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SHORT COMMUNICATION

Development of a bronchospasm device model

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Abstract There is no strong evidence to support ventilatory management for critical limitation of expiratory flow, such as bronchospasm during anesthesia or an acute exacerbation of severe asthma and chronic obstructive pulmonary disease (COPD). Animal models cannot be used to develop reproducible experimental models for conducting mechanical ventilation strategy research relating to these etiologies due to the resulting respiratory and hemodynamic instabilities. Therefore, we developed a device model by modifying a positive end-expiratory pressure (PEEP) valve that can simulate the characteristics of airway bronchoconstriction (i.e., limited peak expiratory flow and a prolonged expiratory phase). These characteristics were found to improve upon narrowing the expiratory port. We believe that this device model will facilitate future mechanical ventilation experiments.

Keywords Asthma · Bronchospasm · Model

Bronchospasm during anesthesia or an acute exacerbation of severe asthma and chronic obstructive pulmonary disease (COPD) is characterized by a critical limitation of expiratory flow. Although it is important to develop a mechanical ventilation strategy for those etiologies that is supported by strong evidence, it is extremely difficult to reproduce such profound pathological alterations in respiratory mechanics using an animal model due to the resulting respiratory and hemodynamic instabilities. Therefore, we developed a bronchospasm device model that would allow us to conduct repeatable and reproducible mechanical ventilation experiments which can mimic severe bronchoconstriction.

We created the device model by modifying a positive end-expiratory pressure (PEEP) valve. Figure 1 shows the model. There are two ports on it: one is attached to the patient side and the other to the ventilator, as depicted in more detail in Fig. 2, which presents a scheme of the interior of the model. By adding a coil spring that pushes the valve down, a gap (X) is maintained during the no-flow state. Port A is connected to the patient side, where expiratory flow occurs. Inspiratory flow is achieved through port B. The air flows in through Q1 and Q2 during the inspiration phase (Fig. 2a). Slow expiratory flow will pass through Q1 and Q2 with minimal resistance (Fig. 2b). When the expiratory flow velocity increases, the valve is pushed up and the air flow through Q1 decreases. More expiratory effort is needed when the valve is maximally displaced upward ($X = 0$). At that point, air flow can only occur through the fixed hole in the valve (Q2) (Fig. 2c). To mimic the "pursed lip breathing" of COPD patients, the diameter of port B was decreased by adding a half-closing lid. When strong expiratory flow passes through port A, with smaller port B airway pressure (P_{aw}) increases and the alveolar pressure (P_{alv}) − P_{aw} decreases relatively, resulting in lower respiratory resistance. This mimics the malignant cycle of increased

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Fig. 1 Photograph of the bronchospasm device model. One port at the bottom (port A) of this picture is attached to the lung simulator (i.e., the patient), while another port on the side (port B) is connected to the ventilator in this experiment

expiratory effort suffered by patients during severe bronchospasm.

A closed loop system with a graphic monitoring device was created by connecting a lung physiology simulator (Lungoo™, Air Water Inc., Osaka, Japan) to port A and a mechanical ventilator (PB840®, Covidien, Mansfield, MA, USA) to port B of the device model described above. A variety of lung mechanics can be obtained with Lungoo™ by setting its muscle pressure (P_{mus}), airway compliance, and resistance appropriately. A respiratory rate of 10 per min, a P_{mus} of 17 cm H_2O, and static compliance and resistance of Lungoo™ were used in our experiment. Graphic monitoring and flow–volume (FV) curve assessment were performed for a series of scenarios, as well as without the device (i.e., the control).

On the flow–time curve, graphic monitoring with the device model indicated a decrease in peak expiratory flow and an increase in expiratory time. Pressure–time curves demonstrated increases in airway pressure and alveolar pressure compared to the control (data not shown).

Flow–volume (FV) curves are shown in Fig. 3. Expiratory peak flow and expiratory tidal volume decreased in the presence of the device model (Fig. 3b) compared to the control (Fig. 3a). When external expiratory resistance was created by semi-occluding port B, expiratory flow per unit time improved (Fig. 3c) compared to the original FV curve obtained with the device.

Thus, our novel bronchospasm device model was observed to accurately simulate the characteristics of airway bronchoconstriction, namely limited peak expiratory

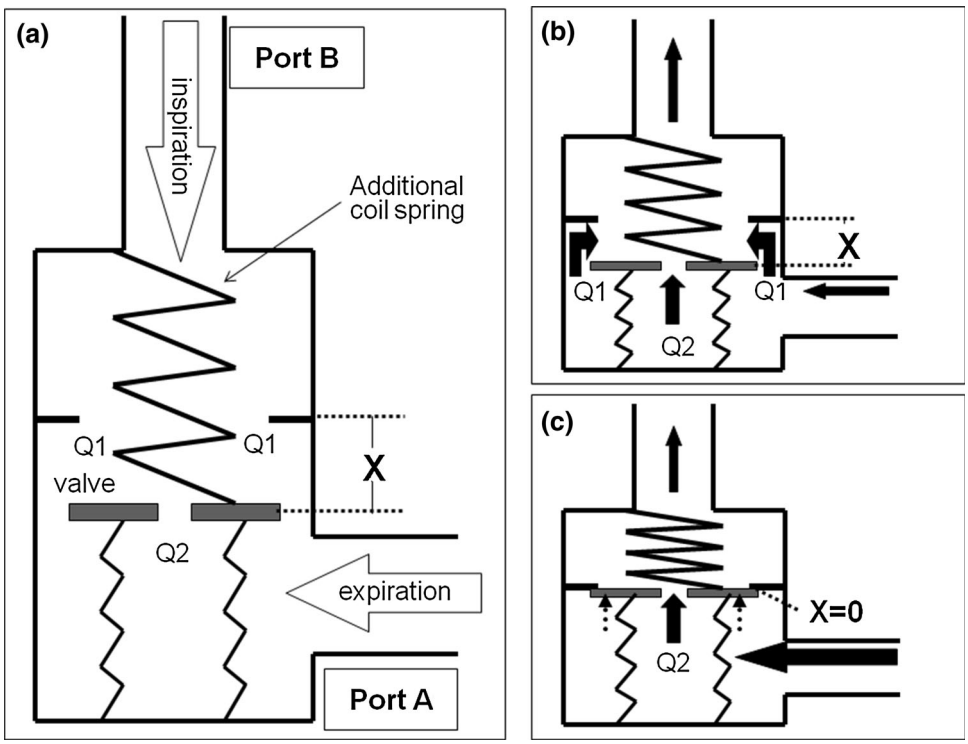

Fig. 2a–c Scheme of the device model. **a** Static state. The model is created by modifying a PEEP valve. The insertion of an additional coil spring produces a gap (*X*). *Q1* space around the valve, *Q2* fixed hole in the middle of the valve. Port A is linked to the patient, and port B to the ventilator. **b** During slow expiration, the expiratory flow pushes the valve up and *X* decreases compared to its value in the static state. Air flows through Q1 and Q2. **c** With increased expiratory effort, the gap *X* is completely eliminated and air flows only through Q2

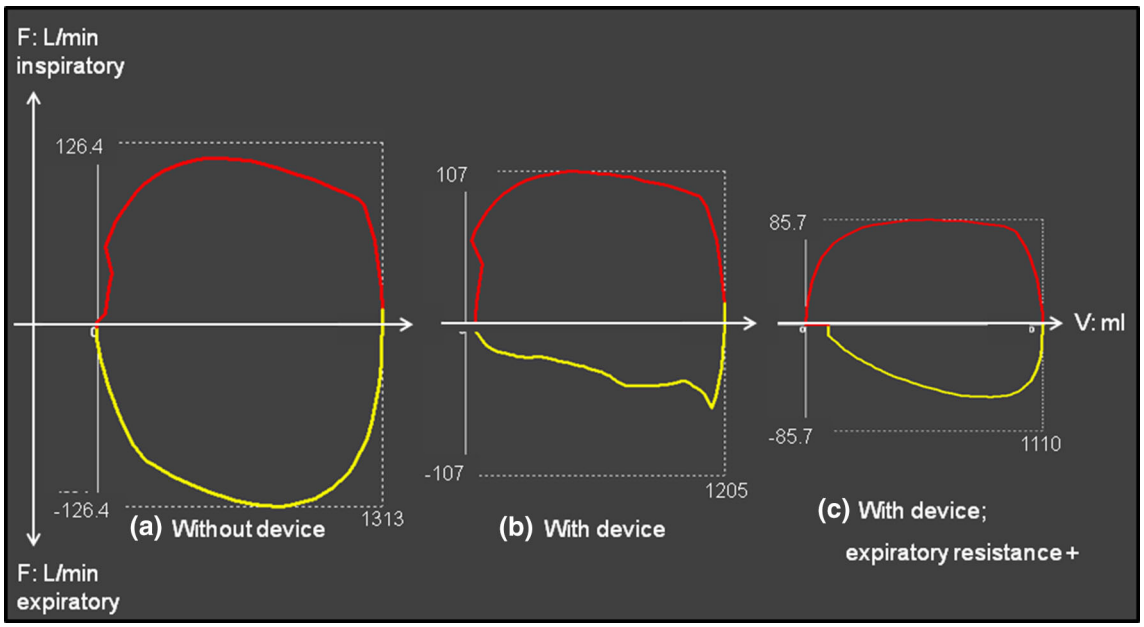

Fig. 3a–c Flow–volume curves. **a** Curves obtained for the closed loop system without the device model. **b** Curves obtained with the device model included: the expiratory peak flow and expiratory tidal volume are smaller than in **a**. **c** Curves obtained when the device model is included and expiratory resistance is present. External expiratory resistance was created by semi-occluding port B. Expiratory flow per unit time is greater than in **b**

flow and a prolonged expiratory phase. These characteristics were found to improve upon narrowing the expiratory port, in a similar manner to the "pursed lip breathing" performed by patients suffering COPD or an asthma attack.

Profound pathophysiologic alterations in the respiratory dynamics occur during severe bronchospasm (e.g., during acute exacerbation of severe asthma, COPD, or medication-induced bronchoconstriction). Increased airway resistance is multifactorial and can be attributed to bronchoconstriction, airway edema, vascular congestion, and luminal occlusion with mucus plugging. These result in reductions in the forced expiratory volume in 1 s (FEV_1), FEV_1/forced vital capacity (FVC) ratio, and peak expiratory flow. Furthermore, critical limitation of the expiratory flow leads to pulmonary hyperinflation [1], and a prolonged expiratory phase leads to incomplete airway emptying prior to inspiration, thus creating auto-positive end-expiratory pressure (PEEP) [2]. Dynamic changes in peripheral airways occur during expiratory effort, which hyperinflated patients tend to suffer from due to limited peak expiratory flow and prolonged expiratory time. High positive intrathoracic pressure during expiratory effort results in external compression of the distal airways [3], which further exacerbates luminal occlusion by creating a negative pressure inside the distal airways with high air-flow velocity. Hyperinflated patients tend to exhale with pursed lip breathing, which is one of the ways of reducing the level of auto-PEEP. Creating this expiratory resistance keeps the peripheral airways open and facilitates expiratory flow during expiration.

Using this device model, we succeeded in reproducing the bronchospasms seen in acute exacerbations of asthma, COPD, and anaphylaxis. Limited peak expiratory flow that worsens with expiratory effort and improves upon narrowing the expiratory port, mimicking the pursed lip breathing of hyperinflated patients, was also simulated. However, there are limitations of this device model: (a) it cannot take into account the severity related to the inspiratory phase, and (b) it represents the lung as a single integrated homogeneous airway and alveolus, whereas real lungs are extremely heterogeneous due to the unbalanced distribution of tidal volume to the distal airways (this distribution depends on the degree of occlusion).

Most of the studies that have been performed using animal models of asthma have focused on the underlying physiological and immunological processes [4]. It is extremely difficult to create a stable in vivo model of severe bronchospasm requiring mechanical ventilation due to the resulting respiratory and hemodynamic instabilities. Our ultimate aim is to discover the optimal mechanical ventilation strategy for bronchospasm and severe exacerbation of COPD. Taking our cue from pursed lip breathing, we are investigating mechanical ventilatory management in which the resistance during the expiration phase is controlled by the ventilator to improve expiration. We believe that this novel device model will prove very useful in our

subsequent experiments and could also potentially find broad application in this field of research in the future.

The development of an ex vivo model of bronchospasm is important as it should lead to improved mechanical ventilation experiments, which will ultimately aid patients suffering from acute exacerbations of obstructive lung diseases. Our device model is able to simulate the dynamics of such patients which could not be achieved by a critical condition of the patients' severe attacks or animal models.

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Conflict of interest None of the authors have any conflict of interest to disclose.

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