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Pulmonary Hypertension

ANDROGEN SUPPLEMENTATION IMPROVES RIGHT VENTRICULAR SYSTOLIC FUNCTION IN A CHRONIC HYPOXIA MODEL

ACC Moderated Poster Contributions
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Session Title: Highlighting Right Ventricular Structure, Function, and Physiology in Pulmonary Hypertension
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Background: Chronic hypoxia (CH) leads to pulmonary arterial hypertension (PAH) . CH in the C57B/I6 mouse leads to PAH and right ventricular (RV) systolic and diastolic dysfunction. While much focus has been paid to the gender differences associated with PAH, the role of androgens in the genesis and progression of RV dysfunction in PAH has never been examined. It has been shown that men with congestive heart failure typically develop androgen deficiency that is thought to have some role in the pathophysiological process. Androgens, specifically dihydrotestosterone (DHT), can induce physiologic cardiac hypertrophy, the role of androgens in CH has never been evaluated. This study evaluates the effect of androgen therapy on RV function in the context of CH associated PAH.

Methods: Adult C57Bl/6 mice were exposed to hypoxia (FIO2=10%; 21 days) and given either testosterone (0.2mg/day) or DHT (0.2mg/day) via subcutaneous pellet. At the end of 21 days, hemodynamics and protein expression in RV and lung were assessed. Using invasive hemodynamics, pressure-volume loops were obtained.

Results: It was shown that there were significant improvements in RV systolic function (Ejection Fraction, and RV contractility (ESPVR) in the right ventricle of animals treated with DHT and testosterone.

Conclusion: These data suggest that androgen supplementation exerts a beneficial effect on RV systolic function in the context of CH associated PAH and suggest that there may be differences in the effects of testosterone versus DHT.

Results

Parameter	Hypoxia	Hypoxia with DHT	Hypoxia with Testosterone	p-valueANOVA
Ejection Fraction	45.27 ± 13.04	59.33 ± 9.89 *	62.00 ± 12.17 *	0.0143
End Systolic Volume	27.82 ± 16.50	11.33 ± 6.50 *	12.13 ± 5.96 *	0.0117
End Systolic Pressure Volume Relationship (ESPVR)	1.406 ± 1.28	3.076 ± 0.39 *	1.991 ± 1.10	0.0371
*P<0.05 vs Hypoxia #P<0.05 vs Hypoxia + DHT				