Uremic toxin concentrations are related to residual kidney function in the pediatric hemodialysis population

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BACKGROUND & AIM

1. Evaluation of a broad array of uremic toxins in a large pediatric HD cohort

2. Exploration impact of residual kidney function

- Deterioration of renal endocrine function
  - Decreased erythropoietin production
  - Calcitriol deficiency
  - Excessive production renin

- Accumulation of uremic toxins
  - Increased generation
  - Decreased renal excretion and/or metabolism

- Dysregulation of fluid, electrolyte & acid-base homeostasis
  - Metabolic acidosis
  - Hyperkalemia

- Related to native kidney disease
  - Auto-immune disorders
  - Hereditary renal disorders

- Related to renal replacement therapy
  - Use of bio-incompatible materials
  - Fluctuation in extracellular fluid volume

HD n = 170
CKD4-5 n = 24

Multicenter European prospective Cross-sectional
ANCOVA, adjustment age, albumin Spearman correlation coefficient
UA, b2M, pCG, HA, IAA, IxS, pCS, CMPF (ELISA, HPLC)
Decrease protein-binding due to altered albumin binding in CKD
- post-translational modifications
- Lower albumin concentrations

Substantially higher levels in anuric HD vs non-anuric HD & CKD4-5
Uremic toxin levels inversely correlated with residual urine volume (mL/BSA/24h) in HD patients

Improved albumin binding properties with preserved residual urine volume

While current HD techniques poorly remove protein-bound uremic toxins, residual kidney function provides a substantial removal of these toxins + improved outcomes!

- Preservation is crucial
- Residual urine volume follow-up in standard pediatric ESKD care
Advisory Board

UZ Gent

Cooperating centers
Back-up slides
|                                | CKD <30ml/min/1.73m² | Non-anuric HD | Anuric HD | p    |
|--------------------------------|-----------------------|---------------|-----------|------|
| **Number**                     | 24                    | 101           | 69        |      |
| **Age (years)**                | 8.4 [3.7; 14.8]       | 13.5 [9.6; 15.8] | 15.1 [11.7; 16.9] | <.01 |
| **Male (%)**                   | 17 (70.8)             | 56 (55.4)     | 35 (50.7) | .23  |
| **Kidney disease (%)**         |                       |               |           |      |
| Glomerular                     | 4 (16.7)              | 18 (17.8)     | 17 (24.6) | .03  |
| CAKUT                          | 15 (62.5)             | 51 (50.5)     | 21 (30.4) |      |
| Cystic disease                 | 1 (4.2)               | 3 (3.0)       | 2 (2.9)   |      |
| Other or unknown               | 4 (16.7)              | 29 (28.7)     | 29 (42.0) |      |
| **eGFR (mL/min/1.73m²)**       | 17 [11; 23]           |               |           |      |
| **Vascular access (%)**        |                       |               |           |      |
| AVG/AVF                        | -                     | 35 (34.7)     | 30 (43.5) | .39  |
| CVC                            | -                     | 66 (65.3)     | 39 (56.5) |      |
| **Dialysis modality**          |                       |               |           |      |
| HDF (%)                        | -                     | 31 (30.7)     | 22 (31.9) | .87  |
| Conventional HD (%)            | -                     | 70 (69.3)     | 47 (68.1) |      |
| **Dialized blood volume**      |                       |               |           |      |
| Blood flow (mL/BSA)            | -                     | 176 [141; 214]| 180 [141; 213] | .78  |
| Dialysis hours/week (h)        | -                     | 10.5 ± 1.2    | 10.7 ± 1.2 | .33  |
| **Dialyzer**                   |                       |               |           |      |
| Low-flux (%)                   | -                     | 40 (39.6)     | 33 (47.8) | .34  |
| High-flux (%)                  | -                     | 61 (60.4)     | 36 (52.2) |      |
| **Dialysis sessions/week (%)** |                       |               |           |      |
| Three                          | -                     | 94 (93.1)     | 66 (95.7) | .77  |
| Two or four                    | -                     | 7 (6.9)       | 3 (4.3)   |      |
| **Average ultrafiltration (mL/m²)** | -     | 968 [364; 1334] | 1364 [755; 1675] | <.01 |
| **Residual kidney function**   |                       |               |           |      |
| Volume (mL/24h/m²)             | -                     | 411 [151; 864]|           |      |
| < 100 mL/24h                   | -                     | 9 (8.9)       |           |      |
| 100 – 200 mL/24h               | -                     | 14 (13.9)     |           |      |
| 200 – 500 mL/24h               | -                     | 24 (23.8)     |           |      |
| +500 mL/24h                    | -                     | 54 (53.5)     |           |      |
| **Dialysis vintage (years)**   | -                     | 0.40 [0.14; 1.14] | 1.26 [0.33; 3.65] | <.01 |
| **Routine blood results**      |                       |               |           |      |
| Albumin (g/L)                  | 43 [41; 47]           | 40 [38; 43]   | 41 [38; 43] | <.01 |
|                                | Healthy children\(^2\) | CKD <30ml/min/1.73m² (n = 24) | Maintenance HD (n = 170) | Ratio HD/healthy | P* |
|--------------------------------|-------------------------|-----------------------------|---------------------------|------------------|----|
| **Water-soluble uremic toxins**          |                         |                             |                           |                  |    |
| UA (mg/dL)                        | -                      | 7.36 [6.55; 8.93]          | 7.02 [5.80; 8.06]        | -                | .09|
| **Middle molecules**              |                         |                             |                           |                  |    |
| β2M (µL/mL)                      | 1.74 ± 0.34            | 9.92 [7.72; 15.4]          | 30.7 [4.4; 39.3]         | 17.6             | <.01|
| **Protein-bound uremic toxins**    |                         |                             |                           |                  |    |
| p-cresyl glucuronide             |                         |                             |                           |                  |    |
| Total levels (mg/dL)             | 0.01 ± 0.01            | 0.02 [0.01; 0.06]          | 0.15 [0.03; 0.33]        | 25.0             | <.01|
| Protein binding (%)              | 17 [0; 31]             | 18.6 [9.18; 23.1]          | 9.31 [5.24; 12.7]        | -                | <.01|
| Hippuric acid                    |                         |                             |                           |                  |    |
| Total levels (mg/dL)             | 0.04 ± 0.04            | 0.39 [0.13; 0.64]          | 1.89 [0.72; 3.43]        | 43.0             | <.01|
| Protein binding (%)              | 64 [53; 70]            | 62.8 [55.1; 66.4]          | 51.7 [45.7; 58.5]        | -                | <.01|
| Indole acetic acid               |                         |                             |                           |                  |    |
| Total levels (mg/dL)             | 0.02 ± 0.01            | 0.06 [0.04; 0.08]          | 0.18 [0.12; 0.27]        | 7.8              | <.01|
| Protein binding (%)              | 90 [88; 94]            | 87.1 [79.2; 89.2]          | 76.1 [69.2; 80.2]        | -                | <.01|
| Indoxyl sulfate                  |                         |                             |                           |                  |    |
| Total levels (mg/dL)             | 0.06 ± 0.03            | 0.56 [0.44; 0.73]          | 2.04 [1.37; 2.70]        | 36.4             | <.01|
| Protein binding (%)              | 94 [89; 99]            | 97.0 [94.9; 97.6]          | 94.5 [91.9; 95.6]        | -                | .02 |
| p-cresyl sulfate                 |                         |                             |                           |                  |    |
| Total levels (mg/dL)             | 0.24 ± 0.18            | 1.67 [0.93; 2.31]          | 2.35 [1.03; 3.27]        | 9.6              | .82 |
| Protein binding (%)              | 95 [91; 98]            | 97.4 [95.4; 97.7]          | 92.4 [88.4; 94.8]        | -                | .03 |
| 3-carboxy-4-methyl-5-propylfuranpropionic acid | |                  |                           |                  |    |
| Total levels (mg/dL)             | 0.01 ± 0.01            | 0.05 [0.02; 0.21]          | 0.12 [0.03; 0.33]        | 12.0             | .97 |
| Residual kidney function in HD | Non-anuric HD\(^\uparrow\) (n = 101) | Anuric HD\(^\uparrow\) (n = 69) | P* |
|-------------------------------|---------------------------------|---------------------------------|----|
| **Small water-soluble uremic toxins** | | | |
| UA (mg/dL) | 6.75 [5.78; 7.70] | 7.44 [6.06; 8.33] | .31 |
| **Middle molecules** | | | |
| β2M (µg/mL) | 29.0 [22.7; 36.8] | 32.4 [26.7; 46.0] | .01 |
| **Protein-bound uremic toxins** | | | |
| p-cresyl glucuronide | | | |
| Total levels (mg/dL) | 0.11 [0.03; 0.30] | 0.19 [0.07; 0.42] | .08 |
| Protein binding (%) | 9.58 [6.46; 13.6] | 7.83 [3.36; 12.3] | .56 |
| Hippuric acid | | | |
| Total levels (mg/dL) | 1.13 [0.57; 2.63] | 3.27 [1.84; 5.56] | <.01 |
| Protein binding (%) | 54.1 [48.9; 60.1] | 49.2 [44.0; 54.8] | .04 |
| Indole acetic acid | | | |
| Total levels (mg/dL) | 0.16 [0.11; 0.25] | 0.20 [0.14; 0.28] | .44 |
| Protein binding (%) | 76.5 [71.7; 81.4] | 72.7 [65.7; 78.3] | <.01 |
| Indoxyl sulfate | | | |
| Total levels (mg/dL) | 1.89 [1.09; 2.48] | 2.29 [1.77; 3.02] | .06 |
| Protein binding (%) | 94.7 [93.2; 96.7] | 93.4 [90.4; 95.4] | <.01 |
| p-cresyl sulfate | | | |
| Total levels (mg/dL) | 2.32 [0.92; 3.09] | 2.50 [1.05; 3.80] | .89 |
| Protein binding (%) | 93.5 [88.9; 95.4] | 91.3 [87.4; 94.0] | .12 |
| 3-carboxy-4-methyl-5-propyl-furanpropionic acid | | | |
| Total levels (mg/dL) | 0.08 [0.02; 0.19] | 0.18 [0.05; 0.44] | <.01 |
