Topic: Heart Failure (Clinical), Cardiomyopathy, Myocarditis

A PRMT5 Selective Inhibitor EPZ015666 Suppressed TAC-induced Left Ventricular Dysfunction

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Background

The mortality of heart disease has been increasing in all over the world. Cardiac hypertrophy is an important risk factor for heart failure. We have previously reported that protein arginine methyltransferase 5 (PRMT5) specific inhibitor EPZ015666 (EPZ) suppressed cardiomyocyte hypertrophy in neonatal rat cardiomyocytes. However, it is unclear whether EPZ can suppress transverse aortic constriction (TAC)-induced cardiac hypertrophy and systolic dysfunction *in vivo*.

Methods and Results

TAC or sham operation was performed on male C57BL/6J mice at 8–10 weeks old. EPZ or vehicle was administrated to mice every morning for 8 weeks beginning on the next day of operation. Echocardiography was performed at 8 weeks after surgery.

Fractional shortening (FS) and ejection fraction (EF) was significantly decreased in TAC+vehicle group and EPZ significantly improved in them. Following the echocardiography, mice were killed and body weight (BW), tibia length (TL), and heart weight (HW) were measured. HE staining and qRT-PCR were performed. There were no significant difference in BW between TAC+EPZ group and TAC+vehicle group. HW/TL ratio, cardiomyocyte diameter, and hypertrophic gene expression were significantly suppressed in TAC+EPZ group compared with TAC+vehicle group.

Conclusion

These results indicated that EPZ suppressed TAC-induced cardiac hypertrophy and systolic dysfunction. EPZ may be a new therapeutic agent for heart failure. ■