LONG-TERM THERAPY WITH BENDAVIA (MTP-131), A NOVEL MITOCHONDRIA-TARGETING PEPTIDE, REDUCES TOTAL BURDEN OF REACTIVE OXYGEN SPECIES IN LV MYOCARDIUM AND PLASMA OF DOGS WITH ADVANCED HEART FAILURE

Poster Contributions
Hall C
Saturday, March 29, 2014, 10:00 a.m.-10:45 a.m.

Session Title: Heart Failure and Cardiomyopathies: Therapy I
Abstract Category: 14. Heart Failure and Cardiomyopathies: Therapy
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Background: Reactive oxygen species (ROS) burden is increased in heart failure (HF) and can lead to damage of cellular DNA, lipids, and proteins and ultimately to cell death. We showed that long-term therapy with Bendavia (BEN), a novel mitochondria targeting peptide, improves mitochondria and LV function in dogs with HF. This study examined the effects of BEN on ROS burden in plasma and LV myocardium of dogs with microembolization-induced HF (LV ejection fraction ~30%).

Methods: HF dogs (n=14) were randomized to 3 months therapy with subcutaneous injections of BEN (0.5 mg/kg once daily, n=7) or saline (control, n=7). Plasma was obtained at baseline (BL), after induction of HF (pre-treatment, PRE) and at 6 weeks (Wks) and 12-Wks of therapy. LV tissue was obtained after 12-Wks of therapy and from 6 normal (NL) dogs for comparison. ROS levels were evaluated luminometrically and expressed as relative luminescence units (RLUx10^5/ml) in plasma and in RLUx10^4/μg protein in tissue.

Results: Plasma ROS levels increased in both study groups at PRE compared to BL (Table). ROS levels also increased in LV of HF Controls compared to NL dogs (1.45 ± 0.18 vs. 0.77 ± 0.04; p<0.05). BEN decreased ROS levels in plasma at 6-Wks and more profoundly at 12-Wks (Table) and in LV tissue compared to Controls (0.90 ± 0.0.06 vs. 1.45 ± 0.18, p<0.05).

Conclusions: Long-term therapy with BEN reduced ROS levels in plasma and LV tissue of HF dogs. Alleviating ROS burden with BEN likely contributed to the observed improvement of LV function in dogs with HF.

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<th>BL</th>
<th>PRE</th>
<th>6-Wks</th>
<th>12-Wks</th>
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<tbody>
<tr>
<td>Plasma ROS in Control Group</td>
<td>5.0 ± 0.3</td>
<td>21.1 ± 3.1*</td>
<td>22.9 ± 3.6*</td>
<td>24.7 ± 3.6*</td>
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<tr>
<td>Plasma ROS in BEN Group</td>
<td>5.3 ± 0.5</td>
<td>20.7 ± 2.6*</td>
<td>18.4 ± 1.8*</td>
<td>10.6 ± 0.8*†</td>
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*p<0.05 vs. BL; †=p<0.05 vs. PRE