Hypertension Research (2010) 33, 778

www.nature.com/hr

COMMENTARY

Effects of angiotensin II receptor blockers on insulin resistance

Pietro Dario Ragonesi

Hypertension Research (2010) **33,** 778; doi:10.1038/hr.2010.100; published online 17 June 2010

In the past decade, there has been an alarming increase in the number of patients with metabolic syndrome, and a clustering of cardiovascular disease risk factors that include hypertension, glucose intolerance/insulin resistance, dyslipidemia and central obesity.[1] The physiological links between abnormalities in glucose regulation, and in particular insulin resistance, and blood pressure provide novel means to treat patients with the metabolic syndrome. Consequently, there is an intense need for better pharmacological treatments of both the underlying insulin resistance and hypertension in affected patients.

Inhibitors that target the renin–angiotensin system are now widely used as therapy for hypertension in diabetic patients.[2,3] Importantly, these agents have shown promise in improving health independent of, or in addition to, blood pressure control.[4] There have been very few reports on the effect of angiotensin receptor antagonists on insulin sensitivity in patients with essential hypertension, showing that not all angiotensin II receptor blockers have the same effect on insulin resistance. Paolisso,[5] for example, reported that losartan improves insulin-mediated glucose uptake through an increase in non-oxidative glucose metabolism and blood flow in hypertensive patients, while Moan[6] found that losartan improves insulin sensitivity in patients with severe essential hypertension, but has neutral effects on insulin sensitivity in those with mild essential hypertension.

On the other side, Higashiura *et al.*[7] reported that candesartan improves insulin resistance in patients with essential hypertension, through ACE inhibition. Several possible mechanisms of improved insulin sensitivity by angiotensin receptor antagonism include vasodilation, which increases the blood flow in skeletal muscles; activation of the glucose transporter and its translocation from an intracellular membrane compartment to a plasma membrane fraction; and suppression of noradrenaline release induced by angiotensin II antagonism.

Furthermore, Yamaguchi *et al.*[8] suggested that tumor necrosis factor α (TNF-α) in skeletal muscle is linked to insulin resistance and that olmesartan may improve insulin resistance either by increasing cAMP or by decreasing TNF-α.

In this context, Derosa *et al.*[9] decided to compare the effects of olmesartan and candesartan in type 2 diabetic hypertensive patients. They did not observe any variations of body weight or glycemic profile with either treatment. Blood pressure was significantly reduced by both treatments, without any difference between them. Retinol binding protein-4, resistin and vaspin values, instead, decreased in the candesartan group, but not in the olmesartan group. *M* value, visfatin and adiponectin increased with candesartan, whereas no significant variations were observed with olmesartan. Both treatments gave a similar reduction of high-sensitivity C-reactive protein.

The implications of these findings need to be considered in clinical practice to achieve a better control of hypertension and insulin resistance.

Dr PD Ragonesi is at the Diabetes Care Unit, S. Carlo Hospital, Milan 20153, Italy.
E-mail: pietrodario.ragonesi@libero.it

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