P10.05: REDUCED MOLECULAR FLEXIBILITY IN THE LARGE ARTERIES OF DIABETIC RATS

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Objective: to test whether 1,25(OH)2D3 (active vitamin D) modifies contractility of proximal resistance vessels, dose-dependently.

Methods: Male Wistar rat mesenteric arteries were investigated by wire myography. The calcium mobilization response to 100 mM KCl (KPS) was the reference for contraction and relaxation measurements. Noradrenaline (NA) responses were measured after 10 min, 30 min and 3 hours incubation with 1,25(OH)2D3, as was endothelial function by Acetylcholine (Ach) response.

Results: KPS-induced contraction was unaffected by 1,25(OH)2D3, but slightly decreased after 3 h incubation in control and 1,25(OH)2D3 groups (generally n = 5 arteries each). After 10 min NA-induced contraction at 10-5 M, a small dose response occurred (controls 192±22%; vitD 10 nM 183%, 100 nM 169%), but after 3 h incubation with 100 nM 1,25(OH)2D3, contraction decreased at 3x10-5 M, and at 10-5 M NA to 118.6±10.3%, compared with controls (mean ± SE: 145.4±13.9%). While differences were individually ‘significant’ (p = 0.04, Wilcoxon test), 2-way ANOVA demonstrated clear vitD (F3,80 6.3, p = 0.001) and NA effects (F4,80 p < 0.000), without interaction. Ach-induced relaxation (at 10-7 to 10-3 M) after 30 min incubation was not enhanced by any 1,25(OH)2D3 dose. After 3 h, higher concentration Ach (10-5 to 10-3 M) induced contraction. Paradoxically, 100 nM 1,25(OH)2D3 marginally increased contractions (105.2±4.8%; control 91.7±4.7%), not individually ‘significant’ but by 2-way Anova & Ach dose effects were (F3,96 = 6.6, p < 0.001).

Conclusion: To our knowledge, these are the first vitD experiments on proximal resistance vessels. 100 nM vitamin D may decrease NA-induced contraction but paradoxical endothelial effects may underlie its variable in-vivo actions.

P10.07 REDUCED MOLECULAR FLEXIBILITY IN THE LARGE ARTERIES OF DIABETIC RATS

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In Type 1 and 2 diabetes tissue stiffening is evident from measurements of the gross mechanical properties of the vasculature. In general, pathological glycosylation of extracellular matrix proteins may play an important role in increasing stiffness in diabetic patients. However, the effects of diabetes on individual elastic fibre components remain poorly defined. Fibrillin microfibrils, a key elastic fibre component, have a ‘beads-on-a-string’ structure with a periodicity of approximately 56 nm. We tested for the first time experiments on proximal resistance vessels. 100 nM vitamin D may decrease NA-induced contraction but paradoxical endothelial effects may underlie its variable in-vivo actions.

P10.08 PULMONARY ARTERY CALCIFICATION IN RACEHORSES

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Vascular calcification (VC) has been sporadically reported in horses, but little is known regarding cause, pathogenesis and clinical significance. We hypothesized that in horses, structural and molecular changes may occur during VC that are comparable to human and mouse models. We surveyed Thoroughbred and Standardbred racehorses (n = 101) for the prevalence, distribution and severity of VC. Histopathological, ultrastructural imaging and energy dispersive X-ray elemental analyses were used to examine the lesions. Immunohistochemistry for cell markers (smooth muscle α-actin, SM22α and Sox9) was performed in selected samples from control (n = 10), mildly (n = 10), and severely (n = 10) calcified arteries. Results showed that calcification of the tunica media of the large pulmonary artery branches, was present in 82% of horses, and both breeds and genders were similarly affected. Lesions appeared as white-to-yellowish, hard, gritty plaques of variable size. Microscopically, calcific elastic fibers were thin, fragmented and calcified, and surrounded by dense collagen matrix, as described for Monckeberg sclerosis. Elemental analysis of the calcified areas was consistent with hydroxyapatite mineral. No immunoreactivity for the smooth muscle cell markers, smooth muscle α-actin and SM22α was observed in cells found at the calcification site. Many of these cells had a chondrocytic phenotype appearance and showed immunoreactivity for Sox9, a chondrocyte marker. Arterial calcification in horses share histopathological features with arterial medial calcification in humans and may result in similar physiological abnormalities such as vascular stiffness. The occurrence of VC in young racing horses indicates the need to investigate its pathogenesis and potential clinical implications.