Deep inspiration and airway physiology: human, canine, porcine, or bovine?

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Dynamic respiratory movements such as deep inspiration (DI) are believed to play an important role in limiting airway narrowing, and a failure of this physiological regulation is offered as a potential pathway to airway hyperresponsiveness in asthma (1). While our understanding of the mechanism(s) involved is incomplete, beneficial effects of DI are believed to be due to an intrinsic response of the airway wall (i.e., airway smooth muscle, ASM) to mechanical stretch (4, 6). A recently published study by LaPrad et al. (8) now challenges our understanding, and questions whether dynamic mechanical stretch to the airway wall impacts on airway function at all.

The authors should first be commended on a highly innovative methodology. The study describes a new application for an existing imaging technology, ultrasound, allowing simultaneous measurement of airway caliber (radius) and wall thickness across the length of an airway segment with an acquisition time suitable for dynamic measurements. This approach represents a powerful means of studying airway function in vitro. Unexpectedly, tidal oscillations and DI were concluded to have little to no effect on airway narrowing. We have two specific comments.

The lack of a bronchodilatory effect of tidal and DI oscillations in LaPrad’s bovine segments is in disagreement with numerous other studies that used a similar experimental design, and for which the authors offer little explanation. Accordingly, volume oscillations mimicking both tidal and DI “breathing” patterns in canine and porcine bronchi produce impressive reductions in airway responsiveness to cholinergic stimulation (2, 3, 6, 9, 12). In apparent contrast, lightly toned (i.e., physiologically) bovine airways constrict when stretched (7). LaPrad et al. address some of the above discrepancies by pointing out that the functional outcome of the majority of the earlier studies (not all, see below) was active pressure, which they suggest is difficult to relate to airway caliber. Active pressure is directly related to wall tension (5), and it is expected that reductions in active pressure after DI will favor reduced airway narrowing. Further, at least one direct imaging study of the airway lumen and radius demonstrated considerable bronchodilation after DI persisting up to 1 min (9). This study alone substantiates the previously cited findings using active airway pressure as a measure of responsiveness. How do LaPrad et al. explain this body of evidence, particularly the latter study which shows directly lumen dilation after DI?

The findings of LaPrad et al. (8) do however put the focus back on the importance of the integrated environment of the airway wall in examining responses to mechanical stretch. Viscoelastic properties of the airway wall influence the amount or nature of the stretching of ASM during breathing (11, 12), which is ultimately responsible for airway caliber. Notably, isolated ASM from all three species discussed here (bovine, canine, and porcine) exhibits responses to length oscillation consistent with bronchodilation, i.e., reduced force (4,13,14). The bovine airway wall may well be unique in its response to mechanical stretch (7,8) and even behave more like the asthmatic (10). However, the more pressing question is “what happens in human airways, in normals, and asthmatics?”

Disclosures

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References


