Methods: A prospective, randomized, open-label, blinded-endpoint, multicenter, parallel-group study was performed in older patients (≥60 years) with systolic blood pressure (SBP) >140 mmHg, diastolic blood pressure (DBP) ≥95 mmHg, and 24-h mean ambulatory SBP >125 mmHg. After a 2- to 4-week placebo run-in, patients were randomized to treatment with telmisartan (T) 40 mg for 2 weeks, with up titration to T 80 mg for 6 weeks and then to T 80 mg + hydrochlorothiazide (H) 12.5 mg for 6 weeks or amlopidine (A) 5 mg, with up titration to A 10 mg for 6 weeks and then to A 10 mg + H 12.5 mg for 6 weeks. Efficacy was determined using 24-h ambulatory blood pressure monitoring. Adverse events (AEs) were monitored.

Results: The reduction from baseline adjusted last 6-h mean SBP (primary endpoint) was 18.8±0.6 mmHg for T+H (n=354) and 17.7±0.6 mmHg for A+H (n=329). The difference in favor of T+H versus A+H of -1.1 mmHg (95% CI 2.7, 0.5 mmHg) confirmed that T+H was at least as effective as A+H. Reductions in 24-h mean SBP (p=0.0010), daytime SBP (p=0.0002), and morning mean SBP (p=0.0105) were greater with T+H than with A+H. T+H was also superior to A+H for DBP endpoints. Drug-related AEs occurred in 40 (8.0%) T-group patients and in 168 (33.4%) A-group patients (p<0.0001). The most common AE was peripheral edema, observed in 6 (1.2%) T-group patients and 122 (24.3%) A-group patients (p<0.0001).

Conclusions: T 80 mg + H 12.5 mg is statistically superior to A 10 mg + H 12.5 mg during the 24-h dosing interval for both SBP and DBP; with both groups being comparable in the last 6 h, the time of heightened cardiovascular risk. The safety profile of T+H is superior to that of A+H.

Key Words: Hypertension

P-237 MP-29
COMBINATION OF TOPROL-XL AND HYDROCHLOROTHIAZIDE: RESULTS OF A FACTORIAL CLINICAL TRIAL
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Most hypertensive patients require 2 or more drugs to achieve target blood pressure. Results of the ALLHAT trial indicate that diuretic-based antihypertensive regimens are effective in reducing cardiovascular morbidity and mortality.

The ATTACH trial evaluated 3 dose levels of hydrochlorothiazide (HCT) (6.25 mg, 12.5 mg and 25 mg), 4 levels of metoprolol succinate extended release (Toprol-XL) (25 mg, 50 mg, 100 mg and 200 mg), 9 of the possible combinations and placebo in an 8 week, multicenter, randomized, double-blind unbalanced factorial trial in patients with essential hypertension (DBP > 95, ≤ 114 mm Hg; SBP < 180 mm Hg).

The investigators randomized 1571 patients; 51% were male, 16% were > 65 years of age and 25% were black. Mean baseline blood pressure was 151/100 mm Hg.

Blood pressure declined significantly relative to placebo (p<0.05) with all combinations (placebo-subtracted range SBP/DBP= 6.1/3.9 to 15.9/12.2 mm Hg) (Figure). Each component contributed to the effect of the combination for both DBP (T-AVE p = 0.0015) and SBP (T-AVE p=0.0006).

Forty-six (2.9%) patients discontinued for adverse events but there was no clustering of events in any one treatment group. Serum potassium declined with HCT and was related to dose.

Toprol-XL-HCT is an effective antihypertensive combination agent over the range of doses (HCT 6.25 mg to 25 mg; Toprol-XL 25 mg to 200 mg).

Key Words: Clinical Trials, Combination Treatment, Hypertension

P-238 HEART RATE VARIABILITY AND ECG CHANGES IN 148 DANISH PATIENTS AFTER TWO YEARS IN THE VALUE TRIAL
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Background: Modulation of the autonomic nervous system through an increase in heart rate variability (HRV) with potential benefits in reducing the risk of ventricular arrhythmias has been demonstrated earlier in ischaemic heart disease with drugs affecting the renin-angiotensin system. The VALUE-trial explored the possible cardiac benefits of a valsartan-based (VAL) regimen compared to treatment with amlodipine (AML) in high-risk hypertensive patients. The purpose of the present substudy was to evaluate the treatment effects on the ECG and HRV calculated from ambulatory electrocardiographic recordings obtained by Holter technique during 24 hours.

Methods: Nine Danish VALUE-centres with a total of 148 patients participated in this substudy. Holter-recordings (2-channel Tracker, Reynolds Pathfinder analysis) were obtained after two years of maintained randomized therapy. From Holter data ventricular arrhythmias were classified according to severity and from 2-hours periods during day and night, time domain HRV measures were derived.

Results: The demographics showed two well-balanced groups with equal blood pressure reduction to 140/80 mmHg. Potassium levels were equal (VAL 4.1 ±0.4 vs. 3.9 ±0.4 mmol/L, ns). Beta-blockers were given as add-on to 37% in both groups. After 2 years the measured ECG criteria for left ventricular hypertrophy and the levels of QTc (VAL 406 ±25 vs. 413 ±27 msec, ns) and QT-dispersion (VAL 35 ±17 vs. 38 ±15 msec, ns) were equal in the two groups. The long term HRV measured as the standard deviation of the average normal to normal intervals (SDANN) was significantly higher in VAL compared with AML during the night (38 ±17 vs. 32 ±13 msec, P=0.019), whereas the SDANN did not differ between the two groups in the daytime. The 24 hour triangular index was significantly higher in VAL compared with AML (32 ±11 vs. 28 ±9, P=0.02). The prevalence of all categories of ventricular arrhythmia as well as the prevalence of atrial fibrillation was equal in the two groups.

Conclusion: Two indices of long-term HRV showed differences in favour of the VAL regimen. Although baseline HRV data were not obtained, the findings in this study substantiate correlation between a treatment regimen based on valsartan and alteration of the autonomic cardiovascular control through an increase of HRV.

Key Words: Amlodipine, Heart Rate Variability, Valsartan