Protein Energy Wasting in Children with Chronic Kidney Disease

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1. Introduction

Nutritional derangements are common in children with chronic kidney disease (CKD) and are associated with significant morbidity and mortality. Studies have reported a prevalence of 20-45% of malnutrition in children with CKD (Iorember et al. 2018). Malnutrition in CKD is not entirely explained by reduced nutritional intake. A complex combination of different factors, including hormonal imbalances, decreased appetite, inflammation, increased catabolism, and metabolic derangements, all predispose CKD patients to malnutrition (Ku et al. 2017, Patel et al. 2017, Oliviera et al. 2017, Kalantar-Zadeh et al. 2003). The exact mechanisms leading to poor outcomes in children with CKD with suboptimal nutritional status are not well understood.

The term protein energy wasting was proposed by The International Society of Renal Nutrition and Metabolism (ISRNM) to describe a state of decreased body stores of protein and fat. Unlike protein energy malnutrition, which describes deficient protein energy explained purely by inadequate dietary protein intake, protein energy wasting (PEW) describes deficient protein energy that cannot be corrected by increasing energy intake alone. The pathogenesis of PEW is not well understood and is shown to be related to many complex factors, including the metabolic, inflammatory, nutritional and hormonal factors mentioned above. PEW is associated with impaired growth and development, increased risk of hospitalizations and death (Abraham et al. 2014). PEW has been well studied in adults and shown to be a risk factor for cardiovascular complications and death, however it is not well characterized in children. A recent study has modified the PEW definition in adults to see if it could be utilized in pediatric populations (Abraham et al. 2014). By including pediatric-focused criterion (e.g. poor growth defined as short stature or poor growth velocity), the study showed that the modified PEW definition was better able to predict rates of hospitalization. A better understanding of the pathogenesis of PEW and better characterization of this condition in children will be important to improve outcomes of children with CKD.

2. Hypothesis

Aim 1: To identify the risk factors and prevalence of protein energy wasting in children with CKD Stages 1-5
Hypothesis 1: Protein energy wasting is prevalent in children with chronic kidney disease in our patient population and several risk factors predict poor outcomes in CKD.

Aim 2: To identify pediatric-focused criteria and other criteria to augment the definition of PEW and improve risk prediction in children with CKD
Hypothesis 2: Inclusion of pediatric-focused and other specific criteria (e.g. bone age, bioimpedance analysis, nutritional diaries, hormonal markers) to the definition of PEW will improve prediction of risk in children with CKD

3. Methods

Aim 1 will be a Retrospective study of previously published markers for PEW. We will use a multiple regression model to identify prevalence of PEW and correlation between significant risk factors ($p<0.05$) and severity of CKD and poor outcomes (hospitalizations, rate of decline of GFR, death).
Aim 2 will be a prospective longitudinal study to collect data to supplement definition of PEW in children (e.g. mid upper arm circumference, bioimpedance analysis, diet journals, hormonal markers). We will partner with the bionutrition core to gather body composition measurements and validate dietary journals. Due to the time constraints of the study we will follow these patients for 1 year and measure outcomes (decline in GFR, growth, hospitalizations) after 1 year. We will also collective retrospective analysis on these patients to trend GFR and growth. We will develop a modified PEW definition based on significant risk factors from the retrospective and prospective portions of the study.

4. **Subject selection**

For the retrospective study, we will perform power analysis to determine the number of subjects required to detect decline in GFR and increased risk of hospitalizations and death. We have medical records for over 200 patients with CKD stages 1-5.
For the prospective study, we hope to recruit 30 patients. Participation in the study will require collecting dietary journals on 3 non-consecutive days, and measurement of body composition (e.g. bioimpedance analysis).

5. **Study questionnaires**

We will partner with the bionutrition core and nutritionists to author a validated nutritional questionnaire that quantifies the energy intake of patients in a day, distinguishing between different sources of energy (carbohydrates, protein or fat).

6. **Confidentiality:** All study materials will be de-identified and stored in a locked office.

7. **Potential conflicts of interest**: None

8. **Location:** New York Presbyterian Columbia University Medical Center and its affiliated clinics

9. **Potential risks:** none

10. **Potential benefits:** No direct benefit to participants, but results of the study could potentially improve outcomes of children with CKD in the future.

11. **Compensation and cost to subjects:** none, except for transportation costs to the bionutrition visits to validate dietary journal data and obtain anthroprometric measurements.

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