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Intermittent positive pressure ventilation increases diastolic pulmonary arterial pressure in advanced COPD

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ABSTRACT

Objectives: To measure the impact of intermittent positive pressure ventilation (IPPV) on diastolic pulmonary arterial pressure (dPAP) and pulmonary pulse pressure in patients with advanced COPD.
Background: The physiological effects of raised intrathoracic pressures upon the pulmonary circulation have not been fully established.
Methods: 22 subjects with severe COPD receiving IPPV were prospectively assessed with pulmonary and radial arterial catheterization. Changes in dPAP were assessed from end-expiration to early inspiration during low and high tidal volume ventilation.
Results: Inspiration during low tidal volume IPPV increased the median [IQR] dPAP by 3.9 [2.5 −4.8] mm Hg ($P < 0.001$). During high tidal volume, similar changes were observed. The IPPV-associated change in dPAP was correlated with baseline measures of PaO_2 (rho = 0.65, $P = 0.005$), pH (rho = 0.64, $P = 0.006$) and right atrial pressure (rho = −0.53, $P = 0.011$).
Conclusions: In severe COPD, IPPV increases dPAP and reduces pulmonary pulse pressure during inspiration.

Introduction

Chronic obstructive pulmonary disease (COPD) is frequently complicated by the development of pulmonary hypertension[1] which is associated with increased mortality,[2–4] increased hospitalizations[5] and reduced functional status.[6] Efforts to treat the pulmonary hypertension in these patients have been disappointing.[7–11] Consequently, there has been renewed interest in the pathogenesis of pulmonary hypertension in patients with COPD[12] in an effort to explore novel therapeutic management strategies.

Although several authors have postulated that gas trapping and dynamic lung hyperinflation contribute to pulmonary hypertension in COPD,[13–18] there is limited evidence to support this. Nevertheless, previous studies have demonstrated that increased intrathoracic pressures are associated with reductions in right ventricular preload, right ventricular cardiac output[19,20] and left ventricular cardiac output.[21] Recently, Pinsky[22] has reviewed heart lung interactions during mechanical ventilation, focusing on pulse pressure and stroke volume variation as a means of identifying volume

Abbreviation: Ax-surgery time, time duration between lung transplant assessment and lung transplant surgery; BMI, body mass index; CI, right ventricular cardiac index; COPD, chronic obstructive pulmonary disease; dBP, diastolic systemic arterial blood pressure; dPAP, diastolic pulmonary arterial pressure; FEV_1, forced expiratory volume in one second; FiO_2, fraction of inspired oxygen; FRC, functional residual capacity; FVC, forced vital capacity; HR, Heart rate; I:E, inspiratory to expiratory; IC, inspiratory capacity; IPAP, inspiratory positive airway pressure; IPPV, intermittent positive pressure ventilation; mPAP, mean pulmonary arterial pressure; PAWP, Pulmonary arterial wedge pressure; $PEEP_E$, extrinsic positive end-expiratory pressure; PVR, pulmonary vascular resistance; RAP, right atrial pressure; RR, respiratory rate; RV, residual volume; sBP, systolic systemic arterial blood pressure; sPAP, systolic pulmonary arterial pressure; SVI, right ventricular stroke volume index; TLC, total lung capacity; $TLCO_{hb}$, transfer factor of the lung for carbon monoxide corrected for hemoglobin; V_T, tidal volume.

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responsiveness due to the effect of raised intrathoracic pressures on right ventricular preload. However, whether raised intrathoracic pressures, as occurs with pulmonary hyperinflation, increase pulmonary vascular resistance (PVR) and whether this subsequently affects right ventricular cardiac output have not been established.

Exploring airway pressure effects upon pulmonary hemodynamics is challenging due to the concurrence of direct and indirect pressure and lung volume effects, pulsatile cardiac contractions, ventricular inter-dependence, pulmonary blood volume changes and the shared anatomical space of the heart and lungs.[23,24] Furthermore, continuous measures of PVR are not readily available nor well validated,[25] especially in human studies. The PVR is also limited in that it is prone to error as an increased cardiac output may recruit more pulmonary vascular bed and thereby reduce PVR in normal subjects. In contrast, the diastolic pulmonary arterial pressure (dPAP) is a useful measure of pulmonary hemodynamics as it reflects both the pulmonary circulation and the back pressure from the left side of the heart, it can be assessed beat-by-beat, is correlated with pulmonary vascular resistance and is minimally affected by right ventricular stroke volume.[26,27]

In this study, we examine the airway pressure effects upon pulmonary hemodynamics in mechanically ventilated patients with severe, stable COPD in the operating theater immediately prior to lung transplantation. We hypothesized that increased airway pressure (as occurs during inspiration with intermittent positive pressure ventilation, IPPV) would increase dPAP, as a surrogate marker of total pulmonary resistance. Secondly, we sought to determine whether baseline cardiopulmonary parameters could predict the dPAP response to inspiration during IPPV.

Methods

Subjects

The study was approved by the institution's Human Ethics Committee. Patients with end-stage COPD were prospectively recruited from the lung transplant waiting list at a single institution and all subjects provided written and informed consent. Baseline demographic and physiologic parameters were taken from lung transplant assessment data. All hemodynamic responses during IPPV were captured once the subjects were anesthetized at the time of lung transplantation, immediately prior to the commencement of surgery.

Primary outcome — diastolic pulmonary arterial pressure (dPAP)

The primary outcome was the change from end-expiration to early inspiration in dPAP. To investigate whether IPPV principally affects dPAP or all systemic and pulmonary pressures equally, the change in dPAP was compared with changes in systolic pulmonary arterial pressure (sPAP), diastolic systemic arterial pressure (dBP), systolic systemic arterial pressure (sBP), right atrial pressure (RAP) and pulmonary arterial wedge pressure (PAWP).

Secondary outcomes

To investigate predictors of the dPAP response to IPPV, we examined the relationship between the percentage change in dPAP and a range of cardiopulmonary parameters that may affect pulmonary vascular compliance, namely $PaCO_2$, PaO_2, PAWP, pH, PVR, RAP, stroke volume index (SVI) and tidal volume (V_T).

Ventilation strategy

Patients were anesthetized using propofol, fentanyl, midazolam and rocuronium. All patients were intubated in preparation for transplantation with an appropriately sized Bronchocath™ (Mallinckrodt, Covidien, Mansfield, Massachusetts, USA) double lumen endotracheal tube. During the study period, patients were ventilated (Aisys Anesthesia Carestation, GE Healthcare, Wisconsin, Milwaukee, USA) with both endotracheal tube lumens connected to a common ventilator.

To determine whether the inspiratory changes to dPAP during IPPV were driven by airway pressure or lung volume changes, we compared the hemodynamic responses during low V_T versus high V_T without changing the delivered inspiratory positive airway pressure.

The "low" V_T protocol comprised inspiratory pressure 15–25 cm H_2O, zero extrinsic positive end-expiratory pressure, respiratory rate of 10 breaths min^{-1}, inspiratory-to-expiratory ratio of 1:3.5, and inspired oxygen fraction of 60%. Ventilation was then adjusted by anesthetist preference to achieve stable hemodynamics, arterial oxygenation of greater than 94% saturation and a stable minute ventilation of 4–6 L min^{-1}. (Hypercapnia was permitted.) The respiratory rate was then reduced to 6 breaths min^{-1} without adjusting inspiratory positive airway pressure, in order to achieve a "high" V_T, whilst attempting to minimize intrinsic positive end-expiratory pressure and maintain minute ventilation. After 5 min with the high V_T strategy, hemodynamic assessment was repeated.

Hemodynamic assessment

All patients had a pulmonary arterial catheter (Edwards Lifesciences, Irvine, California, USA) inserted via the right internal jugular vein. Zero reference was at the midthorax with the patient lying horizontally. Cardiac output was measured using the thermodilution method as the average of three dilutions within 10% of each other. Systemic arterial pressures were measured by a radial artery catheter (Pressure Monitoring Kit with TruWave Disposable Pressure Transducer, Edwards Lifesciences, Irvine, California, USA). Hemodynamics were calculated by the patient monitor (IntelliVue MP90, Philips Healthcare, Andover, Massachusetts, USA) and continuous waveform data was captured by data acquisition software (TrendFace, ixellence GmbH, Wildau, Germany) for off-line analysis.

Pressure measurements

Commencement of inspiration was determined by change in direction of airway flow from negative to positive values (see Fig. 1). For systolic pressure measurement, the complete upstroke limb of the arterial pressure cycle was required to occur during the appropriate phase of ventilation (the upstroke and downstroke limbs were required for diastolic pressure measurement). RAP and PAWP were measured as the mean pressure over a single cardiac cycle during the appropriate phase of respiration. Measurements were averaged over three consecutive breaths during steady state.[28] Changes in PAP, BP, RAP and PAWP were measured from end-expiration to early inspiration.

Statistics

Based on previous animal studies[29] we estimated that a sample size of 14 was required to detect a mean difference of 2 mm Hg (SD ± 1.5 mm Hg) in the primary outcome measure of dPAP with a power of 0.80 at a significance level of 0.05. Differences between low V_T and high V_T parameters were assessed using Wilcoxon