



# The effect of different antihypertensive treatment protocols on oxidant-antioxidant systems in type 2 diabetic patients with microalbuminuria and stage 1 hypertension

Alparslan ERSOY<sup>1</sup>, Müge EREK<sup>1</sup>, Canan ERSOY<sup>2</sup>, Emre Sarandol<sup>3</sup>, Abdulmecit YILDIZ<sup>1</sup>

<sup>1</sup> Uludag University Faculty of Medicine, Department of Nephrology, Bursa, TURKEY

<sup>2</sup> Uludag University Faculty of Medicine, Department of Endocrinology and Metabolism , Bursa, TURKEY

<sup>3</sup>Uludag University Faculty of Medicine, Department of Biochemistry, Bursa, TURKEY

**INTRODUCTION AND AIMS:** Oxidative stress may play a critical role in the pathogenesis of endothelial dysfunction in patients with diabetes or hypertension. Angiotensin converting enzyme inhibitors (ACEI), angiotensin II type 1 receptor blockers (ARB) and third generation beta-blockers, including carvedilol, have beneficial effects on oxidative stress beyond their antihypertensive and antiproteinuric properties. This study was aimed to evaluate short-term effects of losartan (ARB) therapy alone and together with cilazapril (ACEI) or carvedilol on oxidative stress and antioxidants in patients with type 2 diabetes mellitus, microalbuminuria and stage 1 hypertension.

**METHODS:** Fifty-six patients were enrolled and only 30 of the patients completed the study. After 2 weeks follow-up period, all patients received losartan 50 mg/day as a single dose for 6 weeks. Then, patients were randomized into 3 groups at the end of 6<sup>th</sup> week. Losartan dose was increased to 100 mg/day in the first group, and carvedilol (25 mg/day) was added in the second group and cilazapril (5 mg/day) in the third group to losartan 50 mg/day treatment for another 6 weeks. Oxidation and oxidizability of apolipoprotein B-containing lipoproteins (malondialdehyde:  $\Delta$ -MDA, nmol MDA/mg chol, a lipid peroxidation biomarker of oxidative stress), activities of paraoxonase (PON, U/L) and arylesterase (AE, kU/L) (components of the antioxidant system), erythrocyte superoxide dismutase (SOD) and glutathione peroxidase (GSHPx) (antioxidant enzymes) were studied in all patients.

**RESULTS:** Age, gender, diabetes and hypertension durations, oral antidiabetic drug and insulin usage among three groups were comparable ( $p > 0.05$ ). In all three groups, during the losartan 50 mg daily treatment period and post-randomization treatment period, the systolic and diastolic blood pressures (BP) were significantly decreased ( $p < 0.05$ ). Greatest decrease in systolic and diastolic BPs were seen in group 3 (systolic BP:  $16.5 \pm 7.4$  mmHg, diastolic BP:  $10.5 \pm 2.8$  mmHg), and smallest decreases in group 1 (systolic BP:  $9 \pm 6.1$  mmHg, diastolic BP:  $3 \pm 4.8$  mmHg). At the end of the post-randomization treatment period, microalbuminuria levels in all three groups decreased significantly when compared to the period in which 50 mg losartan was administered alone ( $p < 0.05$ ).  $\Delta$ -MDA, SOD and GSHPx levels, PON and AE activities did not significantly change in both 2-week placebo and 6-week 50 mg losartan treatment periods. At the end of 12<sup>th</sup> week 100 mg losartan, 50 mg losartan plus cilazapril and 50 mg losartan plus carvedilol treatments did not affect these parameters when compared to values before pre-randomization.

**CONCLUSIONS:** Our findings indicated that in hypertensive type 2 diabetics with microalbuminuria, carvedilol can be combined with ARB treatment with established efficacy. This combination was not found to be different than other combination treatments used in terms of efficacy and side effects. However, ARB (low or high dose), ACEI and beta blocker agents that are known to have antioxidant effects did not influence oxidant and anti-oxidant systems in this population in a short-period.

**Table 1. The changes in oxidant and anti-oxidant systems of three groups**

Drug	Time	PON	AE	SOD	GSHPx	$\Delta$ -MDA
ARB 100 mg	6 week	247 $\pm$ 119	101 $\pm$ 27	1315 $\pm$ 658	15 $\pm$ 15	52 $\pm$ 26
	12 week	241 $\pm$ 125	103 $\pm$ 27	1102 $\pm$ 414	16 $\pm$ 5	43 $\pm$ 12
ARB+ACEI	6 week	195 $\pm$ 110	93 $\pm$ 25	1322 $\pm$ 887	13 $\pm$ 10	42 $\pm$ 18
	12 week	226 $\pm$ 138	95 $\pm$ 22	1344 $\pm$ 688	13 $\pm$ 12	48 $\pm$ 15
ARB+BB	6 week	159 $\pm$ 56	92 $\pm$ 22	1153 $\pm$ 370	17 $\pm$ 9	43 $\pm$ 11
	12 week	151 $\pm$ 57	90 $\pm$ 25	1084 $\pm$ 270	12 $\pm$ 7	46 $\pm$ 11