate epithelial wound healing by increasing the bioavailability of growth factors, especially FGF, which in turn has been demonstrated to have a pivotal role in angiogenesis, an important phase in epithelial wound healing. In addition, the induction of prostaglandins production as well as cell apoptosis protection by sucralfate can favour the reepithelialization in the wound healing process. The sucralfate biological properties prompted the clinicians to use this molecule as a topical agent to treat different types of epithelial wounds caused by inflammation, infections, vascular occlusion, and physical damage. According to the clinical evidence reported in the literature, it appears that sucralfate favours epithelial wound healing. The bioavailability of growth factors appears to be one of the main and most important molecular mechanisms triggered by sucralfate in epithelial wound healing. Chronic wounds are characterized by abnormal production of growth factors. The local delivery of growth factors has been proposed as a tool to improve epithelial wound healing.[88]

Wound repair depends on neoangiogenesis, the activation of local immune response, and the presence of growth factors including epidermal growth factor (eGF), transforming growth factor b (TGF-b), and basic fibroblast growth factor (bFGF).[9] Sucralfate is known to have multiple beneficial effects on wound healing. This drug induces the proliferation of dermal fibroblasts and keratinocytes in vitro, and inhibits the release of interleukin-2 and interferon-γ from damaged skin cells. The physical barrier feature of sucralfate is to diminish inflammatory reaction and improve mucosal healing. limiting the inflammation might decrease fibrosis and stricture formation and eGF expression as well as the expression of other factors involved in tissue repair processes. Stimulating effects on vascular factors, such as angiogenesis, which play important roles in tissue repair, have been demonstrated by sucralfate. Sucralfate does not have any adverse effects thus it is widely employed in clinical practice to prevent or treat recurrent aphthous stomatitis and several gastrointestinal diseases.[9]

Unfortunately not many in vivo or in vitro histopathological studies about this drug have been carried out.[9]

Tsakayannis et al.[79] first investigated, in a single blind trial, the use of topical sucralfate ointment in non healing venous stasis ulcers in 9 patients not responding to 8 weeks of conventional therapy. At the end of the study, 2 of 5 wounds in the sucralfate treated patients were completely healed, while the other 3 displayed a remarkable granulation tissue, neoangiogenesis and wound contraction. Conversely, wounds in the placebo patient group had no clinical improvement.[79]

Tumino G. et al.[24] investigated the efficacy of topical sucralfate on the healing of chronic venous leg ulcers in 50 patients by a double-blind, placebo controlled randomized study. Study showed that the daily application of topical sucralfate (hydrophilic gel containing precipitated sucralfate at 25 g per 100 g gel) to non infected post-phlebitis/vascular ulcers, for a median time of 42 days, led to complete healing in 95.6% of patients, compared to only 10.9% of patients treated with placebo only. A significant amelioration was observed in the group treated with sucralfate with regard to local inflammation, pain, burning and evolution of the granulation tissue.

Topical sucralphate prepared as either a powder or an emollient (4 g% sucralfate in a eucerin-glycerin-water base) was also used to treat 15 patients with stomal or perineal skin ulceration after other agents had failed. Hayashi et al.[81] demonstrated complete healing in 13 patients. Conversely, one patient had partial healing while in the other patient it was necessary to treat with an additional therapy of an antifungal agent. The authors indicated that the recovery time was dependent on the severity and extent of skin ulceration and that topical application of sucralfate in the management of resistant peristomal and perineal excoriation is soothing, safe and effective.

Similarly, the effectiveness of topical sucralfate on patients with peristomal skin diseases was investigated.[17] The authors reported that in 8 out of 9 patients with faecal or urine excoriation, the daily topical application of sucralfate powder was associated with healing within 4 weeks. Conversely, there was a limited or no response to treatment in 9 patients with excoriated dermatitis (4 patients), pyoderma gangrenosum (3 patients) and traumatic ulceration after colostomy or ileostomy. It

was concluded that sucralfate is an effective and safe treatment for peristomal erosions resulting from faecal or urine irritation.[17]

Likewise, the usefulness of topical sucralfate on peristomal and perineal excoriations was demonstrated.[82] Complete reepithelialization occurred in more than 90% of patients after 110 days of application of sucralfate prepared either as a powder or an emollient (in glycerol base).[82]

Markhan et al.[83] reported the effect of topical sucralfate 4% aqueous cream treatment on erosive dermatitis, which developed in the perineal area, buttocks and upper posterior thighs of a 42-year old woman with spina bifida and paraplegia, due to a previous ileal diversion and urostomy which have led to chronic urethral discharge and diarrhea. The authors showed that after application of the sucralfate cream 4 times daily, the erosion and ulceration healed and the dermatitis resolved within 2 months.

Recently, the potential role of sucralfate as a topical agent to treat intertrigo, a superficial inflammatory dermatitis involving juxtaposed skin surfaces to friction, heat, moisture and maceration was evaluated.[84] A pilot study was designed in which 8 patients with intertrigo were enrolled. Sucralfate was applied twice daily to the affected skin region. The formulated agent contained 20% zinc oxide, 7% sucralfate, and 1% ketoconazole in an adsorption base. The investigators then posed a survey question in which they examined patient satisfaction after the use of topical sucralfate vs. patient' prior therapy. According to the authors, all patients stated improvement of their rash after treatment with the sucralfate preparation.[84]

The utility of the topical application of sucralfate on nonneoplastic vaginal ulceration was also reported. Three patients with vaginal ulceration were treated with vaginal douches of sucralfate 10% suspension twice daily. The authors reported that sucralfate treatment was successful in all three patients.[85]

The efficacy of the topical application of sucralfate on ulcer healing was reported by Alpsoy et al.[86] who topically applied sucralfate suspension for the treatment of oral and genital ulceration developing in patients with Behçet disease. Patients with oral ulceration were given 5 mL of sucralfate to use as an oral rinse for 1-2 minute before sleep, while in patients with genital ulceration, sucralfate solution was applied to external or intravaginal lesions using a cotton-tipped applicator or a vaginal douch, respectively. Sixteen and 14 patients with oral or genital ulceration, respectively, received sucralfate, while 14 and 13 showing matched diseases received only the placebo. Sucralfate topical treatment decreased significantly the frequency, healing time, and pain of oral ulceration and the healing time and pain of genital ulceration.[86]

Lin et al.[87] by reviewing the topical or intralesional treatment for mucocutaneous lesions in Behçet disease, include sucralfate among the different drugs which are considered safe and useful for the treatment of mild to moderate mucocutaneous disease.

Overall, topical sucralfate dressing is efficacious over silver sulfadiazine dressing in terms of early granulation in the healing of second degree superficial burns with comparable antimicrobial resistance pattern to that of silver sulfadiazine dressing. However these findings need further evaluation due to the several

limitations of the study viz, the small sample size, limited study duration of 21 days only, during which all the wounds did not heal completely. Finally, this study was limited to second degree burns and may not be generalized in all the burn injuries.

CONCLUSION

Topical sucralfate dressing is efficacious in terms of development of early granulation in the healing of second degree superficial burns compared to silver sulfadiazine dressing while antimicrobial resistance pattern is comparable to that of silver sulfadiazine dressing.

SUMMARY

Burns are one of the most widespread injuries but, most burns are not severe and could be managed outside the hospital. Many types of medications have been used for burn injuries. The present study was aimed to compare the efficacy of topical sucralfate with that of silver sulfadiazine, in the healing of second degree superficial burns in terms of number of days required for healing or the appearance of healthy granulation tissue and its antibacterial effect.

The present one year randomized controlled trial was done in the Department of General Surgery, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi. A total of 60 patients who suffered from <50% thermal superficial second degree burns during the study period that is, from January 2015 to December 2015 were studied. The selected patients were divided into two groups of 30 each as Group A (treated with Topical sucralfate dressing) and 30 in Group B (treated with Silver sulfadiazine dressing).

Majority of patients were males in group A as well as group B (83.33% vs 16.67%; p=1.000). There were equal number of patients in group A and group B in all age groups except 11 to 20 years and 31 to 40 years (p=1.000). The mean age was comparable in group A and in group B (29.33± 16.94 vs 29.87±16.83; p=0.903). Other characteristics inlcluding burn area was comparable in group A and group B (p=1.000). the mean Pulse rate (p=1.000), systolic blood pressure (p=1.000), diastolic blood pressure (p=1.000) Respiratory rate (p=1.000), and Temperature (p=1.000), personal history of tobacco consumption (90.00% vs. 93.33%; p=0.500), Smoking (76.67% each; p=.1.000) and Alcohol consumption (96.67% each;

p=0.754) were comparable in group A and group B. Most of the patients were moderate and thin built in group A where as in group B most of the patients were moderately built (30.00%), (p= 0.806). All the patients in group A had burn injury in right upper limb (100.00%) compare to left upper limb in group B. This difference was statically significant (p <0.001). the day of granulation was less than 7 days in group A among 50% of the patient While in group B, 56.67% of the patients had granulation between 15 to 20 days (p=0.149). The mean day of granulation was 8.11± 3.92 days in group A compared to 8.93 ± 3.29 days in group B (p=0.396). The wound culture on day 1(40.00% vs. 30.00%; p=0.416), on day 7 (53.33% vs. 46.67%; p= 0.606) and on day 14 (80.00% vs. 70.00%; p=.0.371) did not differ significantly in both the groups.

Overall, topical sucralfate dressing is efficacious in terms of development of early granulation in the healing of second degree superficial burns compared to silver sulfadiazine dressing while antimicrobial resistance pattern is comparable to that of silver sulfadiazine dressing.

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ANNEXURE I

CONSENT FOR PARTICIPATION IN RESEARCH STUDY

Mr. /Mrs. /Miss. _____ we are requesting you to enroll yourself in study titled "A ONE YEAR RANDOMISED CONTROL TRIAL COMPARING THE EFFICACY OF TOPICAL SUCRALFATE VS SILVER SULFADIAZINE IN THE MANAGEMENT OF BURNS" conducted by Dr. ***** ****, Post Graduate in M.S. General Surgery under the guidance of Dr. ***** *****. Professor, Department of General Surgery, and principal, J .N. Medical College, Belagavi under KLE university, Belagavi.

Respected Sir/Madam, We request you to participate in our study as you are eligible for participating in the study. Your participation in the research is absolutely voluntary. Your decision to participate in the study or otherwise will not affect the relationship with KLE hospital. If you decide not to participate, you are free to withdraw at any time. During the study the outcome will be assessed by some questions asked by the post-graduate student and which will have to be answered by you.

Purpose of the study

This study is being done to compare the efficacy of topical sucarlfate dressing when compared with the conventional silver sulfadiazine dressing in patients with <50% superficial thermal second degree burns.

Procedure Involved

Two techniques are used in the dressings of <50% superficial second degree burns, dressings done using topical sucralfate and dressings done using silver sulfadiazine.

Risks and Benefits

There is no increased risk involved in becoming a part of this study and the complications are those which are normally anticipated. This study will help to assess the efficacy of topical sucralfate in comparison with the standard techniques. The results derived at the end of study will benefit all similar patients admitted in this hospital.

Withdrawing/removal from the study

The participant has freedom to withdraw from the study whenever he/she wishes and with any prior notice. Even if you decline to participate, there will not be any change in the line of your management or the relationship with your doctor. You will be told about all the new information that affects your decision to participate in the study. The investigator may also exclude a participant from the study at anytime.

Privacy and Confidentiality

The only people to know that you are a research subject are members of the research team. No information about you or information provided by you during the research will be disclosed without your written permission except:

In emergency to protect your rights and welfare,

If required by law.

Institutional/sponsors policy

If any unforeseen complications or injury occurs during the period of study the participant will be given treatment within the limitations of KLE's Dr. Prabhakar Kore Charitable Hospital.

Financial Incentives for participation

The participant neither gets any financial incentives during the period of study nor will be asked to pay for the purpose of this study.

Authorization to Publish Results

When the results of the research are published or discussed, in a conference, no information will be displayed that would disclose your identity. Any information that is obtained in connection with this study and that can be identified with your identity will remain confidential.

Contact details

The participant can contact me at any time during the study period for clarification of doubts or any questions. In case of any queries, you can contact the following:

DR. *** *******
Postgraduate student,
Department of surgery,
Jawaharlal Nehru Medical College,
KLE University,
Belagavi- 590 010
Ph no: ****** *****

"A ONE YEAR RANDOMISED CONTROL TRIAL COMPARING THE EFFICACY OF TOPICAL SUCRALFATE VS SILVER SULFADIAZINE IN THE MANAGEMENT OF BURNS"

I, Mr. /Ms. /Mrs. _____ voluntarily agree for the participation as a subject of study. By signing this consent form I am not giving up any of my legal rights, I may withdraw from the study anytime. I am signing the consent form after having read or been read for me in vernacular language, including the risks and the benefits and having all my questions answered.

Subject Name: _____

Signature or the Left Thumb Print of Subject: _____

Witness Name: _____ Signature: _____

Investigators Name: _____ Signature: _____

Date: _____

Place: _____

ANNEXURE II – PROFORMA

Name of the patient :

Age :

Sex :

Address :

Occupation :

In Patient number :

Date of admission :

Clinical diagnosis :

History

History of burns :

Percentage of burns over the body:

Systemic symptoms :

Other complaints :

Personal history :

General Physical Examination

Vitals

Appearance :

Local examination

Position of the patient:

Inspection : Burns wound :

Site : Shape :

Skin over surrounding area: Photos :

Day 1	Day 4	Day 8	Day 11	Day 15	Day 18	Day 21

Culture & sensitivity:

Day 1	Day 7	Day 14

Palpation:

Systemic examination

Cardiovascular System : Respiratory System :

Central Nervous system : Per abdomen :

Investigations

Complete blood count :

Urine routine :

Serum urea and creatinine :

Culture and sensitivity :

ANNEXURE III – KEY TO MASTER CHART

-	-	Absent
%	-	Percentage
/min	-	Per minute
+	-	Present
^{0}C	-	Degree centigrade
A. Baumanii	-	Acinetobacter baumannii
Ca	-	Carcinoma
DBP	-	Dialostic blood pressure
deg	-	Degree
E.coli	-	Escherachia coli
F	-	Female
k/c/o HTN on rx	-	Known case of hypertension on treatment
LT U/L	-	Left upper limb
M	-	Male
mmHg	-	Millimeter of mercury
MRSA	-	Methicillin resistant staphhylococcus aureus
NAD	-	No abnormality detected
P.	-	Pseudomonas
RT U/L	-	Right upper limb
SBP	-	Systolic blood pressure
sup	-	Superficial