CHEST

Original Research

INHALATION INJURY

Systemic Inflammation Caused by White Smoke Inhalation in a Combat Exercise*

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Background: **White smoke inhalation is an uncommon but potentially deadly cause of acute lung injury. No clinical spectrum or treatment protocol have been developed.**
Methods: **Twenty patients accidentally been exposed to white smoke during military training were the subjects of this study. We analyzed clinical manifestations, cytokine changes, and treatment outcomes.**
Results: **All patients initially presented with fever, dry cough, chest tightness, and shortness of breath. Twenty-five percent of these patients had severe acute lung injury requiring artificial ventilation support. Elevation of serum tumor necrosis factor-α was observed before treatment with antibiotics and glucocorticoids, but the elevation of transforming growth factor-β_1 was delayed for 2 to 4 weeks after the accident. All the patients had leukocytosis, which correlated positively to disease severity and negatively to intensive treatments. Ninety-five percent of patients had varying degrees of restrictive ventilation impairment, and 85% of these patients had a significantly reduced diffusion capacity in the lungs. Seventy percent of these patients had transient impairment of liver function, which did not correlate to disease severity. The respiratory sequela of restrictive ventilation impairment developed in the most severely affected patients, whereas other tissue toxicities were mostly transient. Treatment included glucocorticoids, antibiotics, and respiratory therapy. All of the patients survived.**
Conclusion: **A proper ventilation strategy, early pharmacologic therapy including glucocorticoids, and complication prevention may contribute to good treatment outcomes after white smoke inhalation.** ***(CHEST 2008; 133:722–728)***

Key words: cytokine; inhalation injury; pulmonary function; smoke bomb; zinc chloride

Abbreviations: ALT = alanine aminotransferase; DLCO = diffusion capacity of the lung for carbon monoxide; FIO_2 = fraction of inspired oxygen; TGF = transforming growth factor; TLC = total lung capacity; TNF = tumor necrosis factor

Smoke bombs are widely used in battles and military training as obscurants. After combustion, the bomb discharges white smoke by igniting a pyrotechnic mixture containing zinc oxide and hexachloroethane. The reaction produces a number of toxic compounds including zinc chloride, hydrogen chloride, and carbon tetrachloride.[1] The mean diameter of the primary smoke particles is approximately 0.1 μm and, after water absorption in the field, the particles swell and reach a final diameter of approximately 2 to 3 μm.[2] Particles of this size are large enough to be captured using lightweight dust mist or high-efficiency particulate air filter respirators as protection.[3] However, if not filtered, particles of this size are small enough to penetrate down to the alveoli of the deep lung.

Massive inhalation of white smoke causes damage to the respiratory tract. Evans[4] reported in 1945 that the inhalation of white smoke leads to chemical pulmonary edema and respiratory failure. Sporadic cases reported in the literature[5–7] all had ARDS, with poor treatment outcomes. We have also demonstrated[8] that accidental white smoke inhalation during military training caused diffuse ground-glass opacities on the high-resolution CT scan and restrictive ventilation impairments on the pulmonary function tests, indicating a predominant parenchymal injury of the lung. However, none of the systemic effects, clinical spectra, treatment protocols, or long-term effects has been identified. We herein analyze the clinical manifestations, cytokine profile, and treatment outcomes of these patients.

Materials and Methods

Patients

Twenty soldiers who had white smoke inhalation during military training were the subjects of this retrospective study. The soldiers had entered a tunnel in single file when a smoke bomb accidentally discharged behind them. A gust of tail wind blew the smoke rapidly forward before the soldiers rushed to the mouth of the tunnel (Fig 1). The estimated exposure time was 1 min for soldiers in the front of this line, 5 min for those at the end of the line, and 3 min for those in between. All patients were transferred to hospital and admitted immediately. Informed consent, which has been reviewed and approved by the Institutional Review Board of Tri-Service General Hospital, was obtained from the patients or their next of kin before any invasive procedures were performed.

Treatment

Accessory oxygen was initially administered to all patients. The patients were transferred to the ICU if they had symptoms or signs of respiratory failure. The patients underwent intubation and mechanical ventilation if they deteriorated clinically or if they could not maintain arterial oxygen saturation > 90% with spontaneous respiration at a 100% fraction of inspired oxygen (FIO_2). A low tidal volume lung-protective strategy was used, targeting tidal volume to 6 mL/kg of the predicted body weight and a plateau pressure < 35 cm H_2O. Positive end-expiratory pressure, FIO_2, and respiratory rates were titrated to maintain PaO_2 > 55 mm Hg or arterial oxygen saturation > 90%. Patients underwent chest tube insertion with chest bottle drainage if pneumothorax developed.

A steroid regimen with IV hydrocortisone (600 mg/d) was started within 3 days of ICU admission and was then tapered off, depending on the improvement in respiratory symptoms. Antimicrobial therapy was not included in the basic protocol, but most patients were treated with β-lactam penicillin or a combination of macrolide and IV cephalosporin before ICU admission. The patients were treated with ceftazidime when they were transferred to the ICU. Standard cardiovascular supports were administered to maintain stable hemodynamics.

Pulmonary Function Tests

The first pulmonary function test was performed as early as possible, when the patient was able to reach the plethysmograph, and was followed up after approximately 2 weeks, 1 month, and 6 months. We performed the pulmonary function tests according to the American Thoracic Society/European Respiratory Society criteria.[9] The diffusion capacity of the lung for carbon monoxide (DLCO) was determined by the single-breath carbon monoxide technique using an infrared analyzer (Model 66200; SensorMedics; Anaheim, CA). Spirometry was performed using a body plethysmograph (Jaeger; Wurzburg, Germany) according to the standard protocol. Each measurement was repeated at least three times, and the highest acceptable measurement was expressed as a percentage of the normal predicted values with adjustments for the Chinese population.[10]

Inflammation Follow-up

WBC counts, serum cytokines (tumor necrosis factor [TNF]-α and transforming growth factor [TGF]-β_1), and liver function (serum aspartate aminotransferase and alanine aminotransferase [ALT]) were monitored periodically until 2 months after the accident. We quantified TNF-α and TGF-β_1 in the serum samples using commercially available enzyme-linked immunosorbent assays.

Data Collection and Statistical Analysis

We classified the patients' clinical conditions into three groups: those who recovered without ICU admission (mild), those who required ICU admission but did not meet the criteria for ARDS proposed by the American-European Consensus Conference[11] (moderate), and those with ARDS (severe). Data are expressed as mean ± SD unless otherwise specified. Categorical variables were compared using the χ^2 test or Fisher exact test when appropriate. Continuous variables were compared among the three severity groups using the Kruskal-Wallis method. When the variables were significantly different, pairwise comparison was made using the Mann-Whitney test; $p < 0.05$ was accepted as significant.

Results

Spectrum of Clinical Courses

Table 1 summarizes and compares the characteristics of patients at the three levels of disease severity: mild (n = 7), moderate (n = 8), and severe (n = 5). Eighty-six percent (six of seven patients) with mild lung injury were in the anterior front of the line in the tunnel, whereas 63% (five of eight patients) of the moderate group were in middle third, and 80% (four of five patents) of the severely affected patients were in the rear third. All patients initially presented with symptoms of intractable cough and chest tightness. Thirteen patients (65%) had symptoms and signs of impending or acute respiratory failure and were admitted to the ICU within 48 h. Of the ICU patients, five patients (38%) progressed rapidly to ARDS and required mechanical ventilation.

Extracorporeal membrane oxygenation was used for one patient with pneumomediastinum, bilateral pneumothorax, and severe ARDS, and was refractory to both ventilatory and pharmacologic interventions.

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