P-508
ADMINISTRATION TIME-DEPENDENT EFFICACY OF STATINS IN HYPERLIPIDEMIC PATIENTS WITH ESSENTIAL HYPERTENSION
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A significant circadian variation has been shown to characterize cholesterol and triglycerides, with predictably highest values at the end of the diurnal active hours, and lowest values after awakening [Am Heart J. 2000;139:164-173]. It has thus been suggested that statins should be administered at night. However, most studies on the efficacy of statins have not evaluated a potential change in effects as a function of the circadian time of dosing. Accordingly, we evaluated the potential administration time-dependent changes in the lipid profile of hyperlipidemic-hypertensive patients treated with statins. We studied 2486 patients (1167 men), 59.7±13.8 years of age, with grade 1-2 essential hypertension and dyslipemia, all under treatment with statins. We evaluated the circadian time of statin administration (awakening-breakfast, lunch, bedtime-dinner, other) and its potential correlation with lipid control, according to NCEP-III criteria (LDL-cholesterol < 160, <130, or <100 mg/dl, according to cardiovascular risk stratification). Therapeutic compliance was evaluated using the Morisky-Green test. Atorvastatin was the statin according to cardiovascular risk stratification. Therapeutic compliance was significantly reduced to 20% in patients taken statins with 36.3% of the patients taken statins at night were controlled. This per-

were taken statins in a single morning dose. With respect to lipid control, NCEP-III criteria (LDL-cholesterol < 160, <130, or <100 mg/dl, according to cardiovascular risk stratification). Therapeutic compliance was also significantly higher

0.001). Therapeutic compliance was also significantly higher when statins were taken at bedtime (87.7%) as compared to midday (78.6%, P=0.001). As a clear example of chronotherapy, in hyperlipidemic patients with essential hypertension the time of treatment with statins should always be recommended to be bedtime, in keeping with the findings of this study. The present results show that the treatment with simvastatin in high-risk patients is associated with a reduction of stimulated ROS production by PMNs. The effect is stimulus specific, and this finding may support an action of simvastatin on intracellular membrane receptor targets in the modulation of the inflammatory response.

Key Words: Chronotherapy, Hyperlipidemia, Statins

P-509
EFFECTS OF SIMVASTATIN ON POLYMORPHONUCLEAR LEUKOCYTE FUNCTION IN HIGH-RISK PATIENTS
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To investigate whether the treatment with simvastatin 20 mg/die may change polymorphonuclear leukocyte (PMN) function in high-risk patients, the chemotactic index (CI, i.e. stimulated chemotaxis/spontaneous migration) and reactive oxygen species (ROS) production were studied in isolated PMNs obtained from patients before institution of statin treatment (1D-e) and thereafter, at 3 days (3D-e) and at 30 days of treatment (30D-e). Functional responses were obtained by stimulation of the cells with fMLP, a chemotactic peptide acting on membrane receptors, and PMA, a direct activator of protein kinase C.

Eight high-risk subjects (mean age 61±8 years; 5 patients with type-2 diabetes in diet treatment, 3 dyslipidemic patients; non-smokers, no heavy sporting activities) were studied. In patients at 1D-e the mean total cholesterol (T-c) was 238±23 mg/dl, LDL-c was 165±17 mg/dl, HDL-c was 47.5±5.3 mg/dl, and triglycerides were 125±50 mg/dl. T-c, LDL-c and ApoB significantly decreased at both 3D-e (202±27 mg/dl, 134±25 mg/dl, and 108±15 mg/dl, respectively) and 30D-e (164±28 mg/dl, 96±21 mg/dl, and 70±32 mg/dl, respectively). Differences were always statistically significant vs 1D-e (P<0.05 by ANOVA followed by Student Newman Keuls post test). The dietary habits (as evaluated by a diary) and the fasting glycemias did not change during the 30-days follow-up. The CI in PMNs from patients was 1.29±0.06 at 1D-e and did not change at 3D-e and at 30D-e, while PMA-induced ROS production was significantly reduced at the 30D-e, both with respect to 1D-e and 3D-e (P<0.05 vs both 1D-e and 3D-e). By contrast, fMLP-induced ROS generation remained unchanged throughout the treatment.

In conclusion, our study suggests that among untreated patients with essential hypertension those with ISH had a more favourable lipid profile. Key Words: Chemotaxis and ROS, Polymorphonuclear Leukocytes, Statin

P-510
LIPID PROFILE OF PATIENTS WITH ISOLATED SYSTOLIC HYPERTENSION
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Isolated Systolic Hypertension (ISH) has been shown to increase cardiovascular disease morbidity and mortality. In this study, we searched for differences in the lipid profile between subjects with ISH and those with essential hypertension.

We studied 442 [212 (48%) were men] hypertensives, who had never been treated. Their median age was 56 (range: 18–83) years. Among them, 135 (30.5%) patients had ISH [Systolic Blood Pressure (SBP) > 140mmHg and Diastolic Blood Pressure (DBP) < 90mmHg]. All patients had a full lipid profile. Persons with ISH were older than other hypertensives (62.0±10.8 vs 53.4±11.9 years, p<0.001). There was no difference in the sex distribution between the two groups [66 out of 135 (48.9%) vs 146 out of 307 (47.6%) were men, respectively]. Those with ISH had significantly greater pulse pressure (PP) (71.6±16.1 vs 60.6±16.8 mmHg, p<0.001) and significantly smaller body mass index (BMI) (29.3±3 vs 30.9±5.2, p<0.001), when compared with the rest hypertensives.

Subjects with ISH had significantly higher high density lipoprotein (HDL) than the rest hypertensives (51.8±17.6 vs 46.9±11.6mg/dl; p<0.001). There were no other significant differences in the rest lipid profile between the two groups.

In conclusion, our study suggests that among untreated patients with essential hypertension those with ISH had a more favourable lipid profile.

Key Words: HDL-Cholesterol, Isolated Systolic Hypertension, Lipid profile