Maine Medical Center  
Department of Emergency Medicine  

Journal Club / Research Article Summary - (Adapted from Schultz Table)

Date: 3/20/13  
Presenter: Alicia Bond  

ARTICLE:

- Country: USA
- Funding Sources: Research grants from the National Institute of General Medical Sciences, the Health Research Administration, the Parker B. Francis Foundation of Kansas City, and the Cardiopulmonary Laboratory Research Foundation of Los Angeles, California

PURPOSE:

- Research Question(s): What is the effect of treatment on intravascular volume status in acute pulmonary edema?

  - Hypothesis: Although it had been proposed that the mechanism of action of furosemide in acute pulmonary edema was to reduce intravascular volume, the authors note that hematocrit is usually elevated in acute pulmonary edema, and hypothesize that intravascular volume is actually depleted during acute pulmonary edema and may be increased by furosemide administration.

DESIGN:

- Study Design: Prospective observational case-control study

  - Dependent / outcome Variable(s): Measurements of plasma volume, hematocrit, plasma osmotic pressure, ABG, total protein, potassium and sodium

  - Independent / research Variable: Acute cardiogenic pulmonary edema vs. healthy controls and controls with chest pain but no MI
SETTING / SUBJECTS:
- Research Setting: Center for the Critically Ill at Hollywood Presbyterian Medical Center in Los Angeles
- Subjects: 21 patients, 11 men 10 women, with acute cardiogenic pulmonary edema
  - Study population: Patients referred to Center for the Critically Ill - minimal demographic data provided

  - Inclusion / Exclusion criteria: Acute onset of respiratory distress, orthopnea, "unequivocal evidence of myocardial disease", with bilateral rales and positive chest radiograph included; exclusion criteria were patients with bleeding, shock, or administration of blood or colloids

  - Number (control / intervention groups): 21 cases, 10 healthy controls, 50 additional controls admitted for chest pain but ruled out

  - Demographics: 11 men, 10 women, ages 44-83, 9 of whom had history of acute pulmonary edema in past; healthy controls were much younger, and admitted controls were somewhat younger. No additional demographic data is presented.

  - Attrition: All 21 patients had two sets of measurements, but only 10 had three sets

METHODS:
- Interventions: ABG, plasma volume, hematocrit, plasma colloid osmotic pressure, plasma osmolality, plasma sodium and potassium, lactate, and plasma protein concentration were measured in study subjects before and 4-12 hours after treatment with furosemide 40-160 mg titrated for diuresis and morphine 5-15 mg titration for relief of dispense. Patients were also treated with oxygen both before and after measurements. Healthy controls had measurements taken before and after at least 3 hours of bed rest.

- Data Collection: Duplicate measurements obtained from single sample of arterial blood in each patient. In patients for whom plasma volume was measured with radioisotopes, measured and calculated volumes were compared to validate the method for calculating plasma volume in the patients who could not have it measures directly due to time constraints prior to therapy.
DATA ANALYSIS:
● Level of data: Real-valued data
● Statistics Used: Student's t-test to evaluate differences between case and control groups

● What, if any, confounding variables were controlled for / adjusted for: None

RESULTS:
● Brief answers to research questions: Mean plasma volume and total blood volume were statistically lower in patients with acute pulmonary edema than healthy controls, and hematocrit, colloid osmotic pressure, and total protein were significantly higher in study patients than in chest pain controls. Despite total net negative fluid balance between measurements, there was a statistically significant increase in plasma volume and decrease in hematocrit, colloid osmotic pressure, and total protein in the study group before and after treatment. However, 5/21 patients had high plasma volume at outset, and a decrease in volume was only confirmed in 14/21 after treatment.

● Other possible explanation for findings: This study was very small, and although the p values are low for the parameters reported, there is some chance that the findings would not be reproducible on a larger scale.

● Limitations?: Very small study. No good real way to measure intravascular volume. Lots of measurements and parameters not reported from control groups - was data selectively presented to support hypothesis? Most importantly, this is not patient-centered information, and while it contributes to our understanding of pathophysiology in acute pulmonary edema, it does not suggest any changes in management or help us to improve our clinical practice.

IMPLICATIONS FOR PRACTICE:
● Applicable to this clinical practice: Does likely apply to our patients

● Feasibility (cost, resources, etc): N/A
Clinically Relevant: No, while this suggests that our understanding of how diuretics work in pulmonary edema was flawed, it does not imply that loop diuretics do not have a role, nor does it have any other immediate implications for clinical practice.

LEVEL OF EVIDENCE / DECISION FOR USE:

- Background

- Level of Evidence:
  - III Well-designed non-experimental studies