Combined Therapy of Sildenafil and Beraprost Improves Arrhythmogenicity Through Connexin 43 Expression and Action Potential Dispersion in Monocrotaline-Induced Rat Pulmonary Hypertension

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Severe pulmonary hypertension (PH) is associated with sudden cardiac death (SCD). Optical mapping analysis (OMP) with electrophysiological study (EPS) and connexin-43 measures were performed weekly in Sprague-Dawley rat with monocrotaline (MCTi, 60mg/kg)-induced PH. Right ventricular pressure (RVP) and pulmonary vascular remodeling (PVR) were measured. EPS for ventricular fibrillation (VF) induction, action potential dispersion (APD) measures and RT-PCR for mRNA expression of connexin-43 (Conx-Ex) were performed. Daily administration of sildenafil (5mg/kg) and beraprost (100μg/kg) was initiated at 2 or 3 weeks after MCTi. OMP revealed abnormal RV conduction with high VF induction rate. Decreased Conx-Ex and APD with high RVP at 3, 4 and 5 weeks after MCTi were observed. Sildenafil with beraprost improved PVR, RV arrhythmogenicity, Conx-Ex, cardiac function and survival rates.

Conclusions: Sildenafil with beraprost therapy improves prognosis by preventing SCD and heart failure. These results give us further insights for understanding PH-induced SCD and therapeutic option for PH.

Keywords: optical mapping, sudden cardiac death, pulmonary hypertension