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SIGNIFICANCE OF IMIDAPRIL IN THE DIRECT INHIBITION OF MATRIX METALLOPROTEINASES IN EXPEIMENTAL ABDOMINAL AORTIC ANEURYSM; COMPARISON WITH LOSARTAN

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Background: Abdominal aortic aneurysm (AAA) is characterized is characterized by the destruction of tissue architecture due to chronic inflammation of unknown etiology. Emerging clinical evidence showed the effectiveness of angiotensin-converting enzyme inhibitor (ACEI) on the progression of AAA more than angiotensin II receptor blockers, although the underlying mechanism has not been fully elucidated.

Methods: We investigated the effects of ACEI, imidapril (10mg/kg/say, n =10), angiotensin II receptor blocker, losartan (10mg/kg/say, n =10), and hydralazine (30mg/kg/day, n =10) on CaCl2-induced AAA in mice. Saline-treated mice was served as controls.

Result: Six week after CaCl2-treatment, imidapril significantly prevented the enlargement of aorta compared to treatments with an angiotensin II receptor blocker, losartan and hydralazine. (28%, 60% and 84%, respectively, $p< 0.01$). Blood pressure was significantly and equally lowered among three groups. The elevated expressions of MCP-1 and TNF-alpha and the recruitment of macrophages to AAA lesion were significantly reduced in imidapril-treated mice compared to losartan and hydralazine-treated mice. The in situ gelatin zymographies showed that lower matrix metalloproteinase (MMP)-2 and MMP-9 activities in AAA in imidapril treated mice compared with losartan and hydralazine treated mice. In addition, in vitro experiment, imidapril significantly reduced the activities of MMPs from AAA tissue and cultured smooth muscle cells more than that in losartan, even after the addition of serine protease inhibitors.

Conclusion: Imidapril attenuated the development of AAA more than losartan in mice. The direct inhibitory action of MMPs in imidapril may contribute to the protection of dilatation of aorta.