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Review Article

Emergency Treatment Approach and Pathophysiology of Burn Related Lung Damage without Inhalation Injury

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Abstract

In this review, it has been evaluated emergency treatment approach and pathogenesis of burn-related lung injury. The release of pro-inflammatory cytokines and the production of oxidants involved the mechanism of burn patients without inhalation injury. In burn-induced animal models, it has been shown that oxygen radicals can be agent for local inflammatory response as well as the development of shock which burn related. Especially, it is very important that there are many deaths due to burn in emergency and still no pharmacological agent to provide radical treatment.

INTRODUCTION

Burn; heat, electricity, radiation and chemical substances, damage to the functional integrity of the skin [1]. Burn is an inflammation, sepsis, systemic inflammatory response syndrome due to the production of reactive oxygen species. Neutrophil infiltration is known to be a potential source of free oxygen radicals contributing to burn injury, and it is thought that neutrophils are responsible for the damage that occurs in local and remote areas after burns [2]. It is thought that neutrophil accumulation is significant in different tissues such as gastric mucosa, liver and lung, especially in the first phase of the burn, and neutrophils may be a source of reactive oxygen derivatives [2]. Free oxygen radicals both damage the tissue directly and allow the accumulation of polymorphonuclear leukocytes [PMNL] in that tissue. Active PMNLs from tissues reveal enzyme such asmyeloperoxidase, elastase, protease, collagenase, lactoferrin, and cationic proteins. These enzymes increase both the damage on the tissue and cause the formation of more radicals. Several mediators and cytokines play an important role in the development of major complications in burn patients without inhalation injury [3-5]. In the development of these complications, the cause of the illness, duration, the layer which the illness progresses, and the immunity play an important role [6]. Especially burn patients without inhalation injury such as thermal injuries, vascular insufficiency can lead to thrombosis, increased inflammatory mediators, histamine release and edema related to increased vascular permeability, multiple organ failure and sepsis [7,8]. Both are the most deadly complications. That is why the most urgent step in the first 24 to 72 hours keeping the burn patient alive is the most important stage. In addition to fluid replacement in emergency resuscitation, the second important step is to reverse the destructive effect aimed at other organs [9].

Respiratory disturbance is one of the most important causes of death after burns [10]. Local inflammation and lipid peroxidation increase in the first few hours after burn injury, which is initiated by oxidants, primarily hydroxyl radicals, leading to a significant increase in the amount of products resulting from lipid peroxidation in lung tissues within 24 hours after burn, and pulmonary it is thought that the damage is caused by oxygen radicals (Figure 1) [11,12].

Pulmonary inflammation and lipid peroxidation are not a simple, transient initial response, on the other hand, last for at least 5 days after burn injury, and there may also be a decline in lung antioxidant defense after burn injury [13]. This inflammation caused the apoptotic pathway especially decreased he expression of Bcl-2/Bax, increase Caspase-3 and Caspase-9 activity. These molecules also contribute to the development of lung damage in burn patients without inhalation injury [14]. Increased microvascular permeability also plays an important role in the pathogenesis of burn-related lung injury. After 24 hours after burn, widespread edema is seen in almost all patients due to burning area, formation and amount of fluid. In a study conducted to investigate the pathogenesis of lung injury, it was found that over the first 24 hours of injury, excessive fluid passage from pulmonary microvascular to interstitium [15]. In this case, the oxygen balance is disturbed due to the damage in the upper airways. Carbon monoxide level increases continuously.

After diffuse bronchospasm develops, secretions increase and oxygenation deteriorates, infection and severe respiratory failure arise [16].

HYPOPROTEINEMIA RELATED TO BURN AND LOW PLASMA ONCOTIC PRESSURE

It is thought that both physiological and immunological factors play a role in the pathophysiology of burn-related lung injury. The most important physiological factors are the effects of lower respiratory pathways due to the duration of exposure to burn, deterioration of oxygenation after epithelial damage, pneumonia due to accumulation of secretions, and death due to increased hypoxia. Inflammatory mediators such as IL-1α, IL-6, IL-8 and TNF-α with oxygen radicals play an important role in the damage which lower respiratory tract in thermal injuries (Figure 2) [17,18]. Yet, when there is more damage, bacterial colonization in the lower respiratory tract is unavoidable and acute respiratory distress syndrome [ARDS] may develop [19].

Hypoproteinemia occurring after burn and its effect on plasma oncotic pressure are believed to be the greatest factor in fluid extravasation to the tissues [15,20]. This is thought to be originated from the loss of plasma proteins from the intravenous infusion of large-volume crystalloid fluids during the period of early resuscitation and from the burn site. Pulmonary interstitial fluid and protein movement can make the rise of hydrostatic pressure worse in pulmonary capillaries [21].

Neutrophıl Activatıon based on Burn Injury

In the pathogenesis of acute lung injury due to burn; complements, neutrophils and oxygen free radicals play an important role [22].

The potent initiator of vascular endothelial cell damage is neutrophils. It is thought that neutrophils have contribution on the local who comprise of the thermal injury and systemic microvascular obstruction [21]. In addition, studies have shown that decrease of neutrophil circulation or inhibition of oxidants by neutrophils in burns, which account for 40% of the total body surface area, prevents protein and fluid extravasation in the rat lung [23,24].

BURN-DEPENDENT TNF- A RELEASE

TNF-α proinflammatories are actualized their effects by directly modifying endothelial cell morphology and intercellular connectivity or by increasing neutrophil-derived cytotoxicity, which is an indirect effect [21].

It has been observed that there was an increase in TNF-α and other proinflammatory cytokine levels early in acute burn injury. In one study, serum concentrations of TNF-α in 31 patients between 1 and 6 days post-burn [mean 2 days] were reported to be 3 times higher than healthy controls. Other clinical and laboratory studies have shown that lungs are an important source for TNF-α release after severe burns. After 48 hours of burning in, it has been observed that TNF-α, IL-6 and IL-8 was in the bronchoalveolar lavage fluid of patients [25-28].

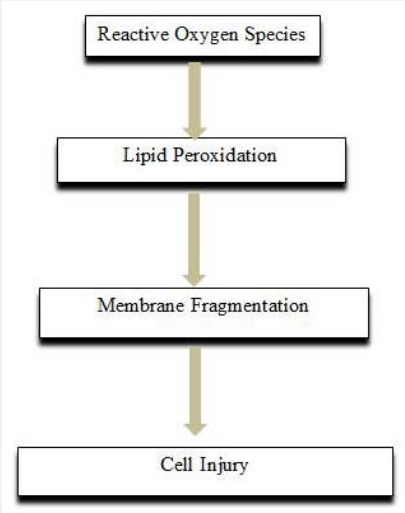

Figure 1 Reactive oxygen species caused to pulmonary injury.

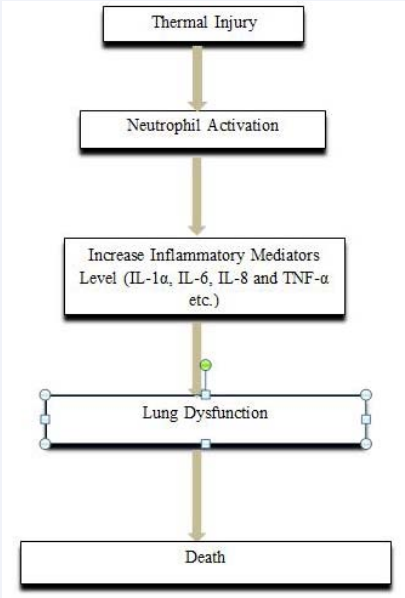

Figure 2 Inflammatory mediators such as IL-1α, IL-6, IL-8 and TNF-α with oxygen radicals play an important role in the lung damage.

CLINICAL FINDINGS AND EMERGENCY PHARMACOLOGICAL APPROACH TO THE LUNG INJURY DUE TO BURN

As a result of burn, hypoxemia is the most common findings. Hyperbaric oxygen treatment may be required if edema in the upper respiratory tract, accumulation of secretions in the lower airways, and persistent epithelial damage are accompanied by high carbon monoxide levels. In the treatment of fluid replacement, the Parkland formula is still accepted the "gold standard" in burn resuscitation [29,30]. Pulmonary damage may require bronchoscopy depending on the duration of exposure and the cause of the burn. A consensus decision should be applied that suggests to the tracheal aspirate >10^5, bronchoalveolar

lavage in the presence of ≥ 10^4 organisms should be assessed as positive for infection [31]. Ventilator support may be required when respiratory failure is severe. But, there is no specific pharmacological agent for the treatment of infection induced by damage. Treatment is dependent on microorganism types.

As a result; there are many factors of lung injury in Burn patients without inhalation injury, such as shock, pulmonary infection, sepsis, diffuse intravascular coagulation [DIC], oxygen poisoning, and surgery, but the most common factors are shock, pulmonary infection and sepsis. Several clinical and laboratory studies have shown that a large number of bacteria, free oxygen radicals, and proinflammatory mediators have been involved in the pathogenesis of burn-induced lung injury. The pathogenesis of lung injury which induces by burn without inhalation injury involves various cytokines Immune cells, Alveolar cells and pulmonary vascular endothelial cell, Inflammatory cytokines, oxygen free radical, and other molecules, as well as cell damage, Apoptosis, Autophagy and repair. The treatment of lung injury includes equipment [Respirator, ECMO], anti-inflammatory drug Glucocorticoid Thalidomide Ulinastatin etc. stem cells and their secretory cytokines /exosomes. The common point in these studies is; the damage is usually caused by increased fluid movement from the vascular area to the pulmonary interstitium [21]. There have not been found any pharmalogical approaches in the approaches that have done until now. It is thought that antioxidant and anti inflammatory agents, which may reduce ROS activity and inflammatory mediators, may be used for treatment, especially in burn induced lung injury. Studies show that development is in this direction. Therefore, every study of burn-related lung injury is valuable and may have the ability to create a new treatment.

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