A Comparative Study Between Nebulized Unfractionated Heparin Versus Nebulized N-Acetylcysteine in Acute Lung Injury After Smoke Inhalation Injury

Thesis

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List of Abbreviations

- **ADP**: Adenosine diphosphate
- **AIS**: Abbreviated injury score
- **ALI**: Acute lung injury
- **AMPA**: α-amino-3-hydroxy-5-methyl-4 isoxazolepropionic acid
- **APTT**: Activated partial thromboplastin time
- **ARDS**: Acute respiratory distress syndrome
- **ASA**: American Society of Anesthesiologists
- **AT**: Antithrombin
- **ATP**: Adenosine triphosphate
- **BSA**: Burn Surface Area
- **BALF**: Bronchoalveolar lavage fluid
- **CO**: Carbon monoxide
- **COHB**: Carboxyhemoglobin
- **CT**: Computerized tomography
- **DNA**: Deoxyribonucleic acid

- **FBO**: fiberoptic bronchoscopy
- **HFOV:** High Frequency Oscillatory Ventilation
- **HIF-1**: Hypoxia-inducible factor-1
- **H_2O_2**: Hydrogen peroxide
- **ICU**: Intensive care unit
- **IL-8**: Interleukin 8
- **INOS**: Isoform nitric oxide synthase
- **LIS**: Lung Injury score
- **LPS**: Lipopolysaccharide
- **mGLUR2\3**: Metabotropic glutamate receptor
- **MPO**: Myeloperoxidase
- **NAC**: N-acetylcysteine
- **NAD**: Nicotinamide adenine dinucleotide
- **NF-kB**: Nuclear factor kB
- **NMDA**: N-Methyl-D-aspartate receptor
- **NO**: Nitric oxide
- **NOS**: Nitric oxide synthase

- **OH^-**: Hydroxyl radicals
- **O_2^-** : superoxide anions
- **PaO2/FIO2 ratio**: Hypoxic index
- **PAPAR 1**: Poly-(ADP ribose) polymerase-1
- **PEEP**: Positive end-expiratory pressure
- **RNS**: Reactive nitrogen species
- **ROS**: Reactive oxygen species
- **SIJ**: Smoke inhalational injury
- **TBSA**: Total burn surface area

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Introduction

Smoke inhalation injury is a major contributer to morbidity and mortality in severely burned patient, in which risk for development of fatal respiratory failure is greater than 50%, the co-presence of bronchopulmonary injury with cutaneous burn covering at least 30% of total body surface area increases mortality rate to more than 70%. Inhalational injury may further predispose burned victim to pneumonia which increase the mortality rate by 90% (***Thai et al., 2010).***

Patient with inhalation injury has a 73% incidence of respiratory failure (hypoxemia, multiple pulmonary infections, or prolonged ventilator support) and a 20% incidence of acute respiratory distress syndrome (ARDS). SIJ occurs through a variety of mechanisms, including direct thermal injury to the respiratory tract mucosa, the magnitude of exposure, the type and properties of the toxic gases and chemicals comprising the smoke, the inhalant's water solubility, and the patient's underlying respiratory function (***Andrew et al., 2009).***

The airways and lungs receive continuous first-pass exposure to irritant or toxic gases via inhalation. Irritant gases, dissolve in the water of the respiratory tract mucosa

and provoke an inflammatory response and inflammatory mediators ***(Bessac and Jordt, 2010).***

The inflammatory mediators lead to intrapulmonary leukocyte aggregation following activation of the classic complement cascade releases even more chemokines and cytokines, leading to the production of oxygen free radicals. The combination of these effects contributes to tissue injury and increased pulmonary vascular permeability, leading to decreased diffusion, oedema and V/Q mismatch. Furthermore, neutrophil infiltration and fibrinogen activation by inflammatory mediators causes airway cast formation and widespread plugging ***(Michael et al., 2010).***

Nebulization of heparin and intratrcheal installed heparin were found to attenuate pulmonary coagulopathy. Nebulization of heparin, as expected, was not found to affect fibrinolysis. Intratracheal-installed heparin reduced pulmonary inflammation and endothelial permeability. In addition intratracheal-installed heparin improved survival, reduced bacterial outgrowth and bacterial adherence to lung epithelium. Furthermore, nebulization of heparin did affect systemic coagulation ***(Hofstra et al., 2010).***

A regimen of aerosolized solution of 20% N-acetylcysteine was studied on adult populations with inhalation injury diagnosed by bronchoscope which act as a mucolytic agent, and diminish airway cast formation. One retrospective case–control study found a significantly decreased mortality, occurrence of atelectasis, and need for reintubation in the treatment group. In a small single-centre study in adults, it was found the nebulized therapy attenuated lung injury and progression of ARDS compared with historical controls ***(Preea and Rebecca, 2014).***

Aim of the Work

This study was conducted to compare nebulized unfractionated heparin to nebulized n-acetylcysteine in attenuating lung injury and inhibition of the progression of acute respiratory distress syndrome in ventilated adult patients with acute lung injury following smoke inhalation.

General Burn Concerns

Successful management of the patient with burn injury begins at the scene of injury and continues in the emergency department with a thorough trauma assessment based on the Advanced Trauma Life Support guidelines. This requires a combined strategy of airway assessment and protection, initiation of resuscitation, and evaluation for coexisting injuries (***Rosenkranz and Sheridan, 2002)***.

Assessing the airway is the first priority during the initial evaluation. The presence of airway injury, signs of airway obstruction, and the presence of preexisting airway abnormality should be assessed as soon as the patient arrives at the hospital. Airway injuries may not be evident initially, but with massive fluid resuscitation airway edema can result. As a general rule, when indicated, it is safer to intubate the patient early than risk a difficult intubation after airway swelling has occurred (***Edward et al., 2015)***.

Different causes of burn:

1. Thermal

In the United States, fire and hot liquids are the most common causes of burns. Of house fires that result in death, smoking causes 25% and heating devices cause 22%. Almost half of injuries are due to efforts to fight a fire. Scalding is caused by hot liquids or gases and most