Postobstructive Pulmonary Edema*

A Case for Hydrostatic Mechanisms

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Background: **Postobstructive pulmonary edema is a well-recognized complication of upper airway obstruction. The mechanisms of edema formation are unclear and may be due to increased hydrostatic forces generated by high negative inspiratory pressure or by increased permeability of the alveolar capillary membrane. Measurement of the edema fluid/plasma protein ratio and the rate of net alveolar fluid clearance are two well-validated methods for classifying the underlying mechanism of edema formation. The goal of the current study was to investigate the mechanisms of pulmonary edema formation in patients with postobstructive pulmonary edema by serial sampling of undiluted pulmonary edema fluid.**

Methods: **A retrospective review of 341 patients who had pulmonary edema fluid collected prospectively after the acute onset of pulmonary edema. All patients had serial samples of edema fluid and plasma collected over the first 8 h after intubation.**

Results: **Ten of the 341 patients with acute pulmonary edema were identified as having postobstructive pulmonary edema. The mean (± SD) edema fluid/plasma protein ratio in these patients was 0.54 ± 0.15. The mean rate of alveolar fluid clearance over 8 h was 14.0 ± 17.4% per hour. Nine of the 10 patients survived the hospitalization.**

Conclusion: **Measurement of the edema fluid/plasma protein ratio and the presence of net alveolar fluid clearance in 10 patients with postobstructive pulmonary edema supports a hydrostatic mechanism for edema fluid formation. The predominantly fast rates of alveolar fluid clearance may explain the rapid resolution of clinical postobstructive pulmonary edema that is typically described.** ***(CHEST 2007; 131:1742–1746)***

Key words: alveolar fluid clearance; edema; fluid/plasma protein; hydrostatic pulmonary edema; postobstructive pulmonary edema

Postobstructive pulmonary edema is an uncommon, but well-described, complication of upper airway obstruction. Two different mechanisms have been proposed for the development of pulmonary edema in the setting of upper airway obstruction. One theory is that postobstructive pulmonary edema is caused by significant fluid shifts due to changes in intrathoracic pressure.[1] Negative intrathoracic pressure is generated in the chest when a patient attempts to inspire against a closed glottis or obstructed airway. The short-term drop in intrathoracic pressure increases venous return to the right side of the heart, which in turn increases pulmonary venous pressure. This increase in pressure in the venous circulation creates a hydrostatic transpulmonary gra-

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dient with fluid moving from high pressure (pulmonary venous system) to low pressure (pulmonary interstitium and airspaces).[1–5] The second proposed mechanism involves the disruption of the alveolar epithelial and pulmonary microvascular membranes from severe mechanical stress, leading to increased pulmonary capillary permeability and protein-rich pulmonary edema.[1–5] The first proposed mechanism of edema formation is similar to hydrostatic pulmonary edema, as seen in patients with congestive heart failure or volume overload states. The latter mechanism is similar to increased permeability pulmonary edema, as seen in patients with acute lung injury or the ARDS.[6]

Measurement of the pulmonary edema fluid/plasma protein ratio is a well-validated method to differentiate between hydrostatic pulmonary edema and increased permeability pulmonary edema.[7–10] Measurement of the rate of net alveolar fluid clearance, with sequential samples of pulmonary edema fluid, provides an assessment of the capacity of the alveolar epithelial barrier to remove alveolar edema fluid, a property that is usually impaired in patients with acute lung injury yet intact in patients with hydrostatic pulmonary edema.[10–13]

We have previously reported four cases of postobstructive pulmonary edema with a mean pulmonary edema fluid/plasma protein ratio of 0.43, which is consistent with a hydrostatic mechanism.[5,14] We now report an expanded series of 10 patients with postobstructive pulmonary edema in whom we measured both the edema fluid/plasma protein ratio and the net rate of alveolar fluid clearance. We postulated that postobstructive pulmonary edema would have characteristics similar to hydrostatic pulmonary edema, with both a low edema fluid/plasma protein ratio and rapid rates of net alveolar fluid clearance, based on a similar physiologic mechanism.

Materials and Methods

The Committee on Human Research at the University of California San Francisco approved this study. We conducted a retrospective review of 341 intubated patients, who were enrolled in a pulmonary edema fluid and plasma databank at the University of California San Francisco over the 20-year period from 1982 to 2002, to identify all cases of suspected acute postobstructive pulmonary edema. All patients had the acute onset of bilateral infiltrates on chest radiograph. The classification of the etiology of acute pulmonary edema as postobstructive was based on a chart review of clinical characteristics at the time of intubation, as well as the hospital course. Patients were selected if "postobstructive pulmonary edema" was documented as a diagnosis and if the study investigators agreed with that diagnosis after reviewing the medical record. Study investigators were unaware of the edema fluid and plasma protein measurements at the time of the chart review. All patients who had a presentation that was consistent with postobstructive pulmonary edema and met the above criteria were included in the present study. Pulmonary edema fluid was obtained by trained respiratory therapists and physicians, using a previously described method.[9,11] Briefly, a soft 14F suction catheter was advanced to a wedged position in a distal bronchus through the endotracheal tube.[9,11] Gentle suction was applied, and samples were collected via a suction trap. Simultaneous plasma samples were collected by venipuncture or aspiration through an already placed IV access site.[9,11] All samples were collected and processed prospectively. Serial samples were obtained from patients over the next 8 h to evaluate the rate of alveolar fluid clearance. Pulmonary edema fluid and plasma fluid samples were centrifuged, and the supernatant was aspirated and stored at −70°C.

The total protein levels in edema fluid and plasma were measured by the biuret method, which has previously been described.[9,11] An edema fluid/plasma protein ratio of < 0.65 is consistent with hydrostatic pulmonary edema, while a ratio of > 0.75 is consistent with high-permeability pulmonary edema.[7–9,11] Patients with a ratio between 0.65 and 0.75 may have a mixed etiology of pulmonary edema or they may have begun to reabsorb some of the edema fluid. This would result in a higher concentration of protein in the edema fluid prior to the initial sampling.[15] The calculation of the rate of alveolar fluid clearance was performed as a percentage of alveolar fluid volume reabsorbed per hour, as has been validated in both clinical and experimental studies.[9,11–13] Briefly, since the removal of protein from the alveoli is slow compared to the removal of fluid, the percentage of alveolar edema fluid reabsorbed can be estimated with the following equation:

$$\text{percentage of alveolar fluid clearance} = 100 \times [1 - (\text{initial edema protein/final edema protein})].^{11}$$

Alveolar fluid clearance $\geq 3\%$ per hour is defined as intact alveolar clearance, while clearance of $> 14\%$ per hour is defined as maximal alveolar fluid clearance.[11,12] All statistical analysis was performed using a statistical software program (SPSS, version 14.0 for Windows; SPSS, Inc; Chicago, IL). The results are reported as either the means ± SD or median and interquartile range, as appropriate. The Spearman correlation coefficient was employed to determine the strength of correlation between variables.

Results

Ten of the 341 patients (3%) were identified over the 20-year period as having postobstructive pulmonary edema. Eight of the ten patients were men. The causes of postobstructive pulmonary edema included suspected postoperative laryngospasm (n = 8), foreign-body aspiration (n = 1), and severe patient-ventilator asynchrony with inspiratory attempts during closure of the ventilator inspiratory valve (n = 1). The mean age of the patients was 37 ± 24 years. The mean simplified acute physiology II score[16] was 25 ± 13. All 10 patients required endotracheal intubation and mechanical ventilation due to hypoxemia. The mean duration of mechanical ventilation was 3.7 ± 4.5 days. Nine of 10 patients survived their hospital course.

The initial edema fluid and plasma protein measurements are summarized in Table 1. The mean