Can High Tidal Volumes Prevent Severe Bronchoconstriction And Ventilation Defects?

**A. H. Golnabi, R. S. Harris, J. G. Venegas, T. Winkler**

1Massachusetts General Hospital and Harvard Medical School, Boston, MA, 2

**Corresponding author's email:** Golnabi.Amir@mgh.harvard.edu

**RATIONALE:** Excessive bronchoconstriction is a main feature of asthma. Studies have demonstrated that tidal breathing is bronchoprotective. However, in asthma, environmental stimuli may cause elevated airway smooth muscle (ASM) activation, which may influence the effects of tidal volume (VT) on bronchoconstriction. We hypothesized that there is an effect of both VT, and relative ASM activation (Tr) on bronchoconstriction, and on the emergence of ventilation defects (VDefs), which are regions with very low ventilation or complete gas trapping.

**METHODS:** We used our integrative model of bronchoconstriction to perform simulation experiments for different conditions. The model consists of a 12-generation symmetric bronchial tree with airway radii that change depending on local conditions caused by airflow, pressure, tidal expansion, parenchymal forces, airway smooth muscle behavior, and airway radii throughout the tree. Using this model, we studied 35 different conditions with VT = 300, 400, ..., 900 ml and Tr = 0.6, 0.7, ..., 1.0. Breathing frequency was 12 breaths per minute. Regional ventilation maps along with the fraction of closed terminal units (Fc) were calculated.

**RESULTS:** At low levels of ASM activation (Tr < 0.8), VDefs did not emerge even at the lowest VT, while at higher Tr, higher VT were necessary to avoid VDefs, e.g. VT = 600 at Tr = 0.8. For maximally activated ASM (Tr = 1.0), VT = 900 ml was required to avert hypoventilation and gas trapping. In addition, both VT and ASM activation affected the time of emergence of VDefs and Fc. In fact, for smaller VT, Fc was larger, e.g., 61% vs. 20% for VT = 300 vs. 800 ml, at Tr = 1.0. In addition, for a given Tr > 0.7, VDefs occurred at a later time for larger tidal volumes.

**CONCLUSIONS:** Our model showed a synergistic effect of tidal volume and ASM activation on bronchoconstriction and on the emergence of VDefs. The higher the tidal volume, the higher ASM activation may be tolerated without occurrence of VDefs. Therefore, during severe asthma attacks with potentially high ASM activation, only a considerably high tidal volume may stabilize airway caliber and prevent severe bronchoconstriction.

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