Letter

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The Effect of an Angiotensin Receptor Blocker on Arterial Stiffness in Type 2 Diabetes Mellitus Patients with Hypertension (*Diabetes Metab J 2011;35:236-42*)

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Atherosclerotic cardiovascular disease is the major cause of death in patients with type 2 diabetes and is accelerated by the coexistence of hypertension. Arterial stiffness, which can be determined noninvasively through the measurement of pulse wave velocity (PWV), is associated with atherosclerosis and known to be an important risk factor of cardiovascular disease [1]. Currently, angiotensin II receptor blockers (ARBs) are recommended as the first-line drugs for treatment of hypertension in type 2 diabetic patients. Several studies have reported that ARBs also reduce arterial stiffness in patients with hypertension and type 2 diabetes, independent of blood pressure reduction [2-4].

In a recent issue of *Diabetes & Metabolism Journal*, Kim and colleagues [5] presented an article regarding the effect of an ARB on arterial stiffness in hypertensive patients with type 2 diabetes. The authors reported that short-term (12 weeks) treatment with valsartan improved arterial stiffness in patients with type 2 diabetes and hypertension, and this effect was influenced by baseline glycemic status. Their study is one of very few studies in Asian people confirming the beneficial effects of ARB on arterial stiffness in hypertensive type 2 diabetic patients. However, there were some limitations to be considered before drawing a firm conclusion.

First of all, as the authors mentioned, we cannot determine whether this effect is specific to ARB as there was no control group using anti-hypertensive agents of another class. Second, one of the drawbacks of this study was that PWV, the main outcome of the study, was measured in less than half (47/98) of the study participants. Although the authors showed that the baseline characteristics of the subgroup of patients with PWV estimation were similar to those of the whole group, we could not exclude the possibility of selection bias, and statistical power was diminished due to the small number of subjects. In addition, it is unclear why patients using insulin or antidiabetic drugs such as metformin or thiazolidinediones were excluded. Third, the authors did not consider several important confounding factors which can potentially influence atherosclerotic process, such as concomitant use of lipid-lowering drugs, antiplatelet agents, or smoking. It has been reported that there was some difference in response of PWV to ARB between smokers and non-smokers [6]. Finally, there might be some differences other than baseline glycemic control between the "PWV decrease" and "no PWV decrease" group, such as a difference in baseline PWV values between the two groups. If glycemic control is an important factor affecting PWV, there must have been significant association between baseline PWV and HbA1c or fasting glucose levels. In addition, although it was not statistically significant, there was also some difference in the change in mean arterial pressure before and after treatment between the two groups (16.2 vs. 10.5 mm

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Hg). Therefore, we cannot exclude the possibility that the "no PWV decrease" group may have higher blood pressure or poor medication compliance.

Although it has been established that ARB can improve arterial stiffness in hypertensive patients with or without type 2 diabetes, the mechanism has not been fully elucidated. The reports of Kim et al. [5] confirmed the beneficial effects of ARBs on arterial stiffness but could not provide insight into the mechanism of improvement. The authors discussed several mechanisms suggested by other researchers such as reduction of vascular smooth muscle cell proliferation and fibrosis, endothelial dysfunction, oxidative stress, or low-grade inflammation. It would have been better if the study investigators were able to measure serum markers of inflammation or extracellular matrix metabolism, which have been shown to be affected by treatment with an ARB [3,7]. The authors of the study concluded that glycemic status at baseline is independently associated with PWV improvement attributable to the action of valsartan. The identification of a significant correlation between PWV and fasting glucose or HbA1c levels at baseline would be supporting evidence for this conclusion.

This study by Kim and colleagues is a clinically important work showing the beneficial effect of ARB in addition to blood pressure reduction in Korean type 2 diabetic patients with hypertension, although this study was only able to provide a limited conclusion and could not elucidate the mechanism of the observed effects. More large-scale, long-term clinical trials directly comparing clinical outcomes, such as cardiovascular morbidity or mortality, with those of other anti-hypertensive agents are warranted. In addition, more mechanistic studies are needed to provide a comprehensive understanding on the pathophysiology of atherosclerosis in type 2 diabetic and hypertensive patients. Finally, I greatly appreciate the devotion of the study investigators to conduct such an important clinical study and wish them continued success in their future research.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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