Abstract: **P1224**

**Angiotensin II-mediated oxidative stress increased the vulnerability of ventricular arrhythmia in cardiac hypertrophy rabbit model, which is suppressed by CaMKII inhibitor**

**Authors:**
YS Lee¹, DG Shin², BC Jung³, HW Park⁴, ¹Catholic University of Daegu - Daegu - Korea Republic of, ²Yeungnam University, cardiology - Daegu - Korea Republic of, ³Fatima General Hospital, cardiology - Daegu - Korea Republic of, ⁴Yonsei University College of Medicine, Cardiology - Seoul - Korea Republic of,

**Topic(s):**
Vascular Biology and Physiology: Ion Channels, Electrophysiology

**Citation:**

Objectives: Angiotensin system is a major cause of heart failure and arrhythmia. Despite a lack of direct evidence that oxidative stress causes ventricular arrhythmia, reversal of oxidative stress is considered a plausible therapy. This study evaluated the Ca²⁺/calmodulin-dependent protein kinase II (CaMKII) inhibitor could suppress arrhythmia in cardiac hypertrophy rabbit model.

Methods: Angiotensin II (Ang II) or saline was administrated for 2 weeks via osmotic minipumps implanted subcutaneously in the midclavicular region. Hearts were perfused, mapped optically to analyze action potential durations (APD), and restitution kinetics, and tested for VF vulnerability. The intracellular calcium dynamics were measured in cardiomyocyte treated with Ang II (10 ng/ml) for 1 hours.

Results: In Ang II rabbit groups, 2(30%) rabbits died and had ventricular arrhythmia and hearts had enlarged left ventricle, longer APD90, slower conduction velocity (CV; P<0.01 versus control) and higher levels of transcripts for CaMKII, PLB, RyR2 (P<0.05 versus control). N-acetylcysteine treatment reversed the transcripts for APD90 and CV (P<0.01). Programmed stimulation triggered VF in Ang II (n=5/6) and Ang II + saline (n=4/6), but not in control (n=0/10, P<0.01).

Cardiomyocyte induced with Ang II showed increased spontaneous Ca²⁺ release (Ca²⁺ Wave Frequency; 1.0±0.0 vs. 5.1±0.5, p=0.001, Ca²⁺ Amplitude; 1.0±0.0 vs. 1.3±0.1, p=0.001) with control. CaMKII inhibitor reversed the change of Ca²⁺.

Conclusion: The Ang II group had an increased incidence of arrhythmia caused by increased phosphorylation of Ca²⁺ handling proteins. These changes were partially reversed by CaMKII inhibition.
Abstract: P1224

Angiotensin II-mediated oxidative stress increased the vulnerability of ventricular arrhythmia in cardiac hypertrophy rabbit model, which is suppressed by CaMKII inhibitor.

Authors: YS Lee, DG Shin, BC Jung, HW Park, 1 Catholic University of Daegu - Daegu - Korea Republic of, 2 Yeungnam University, cardiology - Daegu - Korea Republic of, 3 Fatima General Hospital, cardiology - Daegu - Korea Republic of, 4 Yonsei University College of Medicine, Cardiology - Seoul - Korea Republic of.

Topic(s): Vascular Biology and Physiology: Ion Channels, Electrophysiology

Citation: Objectives: Angiotensin system is a major cause of heart failure and arrhythmia. Despite a lack of direct evidence that oxidative stress causes ventricular arrhythmia, reversal of oxidative stress is considered a plausible therapy. This study evaluated the Ca2+/calmodulin-dependent protein kinase II (CaMKII) inhibitor could suppress arrhythmia in cardiac hypertrophy rabbit model.

Methods: Angiotensin II (Ang II) or saline was administrated for 2 weeks via osmotic minipumps implanted subcutaneously in the midclavicular region. Hearts were perfused, mapped optically to analyze action potential durations (APD), and restitution kinetics, and tested for VF vulnerability. The intracellular calcium dynamics were measured in cardiomyocyte treated with Ang II (10 ng/ml) for 1 hours.

Results: In Ang II rabbit groups, 2(30%) rabbits died and had ventricular arrhythmia and hearts had enlarged left ventricle, longer APD90, slower conduction velocity (CV; P<0.01 versus control) and higher levels of transcripts for CaMKII, PLB, RyR2 (P<0.05 versus control). N-acetylcysteine treatment reversed the transcripts for APD90 and CV (P<0.01). Programmed stimulation triggered VF in Ang II (n=5/6) and Ang II + saline (n=4/6), but not in control (n=0/10, P<0.01).

Cardiomyocyte induced with Ang II showed increased spontaneous Ca2+ release (Ca2+ Wave Frequency; 1.0±0.0 vs. 5.1±0.5, p=0.001, Ca2+ Amplitude; 1.0±0.0 vs. 1.3±0.1, p=0.001) with control. CaMKII inhibitor reversed the change of Ca2+.

Conclusion: The Ang II group had an increased incidence of arrhythmia caused by increased phosphorylation of Ca2+ handling proteins. These changes were partially reversed by CaMKII inhibition.