The Effect of Antihypertensive Dosing on Hypertension in Children with Chronic Kidney Disease

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The Effect of Antihypertensive Dosing on Hypertension in Children with Chronic Kidney Disease
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Background
Hypertension (HTN) is a highly prevalent and major risk factor for poor cardiovascular and renal outcomes in chronic kidney disease (CKD).

Objective
To determine the effect of antihypertensive dose on HTN status in children with CKD.

Methods
Study population: 255 participants studied in the Chronic Kidney Disease in Children (CKiD) study at their third visit.

Inclusion criteria: Age 1-16 years with estimated GFR 30-90 mL/min/1.73m², taking at least one antihypertensive medication, successful 24h ABPM study.

Exclusion: White-coat hypertension (n=5).

Study variables:
- Cumulative Drug Dose Index (cDDI): We developed a new quantitative tool, Drug Dose Index (DDI, Fig 1) which expresses dose as a ratio between the current dose and the maximum potential dose, accounting for age, weight and if indicated, renal dose adjustments. cDDI is the sum DDI for all antihypertensive agents taken by the subject.
- Primary outcome: HTN status classified into controlled HTN (cHTN) or uncontrolled HTN (uHTN = masked HTN or ambulatory HTN) based on 2017 AAP guidelines and 24h ABPM study (see Fig 3).

Statistical analysis:
Univariate analysis: t-test and ANOVA (continuous variables) and chi-square test (categorical variables) used to compare cDDI between the outcome groups (Fig 4): a) cHTN vs. uHTN, b) cHTN, MH vs. AH, and c) LVH vs. no LVH.

Multivariate Logistic Regression Analysis:
- Two outcomes: Table 2) uHTN and Table 3) LVH.

Results
Study population: 255 participants studied in the Chronic Kidney Disease in Children (CKiD) study at their third visit.

Inclusion criteria: Age 1-16 years with estimated GFR 30-90 mL/min/1.73m², taking at least one antihypertensive medication, successful 24h ABPM study.
Exclusion: White-coat hypertension (n=5).

Drug Dose Index:
- cDDI = dose_max / Max dose_max (up to maximum of 1)

Table 1
Summary of Sociodemographic, clinical and pharmacological factors

Table 2 and 3 Logistic Regression Analysis
Model 1: Predictors of Uncontrolled Hypertension
- predictor: uHTN, Odds ratio: 0.001, 95% CI: 0.000-0.004, p-value: 0.02913
- predictor: race (Caucasian), OR: 0.723, 95% CI: 0.326-1.624, p-value: 0.4948
- predictor: eGFR (ml/min/1.73m²), OR: 0.001, 95% CI: 0.000-0.005, p-value: 0.0001

Model 2: Predictors of LVH
- predictor: RAASi and diuretic use, OR: 0.025, 95% CI: 0.000-0.001, p-value: 0.00004
- predictor: non-Caucasian race, OR: 0.000, 95% CI: 0.000-0.001, p-value: 0.00004
- predictor: number of antihypertensive agents, OR: 0.320, 95% CI: 0.130-0.794, p-value: 0.00004
- predictor: higher BMI z-score, OR: 0.000, 95% CI: 0.000-0.001, p-value: 0.00004
- predictor: lower cDDI, OR: 0.000, 95% CI: 0.000-0.001, p-value: 0.00004

Discussion
- This was the first quantitative analysis of antihypertensive dose expressed as a newly developed measure, cDDI, and its relationship with hypertension status in children with CKD.

- No differences in cDDI between uHTN vs. cHTN, or LVH vs. no LVH, but higher cDDI was associated with AH on univariate analysis.

- RAASi and diuretic use were associated with lower odds of uHTN.

- Non-Caucasian race, absence of RAASi and diuretic agents, and higher number of agents were associated with greater odds of uHTN.

- Female gender, higher BMI z-score, lower eGFR, higher number of agents and lower cDDI were associated with greater odds of LVH.

Conclusions
- Lower dose (cDDI) is not a significant predictor of uHTN, however it may be associated with LVH.

Further research is needed to validate the use of cDDI and the roles of medication class and dose on blood pressure control in children with CKD.