An Examination of Lung Physiology in ARDS

Naimish R. Patel

A. Study Purpose and Rationale

The purpose of this study is to examine the static pressure versus volume curves of patients with adult respiratory syndrome (ARDS). ARDS a severe lung condition that is a common endpoint of many other illnesses such as sepis, severe pneumonia, pancreatitis, and multiple traumas. Recent papers using a new ventilation method with a high positive end-expiratory pressure (Peep generally above 15cmH_20) showed a positive benefit with respect to weaning off the ventilator, barotrauma, and mortality at 28 days(1,2). In these papers the patients had a static pressure versus volume (P-V) curve pattern in which at low pressures, the lung was very non-compliant. At gradually higher pressures, the lung would become more compliant. It is thought that in these patients at low pressures, many alveoli are collapsed causing the lung to be non-compliant. At higher pressures however, these collapsed alveoli re-inflate resulting in a more compliant lung(3). It is theorized that keeping these alveoli inflated by using Peep prevents them from sustaining further damage. This has been shown previously in animal models.(4,5,6) However, this "favorable" pattern on the pressure volume curve, in our practice, does not seem to be very common. Many patients tend to have a linear P-V curve. One investigator has suggested that shape of the curve depends upon the stage of disease, although this finding has never been duplicated.(7) Our objective is to take patients in the ICU on a ventilator who have ARDS and measure their P-V curves. We want to determine what the prevalence is of the favorable P-V curve showing a changing compliance. This would allow us to determine how practical this new ventilation strategy really is. In addition, we shall also attempt to show if there is a correlation between the shape of the curve and the number of days on the ventilator and overall survival.

B. Study Design and Statistical Analysis

The study will be designed as a descriptional study looking at patients in the ICU with ARDS. This initial study shall be a pilot study on 25 patients to see how common the different P-V curve patterns are. Given a population of 25 patients and an expected prevalence of at least 25% of the favorable P-V curve, a standard deviation of 8% would be expected for our measured prevalence. In our study, if we measured a prevalence of 9% or 2 of 25 patients with the favorable type of P-V curve, it would be within two standard deviations of 25% and considered significant. This number would be enough to justify further study. P-V curves shall be measured up to day 7 of the patient being on the ventilator. Previous studies have shown that the majority of mortality (approx. 60%) on the ventilator occurs by this day.(8)

We are looking for essentially two patterns on the P-V curves. One pattern in which there is a changing slope, with an initially non-compliant lung that becomes more compliant at higher pressures. The second pattern would be a linear pattern. A (^{2} test can be used to see if there is a significant correlation of the curves with overall mortality. The each patient will also have their Apache II scores calculated so that the overall degree of severity of their condition can be assessed and compared. In addition, a *t* test can be used compare the curves with the number of days on the ventilator.

C. Study Procedures

Each patient shall be put on fixed ventilatory support for 30min, ensuring optimal ventilation using routine arterial blood gas measurements. The patient shall already be on the usual heavy sedation routinely required for ventilated patients - normally fentanyl or propofol.

After a prolonged expiration of approximately 5 seconds, the ventilator mode shall be changed to deliver breaths at a fixed pressure setting (pressure-controlled ventilation). The patient shall be given a

inspiratory pause so that a full tidal volume can be delivered. The average lung volume delivered over 3 breaths shall be obtained from the readout on the ventilator. The patient shall be then put back on the original settings for a minute before conducting another measurement at a different pressure. This will ensure that the patient will not become hypoxemic. If the patient desaturates during the procedure or becomes hemodynamically unstable the original pressure settings will be reset and the measurements shall be ceased. The pressures shall be delivered in a random order and a pressure-volume curve shall be obtained with 8 pressure measurements at 5cm H_2O intervals from 5 to 40cm H_2O. The subject will be completely sedated and will feel no pain or discomfort. No additional instrumentation is needed outside of what is normally used for any patient on a ventilator. The total time needed to obtain one complete curve from a patient is approximately 15 minutes.

The measurements shall be repeated every 2 days for 7 days on each patient.

The study is anticipated to last 3-6 months.

D. Study Drugs

Not applicable

E. Medical Devices

Not applicable

F. Study Questionnaire

In addition to the pressure volume curves, routine clinical data abstracted from the patient's hospital record will also be obtained. No other additional data not normally present in the hospital record will be required for the study.

G. Study Subjects

a. Inclusion Criteria

- males and females 18-70
- patients must meet the criteria for ARDS using a Murray's score(10) which does not require any additional invasive monitoring outside of the usual arterial blood gas measurement.

b. Exclusion criteria

- pregnant females
- history of established underlying lung disease, chest wall disease, or congestive heart failure.
- greater than 20pk/yr smoker
- unstable, out-of-control, or terminal disease

H. Recruitment of Subjects

Patients will be recruited from the medical ICU at CPMC. Patient's families will be approached by the principal investigator only after agreement from the primary physician has been obtained.

I. Confidentiality of Study Data

Unique code numbers will appear on all materials contained study data from the patients. No patient names will appear on any such material All data will be kept locked in the principal investigator's cabinet or on computer under password.

J. Potential Conflict of Interest

Neither the principle investigator or any study personnel have any financial interest, direct or indirect in the principles under investigation.

K. Location of the Study

The study will be conducted in the intensive care units of CPMC.

L. Potential Risks

Risks to the patient are minimal. Using pulse oximeter we will ensure that the patient is being adequately oxygenated at all times during the measurements of tidal volumes. Our preliminary experience using this technique shows that is can be safely done with minimal change in arterial oxygenation or hemodynamic stability. In the previous studies, no complications were encountered in the measurement of the P-V curves(1,2).

M. Potential Benefits

The patient may not benefit from this study. There is a potential benefit to society in that more information shall be obtained about a highly lethal condition.

N. Alternative Therapies

Not applicable because there is no experimental therapy being studied.

O. Compensation to the Patients

No compensation will be provided.

P. Cost to Subjects

There is no cost to the subjects of this study.

Q. Minors as Research Subjects

Minors are excluded from this study.

R. Radiation or Radioactive Substances

No radiation or radioactive substances will be used.

S. References

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