Evaluation of Methods That Estimate Glomerular Filtration Rate in Patients With Prader-Willi Syndrome

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Background

- Prader–Willi syndrome (PWS) is a rare, complex, multisystem disorder caused by the loss of multiple paternally expressed genes on chromosome 15q11–13.
- Characteristics of PWS include low muscle mass and hypotonia, accumulation of excess body fat, short stature, hyperphagia, behavioral problems, cognitive disabilities, developmental delays, and hypogonadism.
- PWS patients have low lean body mass, which may contribute to low serum creatinine (SCr) levels.
- SCr-based methods to calculate estimated glomerular filtration rate (eGFR) may not accurately reflect PWS patient's renal function.

Objective

- To assess methods of estimating renal function in pediatric PWS patients and summarize the relationship between eGFR and patient-specific factors.

Methods

- Retrospective analysis of the pre-treatment data of patients ≥4 years old with genetically confirmed PWS participating in an investigational study of DCCR (diazoxide choline).
- Lean body mass and age were correlated to eGFR/creatinine clearance (CrCl) values calculated using four different equations: Bedside Schwartz (BS), Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI), Modification of Diet in Renal Disease (MDRD), and Cockcroft-Gault (C-G).

Equations Used

Bedside Schwartz[1]	$eGFR = 0.413 * (\frac{\text{Height (cm)}}{\text{SCr}(\frac{mg}{dL})})$
CKD-EPI[2]	$eGFR = 141 * min(\text{SCr}/\kappa \text{ or } 1)^{\alpha} * max(\text{SCr}/\kappa \text{ or } 1)^{-1.209} * 0.993^{Age} *$ (1.018 if female) * (1.159 if African American) $\kappa = 0.7$ for females, 0.9 for males $\alpha = -0.329$ for females, 0.411 for males
MDRD[3]	$eGFR = 175 * (\text{SCr})^{-1.154} * (\text{Age})^{-0.203} * (0.742 \text{ if female}) * (1.212 \text{ if African American})$
Cockcroft-Gault[4]	$CrCl = \frac{(140 - Age) * \text{Weight (kg)}}{72 * \text{SCr}(\frac{mg}{dL})} * (0.85 \text{ if female})$ "Weight(kg)" varies between ideal, actual, and adjusted body weight

Results

- Of the 124 patients enrolled in the study, 99 were <18 years old and 103 were taking growth hormone (GH).

Table 1. Mean (±SD) eGFR calculated by different methods and correlation to lean mass and age

Calculation Method	eGFR or CrCl (from C-G)	Correlation to Lean Mass (Trend)	Correlation to Age (Trend)
BS	120±22 mL/min/1.73m²	Negative	Negative
CKD-EPI	154±23 mL/min/1.73m²	Negative	Negative
MDRD	211±77 mL/min/1.73m²	Negative	Negative
C-G	191±80 mL/min	Positive	Positive

BS = Bedside Schwartz | C-G = Cockcroft-Gault

- Mean SCr was 0.52 mg/dL, with only two subjects (1.6%) having SCr in the normal range (0.84 to 1.21 mg/dL).

Table 2. Mean (±SD) eGFR stratified by age groups in PWS Patients

Age (yr)	N*	SCr (mg/dL)	eGFR (mL/min/1.73m²)			CrCl (mL/min)
			Bedside Schwartz	**CKD-EPI**	**MDRD**	**Cockcroft-Gault**
4-7	28	0.401±0.065	124.05±16.83	176.88±16.28	306.75±71.63	133.11±29.61
8-11	44	0.454±0.074	128.02±19.85	168.60±15.86	254.57±63.69	178.76±59.60
12-17	51	0.563±0.103	121.15±23.99	147.34±13.67	177.42±45.86	222.52±84.92
18+	43	0.655±0.111	104.50±15.72	130.32±13.56	134.25±28.03	211.89±74.47

*This sample size is based on screening data and thus has a total N > 124, which is how many were eventually enrolled

Conclusion

- In PWS patients, low SCr results in eGFR (or CrCl) values that likely overestimate their actual renal function.
- The inconsistent trends in correlation values between eGFR, or CrCl by C-G, and both lean mass and age indicate that current SCr-based methods may be inadequate to accurately estimate renal function in PWS patients that generally have low SCr levels.
- The use of CKD-EPI should be considered in PWS. Otherwise, non-creatinine-based methods to measure renal function need to be evaluated.

References

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