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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.

Methods: A total of 40 Type 2 diabetic subjects, already on 15 mg glibenclamide daily, but with a poor glycemic 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 atherosclerotic complications.

Key Words: C-Reactive Protein, Hypertension, Rosiglitazone

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COMBINED BENZAPEPRIL-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/d), 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 TNFa levels were 2.8±0.24 fmol/ml and 27.9±0.22 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 TNFa reaching 36.54±4.28 fmol/ml and 130±5.22 pg/ml, respectively, at wk 5. Treatment with benazepril alone or combined with amlodipine caused significant reduction in TNFa 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 TNFa.

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

Key Words: Cardiac Ischemia, Lotrel, TNFalp