

**The Effect of Sildenafil on Right Ventricular Failure in Monocrotaline-Induced Rat**

*Hong Y.M.(1), , Kim K.C.(2)*

*Department of Pediatrics(1), Department of Thoracic and Cardiovascular Surgery(2), Ewha Womans University, Seoul, Korea*

Background : Pulmonary arterial hypertension (PAH) leads to right ventricular failure (RVF) as well as an increase of pulmonary vascular resistance. Our purpose was to investigate the hemodynamic effects as well as the cellular and molecular impact of sildenafil on RVF in monocrotaline (MCT)-induced rat models.

Subjects and Methods: The rats were separated into 3 groups. The control (C) group, the monocrotaline (M) group (MCT 60 mg/kg) and the sildenafil (S) group (MCT 60 mg/kg + sildenafil 30 mg/kg/day for 28 days). Masson Trichrome staining was used to measure the collagen content in the heart tissues. Western blot analysis and immunohistochemical staining were performed.

Results: The mean right ventricular pressure (RVP) was significantly decreased in the S group at weeks 1, 2 and 4. The number of intra-acinar arteries and the medial wall thickness of the pulmonary arterioles significantly decreased in the S group at week 4. The collagen content also decreased in the S group at week 4.

The expressions of Bcl-2-associated X (Bax), caspase-3, B cell lymphoma-2 (Bcl-2), interleukin-6 (IL-6), matrix metalloproteinase (MMP)-2, endothelial nitric oxide synthase (eNOS), endothelin (ET)-1 and ET receptor A (ERA) in immunohistochemical staining greatly reduced in the S group at week 4. In western blot analysis, protein expressions of troponin I and brain natriuretic peptide (BNP), caspase-3, Bcl-2, TNF- $\alpha$ , IL-6, MMP-2, eNOS, ET-1, ERA in the heart tissues were greatly diminished in the S group at week 4.

Conclusion: Sildenafil improved right ventricular hypertrophy, mean RVP, lung and heart pathology and gene expressions. There also was improvement in RVF.