Sympathoinhibitory Effect of Diltiazem and Prevention of Aneurysm Formation

To the Editor:

We read with great interest the article by Mieth and colleagues1 dealing with the effect of the benzothiazepine-type calcium channel blocker, diltiazem, on aortic aneurysm formation in a mouse model. The results of their study demonstrated that diltiazem significantly prevented abdominal aneurysm formation in a blood pressure-independent manner in male apolipoprotein E–deficient mice infused with angiotensin II. In addition, the authors showed that diltiazem inhibited the interleukin-6 (IL-6)–induced mRNA expression of IL-1β and the monocyte chemoattractant protein in macrophages and RAW 264.7 cell line. The authors proposed that the antianeurysmal effect of diltiazem might be a result of the suppression of vascular inflammation by blocking the IL-6–induced cytokine expression and macrophage-mediated proinflammatory priming and chemotaxis of inflammatory cells into the vessel wall.

Evidence indicates that the sympathetic nerve activity might have a role in the process of aneurysm formation. An epidemiological study has shown that an increase in resting heart rate, which might reflect the sympathetic nerve activity, was related to an increased risk for mortality of vascular diseases, including abdominal aortic aneurysm.2 Recently, it has been demonstrated that the sympathetic neurotransmitter noradrenaline and the cotransmitter adenosine-5′-triphosphate synergistically induced the release of IL-6 by human dermal microvascular endothelial cell line.3 Because IL-6 might be of major importance for the aneurysmal process in humans,4 it might be possible that production of IL-6 by the sympathetic nerve activation might partially explain the aneurysm formation under conditions of stress. In a study presented previously, we showed that diltiazem significantly inhibited the stimulation-evoked noradrenaline release in the mesenteric arteries of spontaneously hypertensive rats,5 indicating the sympatholytic action of diltiazem in vascular wall in hypertension. In this context, it is strongly suggested that the inhibitory effect of diltiazem on vascular sympathetic nerve activity might contribute, at least in part, to the prevention of aneurysm formation.

Therefore, I would like to know whether IL-6–induced cytokine production in macrophages might be associated with changes in the sympathetic nerve activity, and whether diltiazem could inhibit the sympathetic nerve activity in the aneurysmal model in the study of Mieth and colleagues. Further studies should be performed to assess more precisely the relationships between the sympathetic nerve activity and inflammation, and their relation to the antianeurysmal effect of diltiazem.

Disclosures

None.

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