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**ROSIGLITAZONE LOWERS C-REACTIVE PROTEIN LEVELS IN HYPERTENSIVE TYPE 2 DIABETIC PATIENTS**

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**Objective:** Accumulating data indicate that thiazolidinediones (TZD) present beneficial effects for the cardiovascular system beyond glycemic control, such as triglyceride reduction, HDL-cholesterol elevation and decrease in plasminogen activator inhibitor-1 levels. The aim of this study was to determine the effect of rosiglitazone on C-reactive protein, an inflammation marker associated with an increased risk for cardiovascular disease, in patients with hypertension and Type 2 diabetes.

**Subjects-Method:** A total of 40 Type 2 diabetic subjects, already on 15 mg glibenclamide daily, but with a poor glycomic control, were included in the study. Patients had either established hypertension, poorly controlled under antihypertensive treatment, or newly diagnosed mild hypertension without medication. In 20 of the subjects rosiglitazone 4 mg daily was added-on therapy for 26 weeks, while the rest remained only with the preexisting treatment to serve as control group. At baseline and the end of the study subjects gave blood samples where high sensitive C-reactive protein (hs-CRP) was measured with the use of a latex-enhanced immunonephelometric method.

**Results:** At the end of the study, rosiglitazone treatment was associated with a significant reduction in hs-CRP levels versus baseline (from 0.53±0.11 to 0.39±0.12 mg/dL, P<0.05). In contrast, no significant change in hs-CRP levels was observed in the control group (from 0.49±0.19 to 0.56±0.09 mg/dL, P=0.18). Between-groups comparison revealed also a significant difference for hs-CRP (P<0.05). If the rosiglitazone group is divided in subgroups of men (n=9) and women (n=11), or patients with (n=10) and without (n=10) preexisting antihypertensive treatment, a downward trend in hs-CRP levels is still observed in the subgroups, but the reduction is significant only in that of patients without antihypertensive treatment.

**Conclusions:** Treatment of hypertensive Type 2 diabetic patients with rosiglitazone resulted in a significant reduction of hs-CRP levels. This finding indicates that rosiglitazone possibly exerts a vasculoprotective action, which may be important for this type of patients, who are in high risk for atheroclerotic complications.

Key Words: C-Reactive Protein, Hypertension, Rosiglitazone

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**DIURNAL BLOOD PRESSURE RHYTHM PREDICTS ISCHEMIC BRAIN DAMAGE**

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Altered signal intensity in the subcortical white matter on magnetic resonance imaging (MRI) of the brain, referred to as leukoaraiosis, arises from ischemic injury due to arteriolosclerosis of penetrating end arteries and is associated with increased risk of stroke, cognitive decline and dementia. Elevated blood pressure (BP) and altered diurnal BP rhythm may be major risk factors.

To assess the relationships of leukoaraiosis volume with measures of BP level and diurnal rhythm, we obtained brain MRI’s and 24-hour ambulatory BP recordings (awake and asleep) in 198 adults (70 African Americans from Jackson MS and 128 non-Hispanic whites from Rochester MN; 123 women, 75 men; 62 ± 5.5 yrs old).

In multiple regression analyses that considered age, gender, office BP, and ambulatory measures of BP level and diurnal rhythm, greater leukoaraiosis volume was significantly associated with older age (P <0.0001), higher office BP levels (systolic, P = 0.0475; diastolic, P = 0.0047), and smaller declines in BP between awake and asleep periods (i.e., non-dipping; systolic, P = 0.0080; diastolic, P = 0.0017). Measures of pulse pressure were not significantly associated with volume of leukoaraiosis.

These data suggest that in addition to measures of BP level, the diurnal pattern of variation in BP levels influences the volume of leukoaraiosis. These observations could have important implications for the pharmacological therapy of hypertension to prevent the development or progression of leukoaraiosis and the attendant risks of stroke and dementia.

Key Words: Ambulatory Blood Pressure, Dipping, Leukoaraiosis

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**COMBINED BENAZEPRI-L-AMLODIPINE TREATMENT REDUCES CARDIAC TNFA PRODUCTION POST CARDIAC ISCHEMIA**

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**Background:** Angiotensin converting enzymes inhibitors (ACEIs) have been successfully used in management of heart failure and post myocardial ischemia (MI). Similarly, recent studies suggested that calcium channel blockers (CCBs) and diuretics may have cardiac protective effects. The exact mechanisms induced by these drugs leading to cardiac protection are not known.

**Hypothesis:** We hypothesized that in post MI there is increased myocardial inflammation and ACEIs, CCBs or diuretics may reduce some mediators of this inflammation.

**Methods:** We monitored changes in cardiac interstitial fluid (CIF) levels of angiotensin II (Ang II) and TNFα with and without oral administration of benazepril (40 mg/kg/d), amlodipine (10 mg/kg/d), individually and combined or hydrochlorothiazide (HCTZ, 3 mg/kg), in conscious rats after sham operation or 30 min temporary occlusion of the left anterior descending coronary artery (n=8 each group). Levels were monitored with a microdialysis technique for 5 weeks.

**Results:** There were no changes in heart rate or BP associated with any of these treatments. At wk1, in sham animals, CIF Ang II and TNFα levels were 2.54±0.24 fmol/ml and 27.9±2.02 pg/ml, respectively and did not change significantly throughout the study. In animals post MI, there was a progressive increase in CIF Ang II and TNFα reaching 36.54±4.28 fmol/ml and 130.5±5.22 pg/ml, respectively, at wk 5. Treatment with benazepril alone or combined with amlodipine caused significant reduction in TNFα in post MI to 53.7±2.20 fmol/ml (P<0.01) and 39.5±4.17 pg/ml (P<0.001), respectively, at wk 5 post MI. Neither amlodipine alone nor HCTZ caused significant reduction in TNFα.

**Conclusions:** These data demonstrate that cardiac Ang II and TNFα increase in ischemic hearts. Elevated cardiac TNFα levels are mediated by Ang II since benazepril reduced these levels. TNFα is not influenced by amlodipine or HCTZ, however, combined benazepril and amlodipine treatment causes significant reduction in TNFα levels. This suggests that combined benazepril and amlodipine treatment may be beneficial in management of post-myocardial ischemia.

Key Words: Cardiac Ischemia, Lotrel, TNFalphi