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LEFT VENTRICULAR HYPERTROPHY IN HYPERTENSIVE CHILDREN: A REPORT FROM THE INTERNATIONAL PEDIATRIC HYPERTENSION ASSOCIATION
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Objectives: To determine the prevalence of left ventricular hypertrophy (LVH) by both pediatric and adult criteria in children and adolescents with hypertension.

Methods: Pooled data from 1998 to 2001 from 3 sites belonging to the International Pediatric Hypertension Association were reviewed. Both treated (i.e., antihypertensive meds) and untreated pts undergoing echocardiography to detect LVH as part of the evaluation for hypertension were included for analysis. Left ventricular mass was calculated from 2-D guided m-mode echocardiographic measurements of the LV using the equation reported by Devereux. Measurements of the LV internal dimension, interventricular septal thickness, and posterior wall thickness were made during diastole according to methods established by the American Society of Echocardiography. LVMI was calculated as LVM/height^2.7. LVH by adult criteria was defined as LVMI > 51 gm/m^2.7 and by pediatric criteria as LVMI > 38.6 gm/m^2.7 (based on normative pediatric LVMI data).

Results: 133 pts were included for analysis. Clinical characteristics were: age 13.6 ± 3.6 yrs, male 67%, height 160 ± 18 cm, weight 72 ± 27 kg, and BMI 27.5 ± 7.4 kg/m^2. Mean LVMI was 37.5 ± 13.1 gm/m^2.7. Compared to females, males had greater LVMI (39.2 vs. 34.0 gm/m^2.7, p<0.05) and were taller (164 vs. 152 cm, p<0.001). Males and females did not differ in age, weight or BMI. LVMI correlated significantly with BMI (r=0.41, p<0.0001) and weight (r=0.29, p<0.001), but did not correlate with age. The overall prevalence of LVH by adult criteria was 15.8% and by pediatric criteria was 38.3%. Using either criteria, pts with LVH were heavier (p<0.01) and had greater BMI (p<0.001) than those without LVH. Males were more likely than females to have LVH by pediatric criteria (45% vs. 25%, p<0.001), but not by adult criteria. Among untreated pts (n=77), the prevalence of LVH was 14.3% by adult criteria and 39.0% by pediatric criteria, which did not differ significantly from the overall LVH prevalences.

Conclusions: LVH, even by adult criteria, occurs commonly in children and adolescents with hypertension and is positively associated with increased BMI. Echocardiography may therefore be helpful in the determination of the need for antihypertensive therapy. Further studies are needed to determine whether treatment of the hypertension results in regression of LVMI to the normal range.

Key Words: Left Ventricular Hypertrophy, Child, Hypertension

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GROWTH OF LEFT VENTRICULAR MASS AND ITS MODERATORS FROM CHILDHOOD TO EARLY ADULTHOOD IN AFRICAN AMERICAN AND EUROPEAN AMERICAN YOUTH
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Objective: Increased left ventricular mass has been established as a strong risk factor for cardiovascular morbidity and mortality. The aim of this study was to evaluate growth of left ventricular mass (LVM) from childhood into early adulthood and its possible sociodemographic, anthropometric, and hemodynamic moderators.

Methods: Individual growth curves across age of LVM were created for 687 African American (AA) and European American (EA) males and females, for whom annual LVM assessments were obtained over a 10-year period. Subjects had a mean age (range) of 12.6 (8.2-17.7 yrs) and 19.3 (11.0-27.5 yrs) years at the first and last visit, respectively.

Results: AAs and males had significantly greater LVM levels (P<0.001) than EAs and females, respectively. Males also showed a stronger rate of change in LVM than females. The ethnicity and sex effects on LVM only became apparent in early adolescence and persisted when socio-economic status, anthropometric or hemodynamic variables were taken into account. Body mass index, as a measure of general adiposity, and height were the strongest anthropometric predictors and pulse pressure the strongest hemodynamic predictor of LVM. Pulse pressure no longer added to the prediction of LVM, once body mass index and height were entered into the model. The anthropometric variables explained up to 35% of between-subject variance in LVM from childhood early adulthood.

Conclusion: Increased LVM in males and AAs has its origin in late childhood, and individual differences in cardiac growth are mainly due to body growth and increases in general adiposity.

Key Words: Longitudinal, Sociodemographic, Anthropometric and Hemodynamic Moderators, Left Ventricular Mass

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A RANDOMIZED, PLACEBO-CONTROLLED TRIAL OF AMLODIPINE IN THE TREATMENT OF CHILDREN WITH HYPERTENSION (HTN)
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Amlodipine, a third-generation dihydropyridine calcium channel blocker, has been reported as effective in the treatment of hypertensive children in several single-center studies. To further examine the efficacy and safety of amlodipine in children, a randomized, double blind, placebo-controlled, parallel group dose ranging study was conducted at 49 centers in North and South America. The primary end-point of the study was the effect of amlodipine on systolic blood pressure (SBP). Secondary endpoints included the effect of amlodipine on diastolic blood pressure (DBP), the effect of amlodipine as a function of dose and body size, and safety. 268 children with HTN (seated SBP ≥95th percentile for age, gender and height) were enrolled. Mean age of enrolled subjects was 11.9±3.3 (mean±SD) years, with a range of 1-17 years. 102 children (38.1%) had primary HTN; 177 (66%) were boys. Following a screening visit and washout of prior therapy if needed, subjects were randomized to receive either 2.5 mg or 5.0 mg of amlodipine daily. After 4 weeks of amlodipine treatment, mean SBP and DBP were significantly lower than at baseline (129.8±15.4/70.1±10.4 mmHg vs. 138±12.7/74.2±11.6, P<0.0001). Subjects were then randomized to placebo withdrawal vs. continued amlodipine treatment for 4 additional weeks. Amlodipine recipients had significantly greater reductions in SBP than placebo recipients (mean SBP change: -8.7 mmHg for amlodipine 5 mg QD, -6.9 mmHg for amloidpine 2.5 mg QD, & -3.6 mmHg for placebo). There was
no significant difference in response to amlodipine according to cause of HTN. Linear regression analysis revealed a significant relationship between the dose of amlodipine in mg/kg and changes in both SBP (P=0.03) and DBP (P=0.02), with predicted mean reductions of 9.2/4.9 mmHg for an amlodipine dose of >0.06 mg/kg. Six children (2.2%) were discontinued from amlodipine treatment for drug-related adverse events, and the dose was reduced in one additional child. The most commonly reported adverse effect of amlodipine was headache. We conclude that amlodipine is an effective antihypertensive agent in children. The results of this study should provide valuable guidance to physicians who prescribe amlodipine for children with HTN.

Key Words: Amlodipine, Children, Clinical Trials

OR-70
EFFECTS OF THE ACE INHIBITOR, LISINOPRIL (L), IN CHILDREN AGE 6-16 YEARS WITH HYPERTENSION
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This multicenter study assessed the antihypertensive safety and efficacy of L (PRINIVIL®) in children with hypertension age 6 to 16 yrs. The study was comprised of 115 pts; 41 from the U.S.,74 ex-U.S., 54 (47%) age 5-12 yrs, 61 (53%) age 13-16 yrs, 69 (60%) Tanner Stage ≥3, 75 (65.2%) were male, and 12 (10.4%) were Black.

After an up to one wk washout from prior antihypertensive therapy, pts with trough sitting diastolic BP (SiDBP) > 95 percentile for gender, age and height were randomized to receive 1 of 3 dose groups (Low, Middle, or High) once daily for 14 days: 0.625/1.25 mg (0.02 mg/kg), 2.5/5 mg (0.07 mg/kg), or 20/40 mg (0.61 mg/kg). Pts who weighed <50 kg received the lower dose in the respective treatment groups (0.625, 2.5, or 20 mg), and pts who weighed ≥50 kg received the higher dose (1.25, 5, or 40 mg). Pts in the 20/40 mg group received a half dose for the first 2 days, then were titrated to the full dose. After 2 wks of double-blind therapy (Period I), pts entered a randomized washout period (Period II) where they either continued on their current study regimen or were switched to placebo for up to 2 wks, or when their SiDBP returned to baseline, whichever came first.

Period I SiDBP decreased in all dose groups; -7.6 (Low), -9.3 (Middle), and -16.4 mmHg (High), indicating a strong dose response relationship between the lowest dose 0.625mg/1.25mg, and each of the higher doses, 2.5mg/5mg and 20mg/40mg, in trough SiDBP, resulting in a slope of -0.3 mmHg per unit increase in dose ratio (1:4:32; p<0.001). Period II clearly demonstrated that SiDBP in the placebo group increased after discontinuation of therapy; -0.2 (Low), 9.7 (Middle), and 9.1 mmHg (High), indicating a strong dose response relationship between the lowest dose 0.625mg/1.25mg, and each of the higher doses, 2.5mg/5mg and 20mg/40mg, in trough SiDBP, resulting in a slope of -0.3 mmHg per unit increase in dose ratio (1:4:32; p<0.001). A significant dose dependent reduction in siDBP was also observed.

Angiotensin II levels, as well as tissue renin activity levels are more suppressed in male offspring than in female. Mean arterial pressure [MAP] was the same in adult female offspring of LP [121+/−2mmHg] and NP mothers [120+/−3 mmHg], as was GFR, ERPF, and filtration fraction. In contrast adult male offspring of LP mothers had sig. higher MAP than NP offspring [136+/−2 mmHg vs. 125+/−2mmHg, p =0.004]; they also showed differences in GFR, ERPF and FF. Thus, maternal protein restriction clearly and markedly decrease the expression of the intrarenal RAS in newborn male offspring, leading to permanent changes that influence the subsequent course of cardioenal health, whereas female rats are relatively resistant to programming for adult hypertension by perinatal protein restriction. This resistance may be due to the fact that modest maternal protein restriction does not reduce the number of glomeruli with which females are endowed as it does in males. The intrarenal RAS during development may play a key role in this protective effect of female gender.

Key Words: Perinatal Programming, Renin-Angiotensin System, Nephrogenesis