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Azelnidipine

A Viewpoint by Yukihito Higashi

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Azelnidipine is a new dihydropyridine calcium channel antagonist that is selective for L-type calcium channels. In patients with hypertension, a single dose of orally administered azelnidipine 8mg reaches peak plasma concentrations at 3.7 hours and has a plasma half-life of about 6 hours. This drug has a slow and persistent hypotensive effect, and does not affect the circadian rhythm of blood pressure. Azelnidipine, like amlodipine, is a third-generation dihydropyridine calcium antagonist.

Azelnidipine is generally well tolerated. Notably, azelnidipine is not associated with reflex tachycardia, suggesting that this drug does not cause reflex sympathetic nervous stimulation. Recent epidemiological studies have shown that calcium antagonists are less effective for preventing acute myocardial infarction and heart failure than other classes of antihypertensive agents. One possible reason for this is an increase in reflex sympathetic nervous stimulation with baroreflex stimulation. Since azelnidipine does not affect heart rate, this drug may not have the disadvantages that other calcium antagonists have regarding the heart.

Azelnidipine has a high degree of lipid solubility and a high affinity for vascular tissues. Long-term treatment with azelnidipine reduced the size of the atherosclerotic lesions and levels of total cholesterol and cholesteryl ester in the aortic wall of cholesterol-fed rabbits.

Azelnidipine seems to have an antioxidant effect. The ability of azelnidipine to eliminate hydroxyl radicals is about 5-fold greater than that of other calcium antagonists. Long-term treatment with azelnidipine reduced carotid intimal-medial wall thicknesses and serum lipid peroxide levels in hypertensive patients. The reduction in oxidative stress induced by azelnidipine probably improves endothelial function through an increase in the bioavailability of nitric oxide. Therefore, beyond its effect on blood pressure, azelnidipine is expected to play an important role in antiatherosclerosis via a pleiotropic effect.

Further studies on the effects of azelnidipine on cardiovascular and cerebrovascular disease outcomes in large clinical trials, and on the mechanisms of the pleiotropic effects of lipophilic calcium antagonists, including azelnidipine, are eagerly awaited. ▲