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Assessment of pulmonary vascular smooth muscle remodeling in severe equine asthma

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Abstract

Severe equine asthma (SEA) is characterized by reversible airway obstruction and hypoxemia. Pulmonary hypoxic vasoconstriction occurs during SEA exacerbation, inducing pulmonary hypertension (PH). However, PH is only partially reversed by oxygen administration, and other etiological factors are uninvestigated (Dixon, 1978). In rodent asthma models, airway inflammation is associated with pulmonary artery (PA) remodeling (Rydell-Tormanen *et al.*, 2009), that could contribute to PH, as known in human chronic obstructive pulmonary disease (Barbera *et al.*, 2003). We investigated the presence of PA remodeling in SEA, the involvement of vascular smooth muscle (VSM) alterations and their reversibility following long-term antigen avoidance or inhaled corticosteroids. Using histomorphometry, the PA wall was measured on sections stained with hematoxylin-eosin saffron, collected post-mortem from different lung regions of 12 asthmatic horses and 6 controls. Pulmonary vascular smooth muscle (VSM) mass was measured on sections stained for α -smooth muscle actin collected with *in vivo* thoracoscopy or post-mortem peripheral lung biopsy from 5 controls, 6 asthmatic horses in remission, and 11 asthmatic horses while exacerbation and after 1 year of antigen avoidance alone (5 horses) or treatment with fluticasone (6 horses). Data were compared using unpaired t test with Welch correction or paired t test ($p < 0.05$). PA wall surface percentage was increased in apical ($p = 0.003$) and caudo-dorsal ($p = 0.03$) lung regions (respectively $50,66 \pm 13,16\%$ and $50,56 \pm 15,02\%$) of asthmatic horses, when compared to controls (respectively $35,38 \pm 7,06\%$ and $38,13 \pm 10,18\%$). Similarly, VSM mass percentage was increased ($p = 0.03$) in asthmatic horses ($47,77 \pm 3,17\%$), compared to controls ($41,07 \pm 6,22\%$). A tendency for normalization of the VSM mass was observed after treatment with antigen avoidance ($p = 0.05$; $39,64 \pm 4,02\%$), but not with fluticasone ($p = 0.27$; $45,35 \pm 14,98\%$). Remodeling of the PA occurs in SEA and the increase in VSM could lead to lumen narrowing and enhance hypoxic vasoconstriction, contributing to PH during exacerbation. VSM mass normalization is more effectively obtained by antigen avoidance than by corticosteroids.

References

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