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Respiratory system inertance corresponds to extravascular lung water in surfactant-deficient piglets[☆]

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Abstract

In various cardio-pulmonary diseases lung mass is considerably increased due to intrapulmonary fluid accumulation, i.e. extravascular lung water (EVLW). Generally, inertance is a physical system parameter that is mass-dependent. We hypothesized that changes in lung mass influence the inertive behavior of the respiratory system. EVLW and intrathoracic blood volume (ITBV) were compared with respiratory system inertance (I_{rs}) in four piglets before and after broncho-alveolar lavage (BAL) that induced surfactant deficiency with interstitial edema. EVLW and ITBV were determined using the double-indicator dilution technique, I_{rs} by multiple linear regression analysis. Measurements were taken before, and 1 and 2 h after BAL. EVLW increased threefold (from 6.2 ± 0.8 mL/kg at baseline to 17.7 ± 0.9 mL/kg ($p < 0.001$) after BAL). I_{rs} increased by 35% (from 0.17 ± 0.02 to 0.23 ± 0.04 $cmH_2O\ s^2/L$ ($p = 0.036$) after BAL) and was tightly correlated to EVLW ($r^2 = 0.95$, $p < 0.023$). ITBV did not change significantly after BAL. We conclude that I_{rs} reflects actual changes in lung mass and thus hints at fluid accumulation within the lung.

Keywords: Broncho-alveolar lavage; Lung mass; Multiple linear regression analysis; Respiratory system compliance

1. Introduction

The common final path of various cardio-pulmonary diseases is an increase in lung mass due to accumulation of interstitial fluid and alveolar edema. Either the failing left ventricle increases the filtration pressures in the pulmonary vascular bed or inflammation weakens the endothelial/epithelial barrier function such that both cardiogenic edema as well as ARDS is characterized by increased lung mass (Joachim et al., 1978; Gattinoni et al., 1988; Ruiz-Bailen et al., 1999). Other than compliance (reflecting aeratable lung volume and/or intrinsic parenchymal mechanical properties) or resistance (reflecting airway mechanics), respiratory system inertance reflecting lung mass has received little attention. Certainly, inertance contributes much less to pressure than does compliance or resistance and it does so during phases of significant volume acceleration only, which makes it inaccessible to conventional quasi-static mechanical analysis. Combining, however, information on lung volume distensibility (compliance), and airflow dynamics (resistance) with an estimation of lung mass (inertance) might help distinguishing between pathophysiological conditions that require opposite therapies. An increase in airway pressure, for example, might result from bronchoconstriction or edema. Based on compliance and resistance it is difficult if not impossible to distinguish between the potential causes since usually both parameters are altered at the same time. If inertance allows for an estimation of lung mass the problem could be localized at the airway level (lung mass unchanged) or at the cardiac and/or the epithelial/endothelial barrier level (lung mass increased).

In a retrospective analysis of four piglets of a previous study with increased lung water content resulting from broncho-alveolar lavage we here study whether changes in inertance reflect changes in lung mass. Extravascular lung water was determined using the double indicator dilution technique (Lewis et al., 1982; Pfeiffer et al., 1990) and inertance by multiple linear

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regression analysis (Uhl and Lewis, 1974; Rousselot et al., 1992; Lanteri et al., 1995).

We hypothesized that I_{rs} increases concomitantly with lung mass as indicated by increased extravascular lung water at otherwise unchanged lung fluid compartments.

2. Material and methods

The investigations were performed at the Experimental Laboratories of the Department of Surgical Sciences/Section of Anesthesiology and Critical Care Medicine at the University Hospital of Uppsala, Sweden, in conformity with the Helsinki convention for the use and care of animals. The medical ethics committee for animal experimentation reviewed and approved the protocol. Four healthy male and female piglets of Swedish landrace breed (25 ± 2 kg) were studied.

2.1. Protocol

This is a retrospective analysis of a study, so far unpublished, the protocol of which did not specifically address the problem of lung mass. However, since extravascular lung water, and, hence, lung mass was increased by bronchoalveolar lavage, the data allows for testing the concept of an association between lung mass and inertance. Briefly, the animals were subjected to BAL and lung fluid compartments and dynamic mechanics were determined before BAL, immediately after BAL and, at unchanged settings 1 and 2 h after BAL. Seven animals underwent the protocol. In three animals we could not exclude a leakage around the endotracheal tube (as judged from a minor airway pressure decrease at the end of a 5 s end-inspiratory hold). Since inertance analysis focuses on the end-inspiratory to early expiratory (and the end-expiratory to early inspiratory) phase transition (see below) we excluded those three animals from this analysis.

2.2. Broncho-alveolar lavage (BAL)

BAL was performed as described elsewhere (Lachmann et al., 1980; Lichtwarck-Aschoff et al., 1992a). Briefly, 11 bronchoalveolar lavages with 50–60 mL/kg normal saline each were performed. After each cycle, the animals' lungs were ventilated for 5 min (FiO_2 1.0, PEEP 15 cmH_2O and tidal volume (V_t) 15 mL/kg). After BAL, the animals were allowed to stabilize for 20 min. BAL effects were assessed by changes in gas exchange, respiratory mechanics, and of EVLW and intrathoracic blood volume (ITBV) both determined by the double-indicator dilution technique (Lewis et al., 1982; Pfeiffer et al., 1990).

2.3. Ventilatory setting

The lungs were ventilated through an endotracheal tube (ETT, 8 mm inner diameter, Mallinckrodt, Athlone, Ireland) in the volume-controlled mode, connected by a 60 cm rigid tubing system to a Servo 300 ventilator (Siemens-Elema, Solna, Sweden). Respiratory rate (25 min^{-1}), FiO_2 (0.3), and I:E (1:1) were kept constant throughout all experiments. Preceding BAL, PEEP was set to 7 cmH_2O and V_t to 10 mL/kg; FiO_2 was set to 0.3 both before and after lavage to get comparable conditions of gas exchange, while during lavage with its attendant high risk of hypoxemia FiO_2 was set to 1.0. Since, after lavage, the lack of surfactant makes the lungs particularly prone to collapse, an opening procedure was performed therefore (PEEP to 25 cmH_2O; peak inspiratory pressure to 50 cmH_2O during 2 min). The success of this opening procedure was stabilized with a PEEP of 18 cmH_2O, and V_t was increased from 10 to 12 mL/kg to keep $PaCO_2$ at 5–6 kPa.

2.4. Anesthesia and fluid management

Ketamine anesthesia (20 mg/(kg h)) supplemented with morphine (0.5 mg/(kg h)) was used. Muscle relaxation was obtained with pancuronium bromide (0.25 mg/(kg h)). A solution of 4.5 g/L NaCl with 25 g/L glucose (Rehydrex, Pharmacia Infusion AB, Uppsala, Sweden) was infused at 10 mL/(kg h) together with an initial bolus of 10 mL/kg of dextran-70 (Macrodex 70, Pharmacia Infusion, AB) to ensure normovolemia. Normovolemia was assumed with ITBV between 18 and 22 mL/kg (Lichtwarck-Aschoff et al., 1992b).

The animals were studied in the prone position. At the end of the experiment the animals were killed with an overdose of potassium.

2.5. Double indicator dilution technique

EVLW was quantified using the double indicator dilution method as described elsewhere (Lewis et al., 1982; Pfeiffer et al., 1990). In brief: two indicators, a "thermic" indicator (cold dextrose-solution) and a "color" indicator (indocyanine) of known concentration and amount are injected into a central vein. While indocyanine stays within the vascular compartment, indicating the intrathoracic blood volume, the thermic indicator distributes to all compartments of the lung (pulmonary thermovolume). Via a combined thermistor/fiberoptical sensor concentrations of the indicators are measured in the femoral artery. Subtracting ITBV from pulmonary volume yields extravascular thermovolume or extravascular lung water (EVLW) that can be regarded as indicating all extravascular fluid, mainly interstitial edema but also any fluid in the airways or the pleural space if existing.

2.6. Respiratory system mechanics

Airway pressure (P_{aw}) and gas flow were continuously measured using a pulmonary monitor (CP100, Bicore Monitoring Systems, Irvine, CA). Its pressure-flow transducer was placed between the proximal end of the ETT and the Y-piece of the ventilator tubing. The experimental setup was calibrated according to the manufacturer's instructions. The signals were sampled at 50 Hz and transferred to a laptop computer for off-line analysis. Flow ($\dot{V}$) and P_{aw} were checked for artefacts, the flow signal was integrated to obtain volume (V) and differentiated to obtain volume acceleration ($\ddot{V}$) without any filtering. Flow curves, derived from the ventilator's flowmeters, were continuously displayed