of cellular mechanisms and endothelial dysfunction in the pathogenesis of MS. The ability of the drug to modulate hemostasis may have implications for the use of thrombolytics in cardiovascular disease.

PHARMACOLOGY—CLINICAL

901-114 Effect of Calcium Channel Blockers on the Incidence of Myocardial Infarction in Patients With Left Ventricular Dysfunction

John B. Kostis, Alan C. Willoe, Nora M. Cosgrove, Clifton R. Lahey, from the UMDNJ-Robert Wood Johnson Medical School Clinical Center Based on the SOLVD Database. UMDNJ-Robert Wood Johnson Medical School, New Brunswick, NJ

Recent studies have suggested an increased risk of myocardial infarction (MI) in patients on calcium channel blockers (CCB). We evaluated the effect of CCB on fatal and non-fatal MI in 6797 patients with left ventricular dysfunction (LVD, EF < 55%) in the Studies Of Left Ventricular Dysfunction (SOLVD).

During 40 months average follow-up, fatal or non-fatal MI occurred in 11.5% of the 845 patients on CCB during follow-up versus 7.5% of the 2551 patients not on CCB (p = 0.001, OR 1.6; 95% CI 1.24-2.07) in the enrolment group; and in 14.4% of the 784 patients on CCB versus 9.3% of the 2557 patients not on CCB (p = 0.001, OR 1.64; CI 1.23-2.06) in the placebo group.

By multivariate Cox regression analysis, adjusting for 29 variables describing demographics, comorbidity, etiology and severity of LVD, heart failure, and concomitant drug use, CCB use during follow-up was an independent predictor of increased risk (R.R. 1.37; CI 1.14-1.63).

The increased risk associated with CCB was also observed when the combined endpoint of MI, cardiac death, or hospitalization for angina was considered. The increased MI risk was observed whether CCB were used both at baseline and follow-up or only at follow-up. In addition, the risk was higher when the mean follow-up heart rate of patients on CCB was higher than the median follow-up rate of patients on CCB (74 beats/minute).

In contrast, using the same database analysis, beta blocker use was associated with a lower rate of fatal or non-fatal MI (multivariate Cox R.R. 0.80; CI 0.61-1.05).

In this retrospective analysis of patients with LVD, CCB use was associated with significantly increased risk of MI.

901-115 Is Thrombolytic Therapy Most Effective When Endogenous Fibrinolysis Is Deficient?

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Thrombosis that form as a result of defective endogenous fibrinolysis may be most sensitive to thrombolytic agents. Impaired fibrinolytic activity has been associated with low plasma levels of single-chain urokinase (scu-PA), raised plasminogen(a) [P(a)] and, paradoxically, high t-PA antigen.

We investigated the effect of continuous infusion of fibrinolytic factors on admission and subsequent efficacy of thrombolytic therapy in 51 patients with acute myocardial infarction (AMI) treated within 6 h of symptoms with intravenous t-PA (50-60 MU) and heparin. Pre-treatment plasma concentrations of Lp(a) (mg/dl), t-PA antigen (ug/l) and urokinase (u-PA, ug/l) were measured by ELISAs and of scu-PA (ug/l) by bioimmunoassay. A coronary arteriogram was performed 90 min after the start of lytic therapy. Perfusion of the infarct-artery was defined as TIMI grade 2.

At 90 min, a TIMI 3 infarct-artery was found in 27 pts. The perfused occluded-artery pts did not differ significantly in age, sex, smoking status, delay to treatment, time of day of therapy or rt-PA dose at 90 min. Plasma factors (median and interquartiles) were:

<table>
<thead>
<tr>
<th>Factor</th>
<th>Lp(a)</th>
<th>t-PA</th>
<th>scu-PA</th>
<th>u-PA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pts</td>
<td>10 (7-22)</td>
<td>29 (17-39)</td>
<td>2.0 (1.8-2.1)</td>
<td>2.7 (2.2-3)</td>
</tr>
<tr>
<td>Occluded</td>
<td>9 (5-27)</td>
<td>18 (10-31)</td>
<td>2.6 (1.8-3.9)</td>
<td>2.6 (2.4-2.8)</td>
</tr>
<tr>
<td>pvalue</td>
<td>0.003</td>
<td>0.03</td>
<td>0.36</td>
<td></td>
</tr>
</tbody>
</table>

Thus, in patients with AMI receiving rt-PA, early coronary reperfusion, compared with persistent occlusion, is associated with higher plasma Lp(a) and t-PA antigen levels and lower plasma scu-PA on admission. Pharmacological doses of rt-PA thus appear most effective when natural fibrinolysis is deficient.

901-116 Effect of Prostacyclin Infusion as a Treatment of Pulmonary Hypertension


We have examined the effect of continuous infusion of prostacyclin (PGI2)