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1009-154 **Administration-Time Dependent Effects of Aspirin on Blood Pressure in Untreated Hypertensive Patients**

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Background: Previous studies on the potential influence of aspirin (ASA) on blood pressure (BP) have not taken into consideration the chronopharmacologic effects of nonsteroidal antiinflammatory drugs. This study investigated the effects of ASA on BP in untreated hypertensive patients who received ASA at different times of the day according to their rest-activity cycle.
Methods: We studied 147 patients with mild hypertension (57 men), 43.0±12.1 (mean±SD) years of age, divided in 3 groups: non-pharmacological hygienic-dietary recommendations (HDR); the same HDR and ASA (100 mg/day) on awakening; or HDR and ASA before bedtime. BP and heart rate (HR) were measured every 20 minutes during the day (07:00 to 23:00 hours) and every 30 minutes at night for 48 consecutive hours before and after 3 months of intervention. The circadian pattern of BP in each group was established by population multiple-component analysis.
Results: After 3 months of non-pharmacological intervention, there was a small and non-significant reduction of BP (1.1 mm Hg for systolic BP, 1.0 mm Hg for diastolic BP; P>0.341). There was no effect of ASA on BP when given on awakening (P=0.229). A BP reduction was, however, highly significant when ASA was given before bedtime (decrease of 6 and 4 mm Hg in systolic and diastolic BP, respectively; P<0.001). There was no significant change in HR in any group.
Conclusion: Results indicate a statistically significant administration-time dependent effect of low-dose aspirin on blood pressure in untreated patients with mild hypertension. These results could be related to the circadian-time dependent effects of ASA on b-adrenergic receptors and/or the previously demonstrated time-dependent reduction by ASA of the circulating levels of angiotensin II, an issue that deserves further investigation. In any trial of ASA effects, inquiries about the time when subjects took the drug are indicated and may account for discrepancies in the literature. Moreover, the influence of ASA on BP demonstrated here indicates the need to identify and control for ASA effects in patients using this drug before or during their participation in antihypertensive medication trials.

POSTER SESSION

1010 Benefits of Statins

Sunday, March 30, 2003, 9:00 a.m.-11:00 a.m.
McCormick Place, Hall A
Presentation Hour: 9:00 a.m.-10:00 a.m.

1010-146 **Early Fluvastatin Treatment Reduces the Long-Term Incidence of Major Adverse Cardiovascular Events Following Successful First Percutaneous Coronary Intervention With or Without the Use of Stent: The Lescolfi Intervention Prevention Study**

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Background: The Lescol® Intervention Prevention Study (LIPS), an international double-blind placebo-controlled clinical trial, has shown that early fluvastatin treatment significantly reduces the risk of major adverse cardiovascular events (MACE) compared with placebo in patients with average cholesterol levels after their first successful percutaneous coronary intervention (PCI). The use of stents during PCI is associated with lower early and late adverse cardiac event rates. This study assessed the effects of fluvastatin on MACE in patients treated with either stent or balloon angioplasty.
Methods: In LIPS, 1,677 patients with baseline total cholesterol levels 135-270 mg/dL, and fasting triglyceride levels <400 mg/dL were included. Following successful completion of their first PCI, they were randomized to receive fluvastatin 40 mg twice daily (844) or placebo (833) at hospital discharge. Follow-up was 3-4 years. 1,055 patients had at least one stent implanted (fluvastatin, n=540; placebo, n=515), and 582 patients were treated with conventional balloon angioplasty (fluvastatin, n=287; placebo, n=295). Primary endpoint was the survival time free of MACE, defined as the composite of cardiac death, myocardial infarction, and reinterventions (PTCA or CABG).
Results: In patients treated with balloon angioplasty, fluvastatin significantly reduced the risk of MACE by 28% (RR, 0.72; 95% CI, 0.52-1.00; p=0.048) compared with placebo. Among patients treated with stents, there was a clear trend towards risk reduction with fluvastatin (RR, 0.80; 95% CI, 0.62-1.04; p=0.096). In a prespecified analysis excluding reinterventions due to target lesion revascularization in the first 6 months of follow-up, the benefit of fluvastatin was greater and statistically significant in both groups compared with placebo - a 43% risk reduction in the balloon only group (RR, 0.57; 95% CI, 0.38-0.84; p=0.004), and a 29% risk reduction in the stents group (RR, 0.57; 95% CI, 0.54-0.94; p=0.02). No differences were observed in lipid profiles between the balloon and the stent patients.
Conclusion: Early fluvastatin treatment significantly reduces the risk of MACE in patients after PCI, with or without stenting.

1010-147 **Coadministration of Ezetimibe With Simvastatin**

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Background: This study assessed the efficacy and safety of ezetimibe (EZE), a novel cholesterol absorption inhibitor, coadministered with simvastatin (SIM) in patients with heterozygous familial hypercholesterolemia (heFH), coronary heart disease (CHD), or multiple cardiovascular risk factors.
Methods: Following dietary stabilization, a 6-10-week drug washout, and open-label SIM 20 mg/d run-in, 100 patients with baseline LDL-C ≥130 mg/dL and TG ≤350 mg/dL while on SIM 20 mg were randomized to EZE 10 mg or additional double-blind SIM 20 mg. SIM dose was doubled after 4 or 9 weeks if LDL-C was still >100 mg/dL (maximum of 80 mg with SIM alone and 40 mg with EZE+SIM). The primary endpoint was % LDL-C reduction from baseline for EZE+SIM 20 mg vs. SIM 40 mg alone at Week 4. The key secondary endpoint was the proportion of patients achieving LDL-C≤100 mg/dL at Week 14.
Results: Of 100 randomized patients, 22% had heFH, 42% had CHD and 40% had 2 or more cardiovascular risk factors. EZE+SIM 20 mg (n=66) significantly reduced LDL-C vs. SIM 40 mg (n=34) alone; 24.5% vs. 11.1%, p<0.01 (table). At Week 14, 27% of the coadministration group vs. 3% of the SIM group achieved target LDL-C (p<0.01). EZE+SIM was well tolerated with a safety profile similar to SIM alone.
Conclusion: Adding EZE to ongoing SIM provides significantly greater LDL-C reduction than doubling the SIM dose alone. The coadministration of EZE+SIM offers a highly efficacious and well tolerated new treatment approach to patients with hypercholesterlemia.

Mean (SEM) Baseline, Week 4, and % Change from Baseline Values for LDL-C

Treatment	Baseline LDL-C: mean (SEM) mg/dL	Week 4 LDL-C: mean (SEM) mg/dL	Mean (SEM) % change
SIM 40mg (n=34)	167 (8)	148 (6)	-11.1 (2.0)
EZE+SIM 20mg (n=66)	171 (6)	128 (5)	-24.5 (1.5)*

*p<0.01, EZE+SIM versus SIM alone

1010-148 **Patients After Acute Myocardial Infarction Have for a Prolonged Period Increased Thermal Heterogeneity in Culprit Atherosclerotic Lesions: Additional Effect of Statins on Plaque Stabilization**

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Background: It has been observed that patients with acute myocardial infarction (MI) have increased temperature of the culprit atherosclerotic lesion. The aim of this study was to investigate whether this finding is maintained after acute myocardial infarction.
Methods: In the study we enrolled 31 patients (pts): 12 (mean age: 52.3±12.3 yrs) with a MI 2-4 months before the measurements and 19 pts (mean age: 59.8±11.4 yrs) with chronic stable angina (CSA). All pts underwent coronary angiography and temperature measurements of the culprit lesion. Pts with MI had one vessel disease. We measured temperature difference (TD) between the atherosclerotic plaque and the proximal vessel wall (background temperature) with a thermography catheter (Medispes, ZWG, Switzerland). At the distal end of this catheter a thermistor probe is attached and the measurements are displayed on real-time on the screen of a computer.
Results: The baseline clinical characteristics were similar between the 2 groups. Pts with previous MI did not suffer from post-MI angina. Pts with CSA were stabilized by usual medication at least for the last 2 months. None of pts with CSA had previous MI. The mean value of TD was higher in pts with previous MI than in pts with CSA (0.59±0.61°C versus 0.20±0.18°C, p=0.02). Pts with previous MI (n=6) receiving statins had only a trend towards higher plaque temperature compared to treated pts with CSA (n=9) (0.41±0.35°C versus 0.19±0.20°C, p=0.11). However, pts with previous MI not treated with statins (n=6) had significantly higher TD compared to untreated pts with CSA (n=10) (0.76±0.70°C versus 0.27±0.01°C, p<0.01).
Conclusions: In patients with acute myocardial infarction increased plaque temperature is observed for a prolonged period. Thus, the inflammatory process may be maintained even after plaque rupture. Prolonged treatment with therapeutic agents, such as statins, for plaque stabilization may be required in pts with previous MI.

1010-149 **Effects of Switching to Rosuvastatin From Atorvastatin or Other Statins on Achievement of International Low-Density Lipoprotein Cholesterol Goals: MERCURY I Trial**

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Background: Achievement of low-density lipoprotein cholesterol (LDL-C) goals is an important aim in clinical practice. This multinational trial (4522IL/0081) assessed the efficacy of rosuvastatin to bring additional patients to LDL-C goals and modify LDL-C and other lipid measures vs atorvastatin and other statins in hypercholesterolemic patients with atherosclerosis or coronary heart disease or type 2 diabetes.
Methods: After a 6-wk dietary lead-in period, 3161 adults were randomized to open-label rosuvastatin 10mg (R10), atorvastatin 10mg (A10), atorvastatin 20mg (A20), simvastatin 20mg, or pravastatin 40mg for 8 wks. Patients then remained on these treatments or switched (switch groups) as follows for 8 wks: 1/2 from A10, simvastatin 20mg and pravastatin 40mg to R10; 1/3 each from A20 to R10 and R20. Treatment comparisons were made at wks 8 and 16 using logistic regression analyses for percentage of patients