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Association Between Blood Pressure and ESA Dose in Pediatric Patients on Dialysis

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Background

-Hypertension is a reported side effect of Erythropoiesis Stimulating Agents (ESAs), with mechanisms of action related to elevated hematocrit levels and direct vasopressor effects.

-Limited information exists on the relationship between ESA dosage and hypertension in children receiving maintenance dialysis.

Objectives

-Primary: Determine whether there is a significant association between ESA dose and blood pressure (BP) in pediatric patients receiving maintenance dialysis.

-Secondary: Evaluate the covariates related to ESA dose and BP (hemoglobin level, growth hormone use, number of antihypertensive medications, BMI, total daily output, and dialysis modality)

Methods

-Data entered into the IPDN database from January 2007-September 2019 was analyzed.

-Systolic and diastolic BP measurements obtained at clinic visits were averaged and standardized based on age, height, and sex.

-ESA dose was measured in units/kg/week and categorized into 3 groups (<100u/kg/week, 100-250u/kg/week, >250u/kg/week) with Darbepoetin and continuous erythropoietin receptor activator (CERA) converted to equivalent units of Epopen.

-Kruskal Wallis test was used for continuous variables and Chi-Square for categorical. Logistic Regression was used to evaluate the covariates (SPSS Version 26).

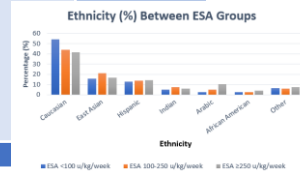
Results

-A total of 3791 children were included in the analysis with mean age of 11 years and 55.7% male. The mean prescribed ESA dose was 218.73 units/kg/week.

Demographics within ESA Groups

| Variable | <100u/kg/week Epopen (N=1293) | 100-250u/kg/week Epopen (N=1636) | ≥250u/kg/week Epopen (N=862) | p-value |
|-------------------------------|-------------------------------|----------------------------------|------------------------------|-------------|
| Age, years (median, SD) | 14.20 (5.45) | 11.46 (5.65) | 6.68 (5.83) | p < 0.001* |
| Sex, M (N, %) | 729 (56.4%) | 901 (55.1%) | 482 (55.9%) | p = 0.771** |
| Ethnicity (N, %) | | | | p < 0.001** |
| 1= Caucasian | 705 (54.5%) | 722 (44.1%) | 358 (41.5%) | |
| 2= East Asian | 205 (15.9%) | 343 (21%) | 145 (16.8%) | |
| 3= Hispanic | 166 (12.8%) | 223 (13.6%) | 123 (14.3%) | |
| 4= Indian | 63 (4.9%) | 125 (7.6%) | 52 (6%) | |
| 5= Arabic | 33 (2.6%) | 79 (4.8%) | 88 (10.2%) | |
| 6= African / African American | 36 (2.8%) | 45 (2.8%) | 33 (3.8%) | |
| 7= Other | 85 (6.6%) | 99 (6.1%) | 63 (7.3%) | |

*Kruskal Wallis, **Chi-Square; p < 0.05 indicates significance



Comparison of ESA Dose and Blood Pressure

| Variable | <100u/kg/week ESA (N=1293) | ≥250u/kg/week ESA (N=862) | Significance | Odds Ratio (OR) ESA dose ≥250u/kg/week: elevated BP (>1.68 standard deviation) |
|---|----------------------------|---------------------------|--------------|--|
| Systolic BP standard deviation for age/sex/height Median | 0.93 | 1.30 | p < 0.001 | OR = 1.40 (95% CI 1.20-1.63) p < 0.001 |
| Diastolic BP standard deviation for age/sex/height Median | 0.72 | 0.87 | p < 0.001 | OR = 1.20 (95% CI 1.01-1.42) p = .035 |

Logistic Regression: Covariates and Systolic/Diastolic Elevated BP (>90th percentile)

| Variable | Systolic BP SD > 1.68 (X ² = 473.089, df= 8, p<0.001) | | | Diastolic BP SD > 1.68 (X ² = 319.937, df= 8, p<0.001) | | |
|--|---|---------|-------------|--|--------|-------------|
| | p-value | Exp (B) | 95% CI | p-value | Exp(B) | 95% CI |
| ESA Dose (<250u/kg/week) | <0.001 | 1.594 | 1.306-1.946 | <0.001 | 1.476 | 1.191-1.829 |
| BMI standard deviation | 0.002 | 1.086 | 1.032-1.143 | 0.759 | -- | -- |
| Dialysis Modality (HD) | <0.001 | 0.557 | 0.466-0.666 | 0.646 | -- | -- |
| Number of Antihypertensive Medications | <0.001 | 1.676 | 1.584-1.774 | <0.001 | 1.586 | 1.498-1.679 |
| Use of Growth Hormone, (No) | 0.201 | -- | -- | 0.098 | -- | -- |
| Total Daily Output/kg | 0.107 | -- | -- | 0.420 | -- | -- |
| Hemoglobin Level gm/dL | <0.001 | 0.930 | 0.893-0.969 | 0.019 | 0.950 | 0.910-0.992 |

Discussion

-Pediatric patients receiving maintenance dialysis were more likely to have elevated blood pressure (>90th percentile for age/sex/height) if they were receiving >250u/kg/week of ESA.

-Elevated BMI, higher number of antihypertensive medications, hemodialysis modality, and lower hemoglobin levels were associated with blood pressure >90th percentile for age/sex/height. Growth hormone use and daily output per kg were not significantly associated with elevated blood pressure.

-There was a significant difference in age between the 3 ESA groups with the higher dose group (>250u/kg/week) being the youngest (median age of 6.68 years). This is likely related to higher ESA doses required to achieve target hemoglobin response in this age group.

Conclusion

Patients with ESA dose > 250u/kg/week may be at higher risk for elevated blood pressure. Further studies are warranted to evaluate the relationship between ESA dosing and blood pressure and to assess the efficacy of anemia management strategies designed to minimize the risk of treatment related complications.

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