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Effect of Telotristat Ethyl on Cardiac Valve Degeneration

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BACKGROUND: Myxomatous mitral valve degeneration increases in prevalence with age. An increasing body of evidence suggests that serotonin signaling is a regulator of valvular degenerative processes. Telotristat ethyl (TE) is an inhibitor of tryptophan hydroxylase 1, the rate-limiting enzyme in serotonin synthesis, and is used in patients with carcinoid syndrome diarrhea. We examined the impact of TE on cardiac valve degeneration.

METHODS: A hypertensive mouse model was established by angiotensin II (A2) delivery. Immunohistochemistry was used to identify myxomatous changes inducible by A2. Telotristat ethyl was administered in two settings: 1) in parallel with A2 treatment, as a preventive approach; 2) after A2 treatment, as a reversal approach. Both settings had four groups: control, control plus TE, A2, and A2 plus TE.

RESULTS: In both settings, A2 increased blood pressure, mitral valve thickness, and mitral valve expression of MMP1, α-SMA, and TGFβ compared to control. In both settings, A2 plus TE reduced circulating serotonin, mitral valve thickness, and mitral valve expression of MMP1 and α-SMA, but not TGFβ compared to A2.

CONCLUSION: Markers of myxomatous degeneration increased in animals treated with A2 and decreased with TE. Clinical research is warranted to examine the impact of TE on cardiac valves.