Editorial Comment

Angiotensin Receptor Blockers: More Than Just Blood Pressure Lowering Drugs?

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Hypertensive patients have an excess of other cardiovascular risk factors, including hyperlipidaemia. Because various antihypertensive drugs, especially diuretics and beta blockers, adversely affect lipid metabolism, these drugs may increase associated risks for coronary artery disease and thus offset some of the beneficial effects of blood pressure reduction.[1] The renin angiotensin system is an endocrine system responsible for the regulation of systemic blood pressure as well as salt and water homeostasis.[2] Therapeutic inhibition has been proposed as a method for reducing blood pressure that can effectively decrease cardiovascular complications. The angiotensin II receptor blocker (ARB) class of hypertensive agents represents an important addition to our therapeutic armamentarium for treating high blood pressure.[3] The ability of these agents to lower high blood pressure is similar to that of older antihypertensive drugs, and recent large international randomised trials have demonstrated that the benefit of ARB extends across the whole spectrum of disease severity and to patients with conditions predisposing to cardiovascular events, such as diabetes, left ventricular hypertrophy and microalbuminuria.[3]

In the interesting study of Kyvelou et al in this issue,[4] the effect of ARB therapy on lipid and apolipoprotein parameters in hypertensive patients was evaluated in a large number (2438) of untreated patients with uncomplicated hypertension. Lipids and apolipoproteins were evaluated before and six months after treatment with five different ARB. Small, but statistically significant beneficial effects were found regarding the lipid and apolipoprotein parameters. Clinical studies have demonstrated that treatment with an ARB decreases plasma cholesterol in hypertensive patients, but other studies of these drugs failed to identify any cholesterol lowering action.[5,6] How can these favourable effects of ARB on blood lipids be explained? Angiotensin II is regarded as a whole homeostatic regulator and its actions include acute and long-term control of blood pressure, body fluid balance, immune and inflammatory responses. Chronic infusion of angiotensin II in experimental studies increases plasma triglyceride levels by stimulating hepatic triglyceride production. There is recent experimental evidence that angiotensin II type 1 receptor activity increases plasma cholesterol levels, whereas type 2 receptor activity has the opposite effect.[7] The excess angiotensin II unbound by an angiotensin type I receptor strongly stimulates angiotensin type 2 receptors with a subsequent decrease in plasma cholesterol levels.

It is interesting, also, that not all of the five ARB used had the same favourable effects on lipids. These changes could not be attributed to confounding factors such as

nutrition, body weight or smoking habits, which may affect lipid profile. In a recent work Derosa et al[8] reported decreases of plasma total and low density lipoprotein cholesterol levels in respond to telmisartan but not to eprosartan in hypertensive type 2 diabetic patients. It must be noted that in the study of Kyvelou et al,[4] the beneficial effects of ARB were seen in spite of the fact that in one third of the hypertensives in the study small doses of a diuretic (12.5 mg of chlorthalidone) were given as an additional therapy in order to control blood pressure. Diuretics are among the antihypertensive drugs that aggravate lipid parameters, especially triglycerides. This may explain, at least in part, why early trials examining the impact of antihypertensive pharmacotherapy with diuretics and beta-blockers showed beneficial effects on coronary artery disease that fell short of the predicted result. In today's clinical practice smaller doses of diuretics are used and so their effect on lipid parameters is more trivial. When antihypertensive drugs are chosen, consideration should be given to their potential influences, either negative or positive, on other cardiovascular risk factors. In addition to its role in hypertension, elevated angiotensin II seems to play a role in abnormal lipid metabolism (hypercholesterolaemia, hypertriglyceridaemia). Angiotensin receptor blockers are effective, well tolerated antihypertensive drugs with potential favourable effects on several metabolic and inflammatory risk factors including lipid profile abnormalities that commonly cluster together in hypertensive subjects.

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