

Skin Burns: Pathophysiology, types and Therapeutic Approaches

Abstract

Burn injury is considered as one of the complex traumatic events affecting multiple organs with local and systemic side effects. Burn trauma may be represented as a type of injury by heat, electricity, chemical, radiation, freezing, and friction. However, profound nerve injury may damage the muscle, bone, vascular, dermal, and epidermal tissues. Burns victims may experience many potentially fatal complications depending upon the location affected and the depth of burns, such as burn shock, electrolyte imbalance, and respiratory failure. This article reviews the pathophysiology, types, and recent advancements with a focus on the therapeutic approaches.

Key Words: Burn Injury, Burn Trauma, Pathophysiology, Recent Advancements

Introduction

Burn can be described as “a systemic inflammatory response syndrome ” (Sepsis et al., 2007). Burns wound infection is mainly caused by several resistant organisms, including MRSA (methicillin-resistant *Staphylococcus aureus*), *Pseudomonas Acinetobacter*, vancomycin-resistance Enterococcus., non-*albicans Candida* spp., and *Aspergillus* (Norbury et al., 2016). Several antimicrobial agents in topical applications such as creams are used to treat burns (Evers, Bhavsar, & Mailänder, 2010; Feck, Baptiste, & Tate Jr, 1979).

Burns

Burns are characterized by a type of severe injury or damage to the skin or other types of tissues that could be triggered by heat, electricity, radiation, abrasion, and chemicals contact.

According to the American burn association, a burn can be described as “Systemic inflammatory response syndrome “ (Sepsis et al., 2007).

Burns can also be caused due to violence or self-harm between people. In case of burns, specific cells in the skin or other body tissues are damaged by hot liquids (scalds), hot solids (contact burn), and fires (Othman & Kendrick, 2010). Flames cause most burns, approximately 55%, while scalds follow it, approximately 40%. However, inhalation injury and mild concomitant trauma are associated with flame burns. Patient age influences the cause of trauma. In

children, due to hyperactive behavior and contact with hot liquid, the majority of burns are scalds burn (70%). The leading cause of burn-in adolescents and young owing to inadequate management of fire, flame, and flammable liquid. In contrast, in adults, flame burns are accidental at work (approximately 1/3) (Evers et al., 2010).

Pathophysiology of Burn

The body has very few specific protective and repair mechanisms for thermal, chemical radiation, and electrical burn. Denaturation of protein is most common for all types of burn. The burn's pathophysiology includes body responses, further divided into local response and systemic response (Keck, Herndon, Kamolz, Frey, & Jeschke, 2009; Palao, Monge, Ruiz, & Barret, 2010). The local response includes three zones of burns characterized by Jackson. Burn zones are of three types

- Coagulation zone
- Stasis zone
- Hyperemia zone

(Hettiaratchy & Dziewulski, 2004).

In the coagulation zone, maximum destruction and irretrievable tissue loss occur due to constituent protein coagulation. Adjoining zone of stasis is well defined by reduced tissue perfusion. Necrosis, hypoperfusion, infection, desiccation, and edema occur in this zone. However, with appropriate wound

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care management, tissue perfusion increased, which prevent irreversible damage. Stasis zone leads to wound widening. The Hyperemia zone is the outermost periphery in which tissue perfusion increased due to viable cells and tissues in this zone consistently recover unless complicated by severe sepsis and hypoperfusion (Hettiaratchy & Dziewulski, 2004).

During the systemic response, when the burn spreads the 30% of total body surface area (TBSA) cytokines and other inflammatory mediators release at the injury site has a systemic effect (Keck et al., 2009). Frank Underhill described the correlation between un-resuscitated burn shock and hematocrit values in the burn patient by providing a complete understanding of pathophysiology. An increase hematocrit value is interpreted as plasma volume deficit (Underhill, Carrington, Kapsinow, & Pack, 1923). Moore and cope described the effect of hypovolaemia caused by fluid and plasma protein translocation from both burned and non-burned tissues (Cope & Moore, 1947).

The pathophysiological changes appear from a severe thermal burn injury. It involves the cardiovascular changes (increase capillary permeability, hypovolaemia, and myocardial depression owing to tumor necrosis release factor α). As a result of these changes systemic hypotension and end-organ hypoperfusion develops (Hettiaratchy & Dziewulski, 2004). Pulmonary (bronchoconstriction and respiratory distress syndrome), gastrointestinal (impairment of gastrointestinal motility and splanchnic vasoconstriction, decrease catabolism, increase gastric pH and maintain gut integrity), hematopoietic (renal, immunodepression) and renal vasoconstriction (Evers et al., 2010).

Epidemiology

Burn is considered as the 4th main cause of injury followed by road traffic (RT) injuries, drop injuries and social violence, counting 5-12% of all worldwide injuries (Peck, 2011). According to WHO, approximately 265,000 people died each year by burn injuries (Organization, 2008). The present burn injuries burden is profoundly disproportionate, with a frequency excessively affecting the poor and helpless (Forjuoh, 2006). Approximately 80% of thermal burns are from dry sources (fire & flame) and wet sources (scalds) (Sepsis et al., 2007). About half a million Americans affects each year with thermal injuries, with approximately 40,000 hospitalization

and 3,400 deaths annually (Gibran et al., 2013). However, over the past four decades, survival rate for burn patient has been improved consistently (R. Mann & Heimbach, 1996). The WHO states that over 95% (the vast majority) of fire burn injuries are related to low and middle-income countries (Othman & Kendrick, 2010). According to the Pakistan national emergency department, 146.8 burn injury patients per 100,000 ED visits in Pakistan. Male comprised 67.2% and female 32.8%. The leading causes of burn-in Pakistan were scalds (64.3%) associated by fire, flame, or smoke burns (16.4%).

Etiology

Burns wound infection is mainly caused by several resistant organisms, including Gram+ve bacteria, Gram -ve Bacteria, virus and Fungi.

Examples of Gram +ve bacteria

- MRSA (Methicillin-resistant *Staphylococcus aureus*)
- Vancomycin-resistance *Enterococcus*
- Streptococcus (*S.pyogenes*, *S.agalactiae*)

Examples of Gram -ve bacteria

- Pseudomonas (*P.aeruginosa*)
- *Acinetobacter*
- *Enterobacteriaceae*
- Anaerobes (*Bacteroides*, *fusobacterium*)

Fungi/yeast includes

- *Candida* sp.,
- *Aspergillus*.
- *Fusarium*

Viruses include

- *Herpes simplex*
- *Varicella-zoster*

(Norbury et al., 2016).

Sign and symptoms

Burn injury is a complex, painful incident through several local and systemic effects and also affects a number of organs outside the skin. Burn patient shows a complex inflammatory response reaction. However, in the acute phase, inflammation shows adverse effects due to capillary leakage, proliferation of inhalation injury with failure of other organs (Evers et al., 2010).

According to the reported burn data, heating burns from dry source (flame, fire) or wet source (scalds) accounts for around 80%. Thermal and local injury at the location of burn and thermal injury causes the systemic response collectively known as burn shock. Thermal injury covers 20% of the total

body surface area. An increase in capillary permeability describes burning shock. Hydratic pressure through the microvasculature also increased fluid and protein drive from intravascular spaces to interstitial spaces. Cardiac output decrease and hypovolemia, often demanding volume resuscitation (Pham, Cancio, & Gibran, 2008). Formation of edema initially within 8hrs of injury, and it continues slowly at least 18h after injury (Shirani, Vaughan, Mason, & Pruitt, 1996). However, the volume requirement for resuscitation is estimated by patient body weight and complete burn area (Pham et al., 2008). The actual fluid infusion rate depends upon the body's physiological response, e.g., urine output (Dries, 2009). After successful resuscitation, chronic inflammation, severe hypermetabolism, and lean body mass wasting develop among burn patients (Porter, Hurren, Herndon, & Borsheim, 2013).

Additionally, systemic inflammation may lead to sepsis because the immune system is altered due to an increase in infection susceptibility (Farina, Rosique, & Rosique, 2013). So, impairment in wound healing via delay re-epithelialization is mainly caused by sustained hypermetabolism and inflammation (Edgar, Fish, Gomez, & Wood, 2011; Sommer et al., 2013). There is a correlation between the extent of the inflammation and hypermetabolism with the burn's extent and depth. However, a higher level of circulating cytokines in the deeper burn shows a higher metabolic response (Sakallioğlu et al., 2006). The burn's extent determines the hospital stay length and mortality (Wilmore, Long, Mason Jr, Skreen, & Pruitt Jr, 1974).

Table 1. Diagnostic Parameters for Burn

Tests	Findings	References
Risk Factors	Extent and deepness of the burn, full thickness of burn, presence or absence of inhalation in the burn, burn injury, and age of burn patient are connected with the amplified risk of mortality of burn patient.	(Rowan et al., 2015)
Physical Examination	During the physical examination, it is essential to assess the following edema tissue necrosis sepsis systemic changes pain, erythema, color changes premature separation of burn eschars unexpected changes in the depth and appearance of the wound	(Farina Junior, Rosique, & Rosique, 2013; Rowan et al., 2015)
Lab test for diagnosis of wound infection	Quantitative biopsy Quantitative swab (flawed test but may help in identifying organism) Tissue histology Use of C reactive protein and white blood cell account	(E. A. Mann, Wood, & Wade, 2011; Sepsis et al., 2007)

Phases of Wound Healing

Although there is a difference between burns wound and other skin wounds concerning grade of systemic inflammation (Tiwari, 2012), healing is driven by a process with overlying phases (Gurtner, Werner, Barrandon, & Longaker, 2008). The first stage of wound healing is Hemostasis stage. Second stage is known as the inflammatory phase. This phase can bring the neutrophils and monocytes through localized vasodilation and fluid extravasation to the injury site to initiate the immune response, further

maintained by the enrollment of macrophages by chemokines (Tiwari, 2012). The inflammatory phase degrades the necrotic tissues and activates the signal essential for wound healing and the prevention of infection. The third phase is the proliferative phase, overlapping the inflammatory phase, determined by keratinocytes' activation and fibroblastic cells by cytokinesis and growth factors (Werner, Krieg, & Smola, 2007). So, keratinocytes can migrate above the wound, restore and close the vascular linkage because it is the primary step of the wound healing

process (Pastar et al., 2014). A communication network between the stromal, endothelial, and immune cells formed is favorable in determining the healing course and closure and revascularization. Remodeling of the wound is the final phase of wound healing, followed by the proliferative phase (Widgerow, 2011). During this phase, the wound scars mature because elastin and collagen are deposited and reformed as a fibroblast, which further

becomes myofibroblasts (Singer & Clark, 1999). Myofibroblasts intricate wound contracture due to contractile phenotype. A gentle balance among the contraction and re-epithelialization is controlled by the conversion of fibroblasts to myoblasts, and it also controls the flexibility of the restored wound (Snowden, 1984). The key step is the apoptosis of keratinocytes and inflammatory cells (Shih, Garside, McGrouther, & Bayat, 2010) **Table 2.**

Table 2. Stages of Wound Healing

Stage	Features	Key Player
Hemostasis stage	Wound closed by clotting Fluid extravasation	Blood Clot Neutrophils
Inflammatory stage	Edema Dilation of blood vessels	Monocytes Macrophages Keratinocytes
Proliferative stage	Wound edge contract Re-vascularization	Granulation Tissues Epithelial Cells Fibroblasts Elastin
Maturation stage (Remodeling)	Wound recover Scaring	Cartilage Connective tissue Fibroblasts/myofibroblasts

Treatment Plan

The objective of the treatment for burns wound infection is to cure the burn area of the skin. Burns

wound infection is mainly treated according to the type of microorganism which causes the infection as reported (Norbury et al., 2016) and enlisted in the **table 3.**

Table 3. The Treatment Plan for Burn Wounds Infection

Source of Infection	Treatment
Methicillin-resistant <i>Staphylococcus aureus</i>	Vancomycin
	Linezolid
	Tigecycline
	Daptomycin
	Quinupristin-dalfopristin
vancomycin-resistance <i>Enterococcus</i>	Dalbavancin
	Linezolid
<i>Pseudomonas</i>	Ampicillin + Aminoglycosides (Quinupristin-dalfopristin)
	Piperacillin-tazobactam
<i>Acinetobacter</i>	Polymyxin E
	Carbapenems (imipenem & meropenem)
<i>Enterobacteriaceae</i>	Carbapenems
	Fourth-generation cephalosporin
Anaerobes (<i>Bacteroides. fusobacterium</i>)	Broad-spectrum antibiotics
<i>Candida sp.,</i>	Voriconazole followed by amphotericin B
<i>Aspergillus</i> and <i>fusarium</i>	Casprofungin
Herpes virus (Herpes simplex & varicella-zoster)	Topical antiviral
	(Acyclovir)

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