Effect of vitamin D in experimental pulmonary arterial hypertension in rats: Possible role of eNOS mediated signaling pathways

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BACKGROUND

Several clinical studies reported that patients of pulmonary hypertension with co-existing vitamin D deficiency exhibit exaggerated disease manifestations; however, the pathophysiology is unclear. We, therefore, investigated the role of vitamin D deficiency and associated signaling pathways in an experimental model of pulmonary hypertension in rats.

OBJECTIVE

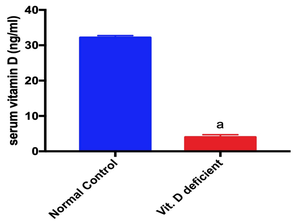
To elucidate the role of eNOS signalling pathway in vitamin D induced amelioration of pulmonary arterial hypertension in rats.

MATERAIL & METHODS

Wistar rats were placed on either vitamin D control diet or vitamin D deficient diet for 16 weeks. Pulmonary arterial hypertension (PAH) was induced with a single dose of monocrotaline (MCT) 50 mg/kg s.c. Rats were randomized to 5 groups: Group I: Control, Group II: MCT, Group III: MCT + sildenafil, Group IV: MCT + vitamin D (100 IU/day), and Group V: MCT + L-NAME (eNOS inhibitor) + vitamin D (100 IU/day). Hemodynamic (Right ventricular systolic pressure RVSP), echocardiographic (right ventricular outflow tract dimension to aortic tract dimension ratio), histopathological and immunohistochemical, and the level of eNOS was measured at the end of 28 days.

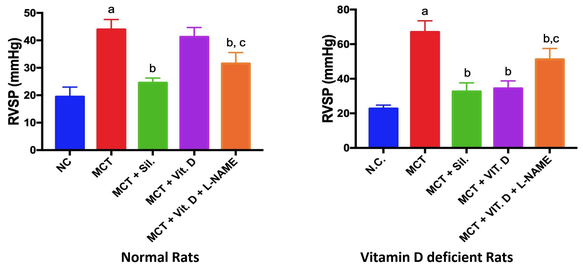
RESULTS

Fig. 1: Levels of vitamin D in rats fed with normal pellet diet and vitamin D deficient diet



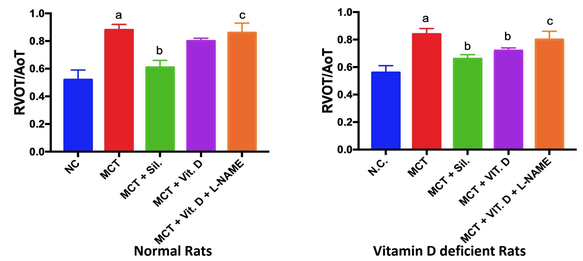
[a]p<0.05 vs. normal control (rats fed normal pellet diet)

Fig. 2: Effect of vitamin D treatment on right ventricular systolic Pressure (RVSP) in normal and vitamin D deficient rats



[a]p<0.05 vs. normal control, [b]p<0.05 vs. MCT, [c]p <0.05 vs. MCT + Vitamin D

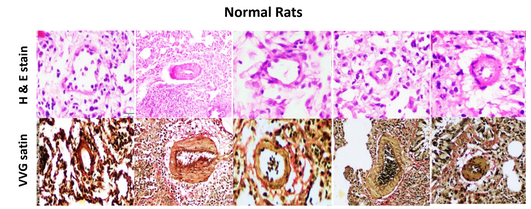
Fig. 3: Effect of vitamin D treatment on right ventricular outflow tract dimension to aortic dimension ratio(RVoT/AoT) in normal and vitamin D deficient rats



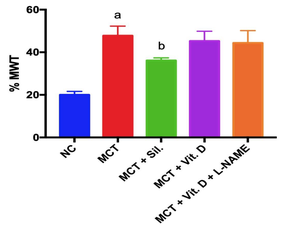
[a]p<0.05 vs. normal control, [b]p<0.05 vs. MCT, [c]p <0.05 vs. MCT + Vitamin D

RESULTS

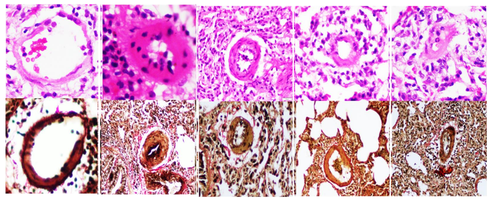
Fig. 4: Effect of vitamin D treatment on histopathology of lungs in normal and vitamin D deficient rats



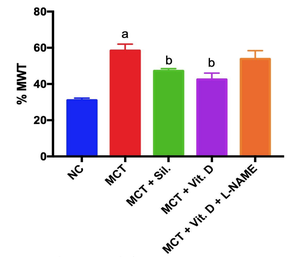
I-NORMAL CONTROL; II-MCT; III-MCT + SILDENAFIL; IV-MCT + VITAMIN D; V- MCT + VITAMIN D + L-NAME



[a]p<0.05 vs. normal control, [b]p<0.05 vs. MCT

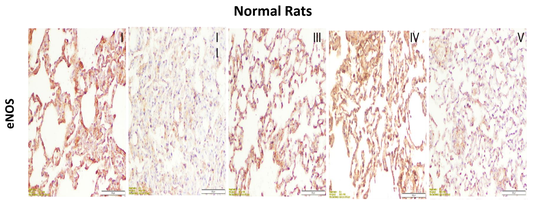


I-NORMAL CONTROL; II-MCT; III-MCT + SILDENAFIL; IV-MCT + VITAMIN D; V- MCT + VITAMIN D + L-NAME



[a]p<0.05 vs. normal control, [b]p<0.05 vs. MCT

Fig. 5: Effect of vitamin D treatment on the expression of eNOS in the lungs of normal and vitamin D deficient rats



I-NORMAL CONTROL; II-MCT; III-MCT + SILDENAFIL; IV-MCT + VITAMIN D; V- MCT + VITAMIN D + L-NAME

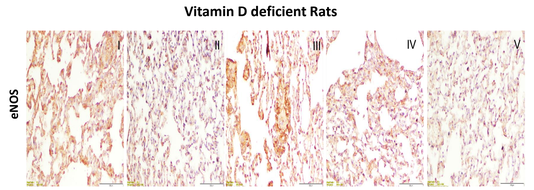
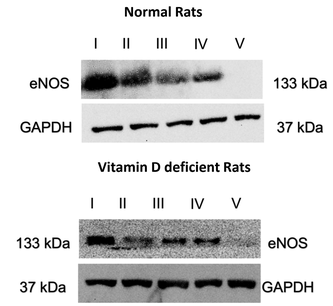


Fig. 6: Effect of vitamin D treatment on the levels of eNOS in the lungs of normal and vitamin D deficient rats



CONCLUSION

These data suggest a major role of vitamin D in pulmonary vascular homeostasis which is regulated via the endothelial nitric oxide synthase pathway. It also supports the clinical evaluation of vitamin D levels in patients with pulmonary hypertension to prevent disease severity and progression.