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

ACC Moderated Poster Contributions
McCormick Place South, Hall A
Sunday, March 25, 2012, 11:00 a.m.-Noon

Session Title: Highlighting Right Ventricular Structure, Function, and Physiology in Pulmonary Hypertension
Abstract Category: 30. Pulmonary Hypertension
Presentation Number: 1130-477

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Background: Chronic hypoxia (CH) leads to pulmonary arterial hypertension (PAH). CH in the C57B/16 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

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Hypoxia</th>
<th>Hypoxia with DHT</th>
<th>Hypoxia with Testosterone</th>
<th>p-value ANOVA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ejection Fraction</td>
<td>45.27 ± 13.04</td>
<td>59.33 ± 9.89 *</td>
<td>62.00 ± 12.17 *</td>
<td>0.0143</td>
</tr>
<tr>
<td>End Systolic Volume</td>
<td>27.82 ± 16.50</td>
<td>11.33 ± 6.50 *</td>
<td>12.13 ± 5.96 *</td>
<td>0.0117</td>
</tr>
<tr>
<td>End Systolic Pressure Volume Relationship (ESPVR)</td>
<td>1.406 ± 1.28</td>
<td>3.076 ± 0.39 *</td>
<td>1.991 ± 1.10</td>
<td>0.0371</td>
</tr>
</tbody>
</table>

*P<0.05 vs Hypoxia
#P<0.05 vs Hypoxia + DHT