Current Prospective in Smoke-Inhalation: Acute Lung Injury

R.A. Karlnoski, E. Elamin, E.M. Camporesi
Department of Anesthesiology and Critical Care Medicine, University of South Florida
Tampa, FL USA

Introduction

Acute lung injury (ALI) is a pathological condition resulting from the aspiration of superheated gases, steam, or noxious products of incomplete combustion. ALI carries a serious health threat to burns victims. The association of ALI with cutaneous burns is known to adversely complicate the outcome of those victims. When associated with pneumonia, ALI added to burn induced morbidity and increased expected mortality by 20-80% (1-2). In addition, about 70% of all fire victims who die within the first 12 hours post burns, died from ALI related complications (3). ALI involves the entire respiratory system, from the upper airway to the alveoli. The extent of injury depends on the toxic composition of the inhaled smoke (CN, NO2, and SO2), the inhalant’s water solubility, the patient’s underlying respiratory function, and the duration of exposure.
the pulmonary vascular bed is extremely large with narrower pulmonary capillaries compared to systemic capillaries. In addition, there is more cytokine production in the lung secondary to the presence of alveolar macrophages (4).

Activated neutrophils adhere to the activated endothelial cells and injure them, resulting in an increase in pulmonary vascular permeability. The exuded plasma contains coagulation factors such as fibrinogen and/or prothrombin. In addition to the exudation, pulmonary epithelial cells and alveolar macrophages express tissue factor. Tissue factor is an initiator of the extrinsic pathway of coagulation and is known to cause fibrin deposition (clots) in the alveolar space. Fibrin formation and deposition in the alveolar space is considered to be a hallmark of ALI and acute respiratory distress syndrome (ARDS). Fibrin is also known to inhibit various surfactant activities.

The pathophysiology of ALI includes variable degrees of airway edema from direct thermal injury, bronchospasm from aerosolized irritants, alveolar flooding from epithelial disruption, and small airway occlusion from sloughed endobronchial debris (“casts”). These casts cause atelectasis in the occluded lung and hypoxia and barotrauma to the ventilated areas. Within the first 24 hrs, the clinical consequences are usually airway obstruction and bronchospasm, while intrapulmonary shunting, diminished compliance, and pulmonary infection develop over the subsequent several days.

**Recommended Treatment**

There is no specific treatment for inhalation injury; management involves providing the degree of support required to compensate for decrements in gas exchange while the injured endobronchial and alveolar mucosa regenerate (5). Treatment consists of intubation for standard indications, positive pressure ventilation, pulmonary toilet, and antibiotics for established infection. There is no value to prophylactic intubation, steroids, or antibiotics (6). In practical terms, one can only support such patients while they go through a predictable 7- to 21-day period of endobronchial slough, secondary failure of gas exchange and compliance, infection, and healing. There are, however, clinical problems that may need to be addressed in patients with inhalation injury. Intense bronchospasm from aerosolized irritants occurs during the first 24 to 48 hours, especially in young children. This is managed with nebulized beta-agonists, although some will require intravenous bronchodilators such as terbutaline, aminophylline, or racemic epinephrine infusions (7). Steroids are only indicated in the initial 24 hours after inhalation injury.

Approximately half of those with ALI can be expected to develop pulmonary infection, either pneumonia or purulent tracheobronchitis (8). Infection typically occurs toward the end of the first week following injury. It is common to see patients with serious inhalation injuries deteriorate at this time. Treatment begins with prevention-meticulous nursing care with respect to cleanliness, pulmonary toilet, early removal of central lines, and early extubation. W hite blood cell count, sputum culture, and chest x-ray must be closely monitored in susceptible individuals to combat infection.

Carbon monoxide poisoning commonly occurs in conjunction with inhalation injury. Its primary pathophysiology involves the reversible displacement of oxygen on the hemoglobin molecule. Some investigators recommend hyperbaric oxygen as a means of improving the prognosis of those suffering serious CO exposures and to prevent the development of neurologic sequelae.

Small airway obstructions, caused by the formation of casts, may occur as necrotic endobronchial debris slough. Studies have shown that the obstructing material is composed mainly of fibrin that has entrapped migrated neutrophils, shed bronchial epithelial cells, and thickened mucus (4). In many cases, the cast is solid and hard to remove secondary to ALI induced damage to the ciliary transport function (9). Toilet bronchoscopy can greatly facilitate clearance of the airways. Vigilant pulmonary toilet is an essential component of the management of patients with inhalation injury. Nebulized heparin and N-acetylcysteine has been proposed as an adjunct to prevent small airway obstructions and improve pulmonary toilet in patients with inhalation injury. These data are described in more detail below.

**Heparin**

Research in lung inhalation injury has focused on reducing airway obstruction and progressive ventilation/perfusion mismatch by preventing the formation of casts. Administration of nebulized or systemic heparin has been shown to decrease tracheobronchial cast formation and pulmonary edema in smoke inhalation injury. Activation of the tissue factor-induced coagulation pathway in the alveolar compartment, accompanied by inhibition of the regional fibrinolytic system promotes the deposition of fibrin in alveoli and contributes to the formation of casts and the functional impairment of the lung. Microscopic evaluation of airway obstruction in sheep with ALI showed that aerosolized heparin significantly prevented cast formation, edema, cellular infiltrates, and congestion (10). A retrospective comparison of 47 consecutive pediatric patients with smoke inhalation injury treated with mechanical ventilation plus nebulized heparin (NH) (5,000 IU) and the mucolytic agent N-acetylcysteine (NAC) (3 ml of 20% aerosolized solution), every 4 hours for the first 7 days after injury, revealed a significant decrease in reintubation...
rates, incidence of atelectasis, and mortality in patients treated with nebulized heparin and N-acetylcysteine compared to controls (11).

The beneficial effect of N.A. is related to its mucolytic effect. On the other hand, N.H. benefits are related to its ability to prevent fibrin formation and its deposition in the alveolar space. This effect can be crucial in halting the development of ALI/ARDS or damage to the surfactant. The concentration of N.H. used in this study did not change platelet count or the partial thromboplastin time (PTT) in the pediatric patients (11).

Considering the anatomical and histological differences between the pediatric and adults airways, nebulized heparin and N-acetylcysteine has been tested in adult patients with ALI. In a retrospective review, daily lung injury scores generated from the averaged scores of chest roentgenograms, PaO₂ to FiO₂ ratios, positive end expiratory pressure requirements (PEEP), and respiratory compliance showed that nebulized heparin and N-acetylcysteine significantly reduced lung injury scores and significantly reduced mortality within the first week of treatment compared to the control group (12).

Systemically administered heparin has also been shown to ameliorate ALI. Cox et al. (13), compared adult sheep with smoke inhalation injury treated with mechanical ventilation plus continuous heparin infusion to sheep treated with mechanical ventilation alone. The heparin group received a 400 unit per kilogram bolus of heparin followed by a continuous infusion to maintain the activated clotting time between 250 to 300 seconds. The control group received a saline solution vehicle. Heparin-treated sheep showed improved PaO₂ to FiO₂ ratios, lower PEEP requirements, fewer casts, and less pulmonary edema.

Drug treatment for lung injury after smoke inhalation is being addressed in clinical trials and animal models. Presently, we do not know the mechanism of action for heparin in smoke inhalation injury. The inhibition of clot formation in the blood vessels by heparin is common knowledge, but the inhibition of cast formation in the airway by heparin is a novel idea. Experiments have shown that heparin decreases tracheobronchial cast formation, improves oxygenation, minimizes barotrauma and reduces pulmonary edema in ovine models of severe smoke inhalation injury and in adult and pediatric patients with inhalation injury. In light of the high mortality associated with inhalation injury, the risk/benefit of heparin appears very favorable.

References