Blockade of Angiotensin II Receptors Reduces the Expression of Receptors for Advanced Glycation End Products in Human Endothelial Cells

Masashi Fujita, Hiroko Okuda, Osamu Tsukamoto, Yoshihiro Asano, Yulin Liao, Akio Hirata, Jiyoong Kim, Takeshi Miyatsuka, Seiji Takashima, Tetsuo Minamino, Hitonobu Tomoike, Masafumi Kitakaze

Objectives—Receptors for advanced glycation end products (RAGEs) play crucial roles in atherogenesis. Because tumor necrosis factor α (TNFα) is expressed and upregulates RAGE expression in atherosclerotic lesions, the TNFα-RAGE interaction might be involved in the inflammatory process of atherogenesis. On the other hand, an angiotensin II type-1 receptor blocker (ARB), widely used as an antihypertensive drug, has been reported to have also antiatherosclerotic effects. Thus we investigated whether an ARB exerts antiatherosclerotic effects via inhibiting the TNFα-RAGE interaction.

Methods and Results—Stimulation of human endothelial cells with candesartan as well as olmesartan decreased TNFα-induced RAGE expression in both mRNA and protein levels along with the decrease in the activity of nuclear factor κB and the expression of inflammatory mediators such as vascular cell adhesion molecule (VCAM)-1. Both candesartan and olmesartan inhibited the binding of nuclear factor κB to the RAGE gene promoter. Furthermore, gene silencing of RAGE by RNA interference decreased the expression of TNFα-induced VCAM-1 in both mRNA and protein levels.

Conclusions—RAGE contributes at least partially to the TNFα-induced VCAM-1 expression in both mRNA and protein levels. Blockade of angiotensin II receptors might exert antiatherosclerotic effects via reducing TNFα-RAGE interaction. (Arterioscler Thromb Vasc Biol. 2006;26:e138-e142.)

Key Words: angiotensin II type-1 receptor blocker (ARB) ■ receptors for advanced glycation end products (RAGEs) ■ endothelial cell

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