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VALSARTAN INHIBITS AORTIC REMODELLING BY BLOCKING THROMBOSPONDIN-1 MEDIATED TRANSFORMING GROWTH FACTOR-β 1/SMADS PATHWAY IN DIABETIC RATS

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Objectives Angiotensin II (Ang II) and transforming growth factor β (TGFβ) are closely involved in the pathogenesis of diabetic complications. The aim of the study was to determine whether aberrant thrombospondin 1 (TSP1) mediated TGFβ1/Smads signalling pathway specifically impacts vascular fibrosis and valsartan exerts an anti-fibrotic effect in diabetic rats.

Methods Age-matched male Wistar rats (200–240 g) were randomly divided into control group (n=8), diabetic group (n=16) and valsartan group (n=16). Type 2 diabetes mellitus (T2DM) was induced by high-calorie diet and streptozotocin injection. Morphological and biomechanical properties of thoracic aorta were assessed by echocardiography and cardiac catheterisation. Masson staining was used for histological evaluation of collagen. The expressions of components in TSP1 mediated TGFβ1/Smads signalling pathway were analysed by immunohistochemistry and real time quantitative reverse transcription PCR.

Results In comparison with controls, the thoracic aorta in diabetic rats was reduced in distensibility and compliance, with excessive collagen deposition. Components in TSP1 mediated TGFβ1/Smads signalling pathway, including TSP1, TGFβ1, TGFβ type II receptor (TβRII), Smad2 and Smad3, were accumulated in the cytoplasm of vascular smooth muscle cells. Their protein and mRNA levels were up-regulated by hyperglycaemia. All these abnormalities were obviously attenuated by valsartan, an Ang II subtype 1 receptor blocker.

Conclusions TSP1-mediated TGFβ1/Smads activation plays an important role in marcovascular remodelling of T2DM. Valsartan can block the TSP1 mediated TGFβ1/Smads signalling pathway and alleviate vascular fibrosis.