Abstract: **P5439**

**Protective effect of angiotensin-neprilysin inhibition compared to angiotensin inhibition on ventricular arrhythmias in spontaneous hypertensive rats**

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**Topic(s):**
Chronic Heart Failure: Pharmacotherapy

**Citation:**

Background

Angiotensin-neprilysin inhibition compared to angiotensin inhibition decreased sudden cardiac death in patients with reduced ejection fraction heart failure. The protective effect from ventricular arrhythmia in diastolic heart failure (DHF) remains unknown.

Methods

The spontaneous hypertensive rat (SHR) has been well established as a suitable model for studies of DHF. A total of 18 10-week-old male SHR were divided into three groups: sacubitril/valsartan, valsartan and saline (0.9%) (n=6 in each group). Eighteen 10-week-old male Wistar-Kyoto rats (WKY) were served as the control group. After two weeks feeding with sacubitril/valsartan, valsartan and saline in SHR and WKY. Optical mapping was performed to measure the electrical dynamic of cardiac ventricle and the maximal slope of action potential duration restitution was calculated. An S1–S2 pacing protocol was applied at the right ventricle to determine inducibility of ventricular tachycardia and fibrillation (VT/VF).

Results:

SHR revealed increased LV mass than those treated with sacubitril/valsartan, and valsartan. Compared with WKY, SHR had significantly higher max slope (1.32±0.12 vs. 0.28±0.08, p<0.001). SHR was less prone to arrhythmogenicity after treated with valsartan than saline (0.29±0.04 vs. 1.32±0.12, p<0.001). Furthermore, the max slope was even lower in SHR treated with sacubitril/valsartan than those with valsartan (0.10±0.03 vs. 0.29±0.04, p=0.005). The incidence of induced sustained VT/VF (duration > 2 second) was significant higher in SHR compared with WKY (18 ± 11.1 % vs. 0%, p<0.001) and also higher in SHR treated with valsartan compared with those with sacubitril/valsartan (7 ± 6.5% vs. 5 ± 2.9%, p=0.036).

Conclusions

Angiotensin-neprilysin inhibition could provide better protection from ventricular arrhythmia than valsartan in SHR, warranting the further investigation of angiotensin-neprilysin inhibition in DHF patients.
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<table>
<thead>
<tr>
<th>Group</th>
<th>Max. slope</th>
<th>P-value</th>
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<tbody>
<tr>
<td>WKY</td>
<td>0.28±0.08</td>
<td>WKY vs. SHR: p value 0.001</td>
</tr>
<tr>
<td>SHR</td>
<td>1.32±0.12</td>
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<tr>
<td>SHR-val</td>
<td>0.29±0.04</td>
<td>SHR vs. SHR-val: p value 0.001</td>
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<tr>
<td>SHR-sacu/val</td>
<td>0.10±0.03</td>
<td>SHR-val vs. SHR-sacu/val: p value 0.005</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Group</th>
<th>Sustained arrhythmia incidence (%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SHR</td>
<td>18 ± 11.1</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>WKY</td>
<td>0</td>
<td></td>
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<tr>
<td>SHR-val</td>
<td>7 ± 6.5</td>
<td>P&lt;0.036</td>
</tr>
<tr>
<td>SHR-sacu/val</td>
<td>5 ± 2.9</td>
<td></td>
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</tbody>
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