

D053

AMBULATORY BLOOD PRESSURE MONITORING FOR THE EVALUATION OF THE TIME-EFFECT PROFILE OF AMLODIPINE VS PERINDOPRIL

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In a double-blind randomized parallel group study, we compared the effects of amlodipine 5-10 mg (Aml) vs perindopril 4-8 mg (Per) in 101 hypertensive patients (Office DBP between 90 and 109 mmHg) aged 51 ± 11 years. All received placebo during a 2 week run-in period followed by 2 months of active therapy. An ambulatory blood pressure measurement (24 hour ABPM) was performed before and after active treatment, with similar daily physical activity. Time-effect profile was evaluated using the trough/peak (T/P) ratio and the smoothness index (SI) calculations. In each patient, T effect was measured as the pre-treatment difference of mean SBP/DBP during the 2 last hours of the inter-dosing interval and P effect as the largest difference of SBP/DBP hourly averages during the first 12 hours post dosing. The SI was calculated in each patient as the mean 24 hour BP reduction/ standard deviation of this reduction.

Office blood pressure response rate was similar in both groups (Aml vs Per: 65% vs 59%) and so were the effects on ABPM 24 hour -average SBP/DBP. Safety was comparable in both groups (50% adverse events in each group, 14% cough with Per vs 19% leg edema with Aml). Individual T/P ratios were not normally distributed and 95% confidence intervals (CI) were very large. Mean individual DBP T/P ratios were, respectively for Aml and Per: (n = 49 vs 46) 50 ± 69% vs 15 ± 327% (medians: 42 vs 33%) (ns). Standard deviations were significantly larger in the perindopril group. Group averages of T/P ratios for SBP/DBP were respectively for Aml and Per: 83/80% vs 68/81%. Mean individual SBP/DBP SI were, respectively for Aml vs Per: 0.85 ± 0.85 / 0.65 ± 0.75 vs 0.74 ± 0.86 / 0.49 ± 0.60.

These results suggest that, even in controlled conditions T/P evaluation using ABPM yields individual T/P values non normally distributed and with very large standard deviations. Group T/P ratios were consistently higher than mean and median individual T/P ratios. Although not significantly so, Per tended to produce lower T/P ratios as well as smoothness indexes with larger standard deviations than did Aml. In order to reach statistical significance, much larger sample sizes are needed.

Amlodipine, perindopril, hypertension, ambulatory blood pressure monitoring

Key Words:

D055

INCREASED DEMANDS IN RECRUITMENT EFFORT FROM THE PILOT TO THE FULL-SCALE PHASE IN THE AFRICAN AMERICAN STUDY OF KIDNEY DISEASE AND HYPERTENSION (AASK). RA Phillips*, K. Britain, J Charleston, F Johnson, J Kusek, A Richardson, R Thompson, for the AASK Study Group, NIDDK, Bethesda, MD.

The AASK is an on-going NIH-sponsored 21-center randomized clinical trial studying whether 4 years of strict blood pressure (BP) control (MAP < 92 mm Hg vs 102-107 mm Hg) and 3 antihypertensive drug regimens (either beta-blocker, calcium channel blocker or ACE inhibitor as initial therapy) can blunt decline in renal function (GFR) in African Americans with renal disease due to hypertension. 80% of subjects were randomized as of October 1997; enrollment ends May 15, 1998. Inclusion criteria are African American/black, diastolic BP ≥ 95, age 18-70, and GFR between 20 and 65 ml/min/1.73m². Exclusion criteria include diabetes mellitus, heart failure and symptomatic coronary artery disease. A pilot study at 12 sites suggested that chart review was the most efficient strategy to identify subjects. Review of approximately 10 charts yielded one randomized patient. Many of these patients were previously well known to the sites with regard to serum creatinine and absence of exclusion factors. This data was used to estimate the effort and resources required for the full-scale trial. The pilot was both predictive and also highly misleading. As suggested by the pilot, in the full-scale trial 83% of randomized patients were identified by chart review, or by referral by a health professional; only 5% were recruited by mail, and < 1% by either flyer, health fair, poster, bus ad, church bulletin, newspaper article or advertisement. However, as opposed to the pilot, 421,792 charts were reviewed to yield 844 randomized patients (500 charts per randomized patient), a proportion which is 50 times greater than the pilot. Efficiency of recruitment varied from site to site, possibly as a function of the degree to which computerized databases were used to identify and exclude potential subjects. This enormous effort at only 21 sites (average 20,100 charts/site) required a one year extension of the recruitment period. The full scale trial illustrates that pilot data, which may be generated from with subjects with previously recognized disease, may seriously underestimate the effort, time and resources required for a full-scale recruitment.

Key Words:

renal disease, hypertension, clinical trials, African Americans

D054

Visit (VAd) and Medication Adherence (MAd) in the Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack Trial (ALLHAT): Effect of Age and Other Factors.

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Background: ALLHAT has achieved the randomization targets of both the antihypertensive and lipid-lowering components of the trial (40,000 and 10,000 patients respectively). The next challenge is to maintain a high percent patient retention and adherence to drug during follow up.

Objective: To determine whether age is a predictor of VAd and MAd in ALLHAT, we tested the hypothesis that there is no difference in VAd and MAd between older (≥ 65 years old) and younger (55 - 64 years old) patients enrolled in ALLHAT.

Design and Methods: Included in this analysis were randomized patients still alive and with at least 1 year of follow up. For VAd we compared the proportion of younger patients who attended > 80% of their scheduled visits to the same proportion of older patients. For MAd the proportions of younger and older patients who were on assigned blinded drugs at their last clinic visit were compared. Tests of proportions were done by the χ^2 method.

Results: 22,007 of the patients currently enrolled in ALLHAT met the criteria for inclusion in the two analyses. The distribution of younger and older patients differed by gender, race, and geographic region. The percentage of the 8,463 younger and 13,544 older patients attending > 80% of scheduled clinic visits were 65.7% and 67.2% respectively (p = 0.02). 76.6% of younger patients were still on assigned treatment, while among older patients this was 72.7% (p < .001).

Conclusion: Younger patients are more likely to be on their assigned medication than were older patients, while older patients were more likely to adhere to their visit schedule. The absolute differences in the percentages are small. One possible explanation is that younger patients adhering less well to medication may avoid physician encounters, while older patients may seek physician advice more frequently for perceived problems. We will be investigating additional potential predictors of adherence such as gender, ethnicity, cigarette smoking, baseline comorbidities, clinic setting (VA, HMO, community health center, solo practice) and geographic location in the ALLHAT study group.

Key Words: Hypertension, antihypertensive, adherence, clinical trial

D056

ASSOCIATION OF METABOLIC FACTORS WITH THE EARLY CEREBROVASCULAR MANIFESTATIONS IN MILD HYPERTENSIVE MALES. AN Britov, DV Nebieridze, MN Mamedov, RG Oganov, National Research Centre for Preventive Medicine, Moscow, Russia.

In this study attempt was made to investigate the association of different metabolic variables with the development of persistent blood pressure elevation (PBPE) and early cerebrovascular manifestations in mild hypertensive (MH) patients (pts). Plasma cholesterol, HDL cholesterol, triglycerides, body mass index (BMI — kg/m²) were determined in 215 MH males, aged 30-49 (diastolic BP within 90-104 mm Hg) out of 810 screened subjects. Besides, in 50% randomly selected MH pts fasting plasma insulin was measured by radioimmunoassay. All MH pts were followed up for 5 years repeatedly measuring of BP (altogether 5 measurements). In the end of follow-up they were questioned on the appearance of headache, dizziness, reduction of memory and mental activity. PBPE (diastolic BP ≥ 95 mm Hg in all follow-up visits) was found in 99 MH pts (46%). Comparing with the rest MH pts they had higher initial levels of: insulin — 14.0 ± 3.09 μU/ml against 7.3 ± 1.7 μU/ml (p < 0.001), atherogenic index (total cholesterol — HDL cholesterol/HDL cholesterol) — 5.4 against 3.5 (p < 0.05), triglycerides — 173 ± 24 mg/dl against 127 ± 13 mg/dl (p > 0.05), BMI — 27.1 ± 3.3 against 25.8 ± 3.3 (p < 0.05). On the other hand, MH pts with PBPE had higher frequency of: headache — 18% against 9% (p < 0.05), dizziness — 21% against 10% (p < 0.05), reduction of memory — 30% against 15% (p < 0.05) and mental activity — 20% against 8% (p < 0.05).

We conclude that hyperinsulinemia, connected lipid abnormalities and obesity may promote to the progression of mild hypertension and development of early vascular complications.

Key Words: metabolic factors, mild hypertension, cerebrovascular manifestations.