Children's Hospital of Philadelphia

Hypernatremia and diaphoresis in two dialysis patients

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Case 1

A 19-month old male who presented with 2 days duration of diaphoresis.

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Past Medical history

- Prematurity at 35 weeks
- A single solitary pelvic dysplastic kidney with ESKD receiving chronic peritoneal dialysis;
- Pulmonary hypoplasia; tethered cord s/p release; umbilical hernia; GERD and G tube dependency.
- He has residual urine output and receives dialysis mainly for clearance.

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Case history-1

- Medications: Calcitriol, Calcium Carbonate, Epogen, Ferrous sulfate, Growth hormone, Bethanecol, Simethicone, Benadryl, Omeprazole
- PD prescription : All 1.5% low calcium (2.5 mmol/l) dialysate solution, low fill mode – 300 ml fill volume, 8 cycles, 8 hours.

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Case History -2

- Soaking of his cloths and sheets starting 1-2 days prior to admission with a single temperature of 99.9 F.
- Playful
- Decreased wet diapers
- Sleepier
- His PD fluid remained clear.

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Case History -3

- Vitals: HR 160, BP 90/50, Weight 8.18 kg (Dry weight 8.5kg), RR 30, SAT> 95%
- Nontoxic, well appearing, dry mucus membranes, abdomen soft nontender, reducible small umbilical hernia with normal PD catheter and G tube sites, lung and CV exam were WNL.

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Case History -4

- Labs: Cr-5.5 mg/dl, BUN-26mg/dl, **Na-154 mmol/l**, WBC-10.4K.
- PD fluid count: 107 WBC, 10% PMN no bacteria on the gram stain.
- PD fluid and blood cultures were obtained.

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What would be the differential for significant **diaphoresis** among a patient on peritoneal dialysis?

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Diaphoresis DDx

- Infection/sepsis (also if prolonged think of HIV, TB)
- Endocrine (hyperthyroidism; hypoglycemia; hormonal agents)
- Malignancy
- Pheochromocytoma; carcinoid
- Medication induced

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Case 2

A 3-year-old male with ESKD on hemodialysis (HD) presented over several months with multiple episodes of diaphoresis

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Past Medical History

- Autosomal recessive polycystic kidney disease s/p bilateral nephrectomies
- Hypotension and presumed dysautonomia
- Congenital hepatic fibrosis
- Pulmonary hypoplasia and associated chronic lung disease- tracheostomy dependence
- G-tube dependence, GERD
- Seizure disorder.

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- Medications : Calcitriol, Calcium carbonate, Epogen, Ferrous sulfate, Simethicone, Probiotics, Omeprazole, Bethanecol, Flovent, Albuterol, Keppra
- HD – 3 times a week MWF K-2/Ca-2.5 for 3 hours

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Case History-1

- Vitals: HR 139 bpm, BP 60/40 mmHg, Weight 13 kg (Dry weight 12kg), RR 22 breaths per minute, oxygen saturation> 95%.
- Nontoxic, well appearing, moist mucus membranes, abdomen soft and non tender with previous well healed surgical scars, tracheostomy site clean and intact, HD catheter site C/I

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Case History-2

- Creatinine -6.9 mg/dl, BUN-66mg/dl, serum **sodium-153 mmol/l**, WBC-17.4K. Blood cultures were obtained.

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- What would be the differential diagnosis for **hypernatremia** in a child on hemodialysis ?

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Hypernatremia DDx

- Dehydration (free water losses : skin, GI)
- Salt intoxication (oral vs intravenous)

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Case 1

- He received a 0.9% normal saline (NS) bolus of 10 ml/kg and then was initiated on a continuous infusion of D5 water (D5W). Given the concern for an infection he was initially treated with vancomycin and cefepime.

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Case 1

- Cultures negative
- TSH/TFTs normal
- Bethanecol, Benadryl held.
- Symptoms and hypernatremia resolved
- Benadryl resumed with no return of his symptoms.
- Discharged home off Bethanecol with a sodium of 137 mmol/l.

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Case 2

- Received a 0.9% NS bolus of 20 ml/kg.
- Vancomycin and cefepime were administered.
- Diaphoresis persisted throughout admission
- Cultures negative
- Repeated episodes of profuse diaphoresis prompting trial off Bethanecol with resolution of symptoms.

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Discussion

- The most common diagnosis for any dialysis patient presenting with both diaphoresis and hypernatremia is acute infection with increased insensible losses due to fevers.
- Our two patients had persistent symptoms despite adequate antimicrobial coverage without evidence of infection

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Bethanecol induced hypernatremia

- Muscarinic receptor cholinergic agonist :
  - non-obstructive urinary retention
  - decreased gastrointestinal motility
  - GERD
- Reported side effects : hypotension, diaphoresis, and diarrhea
- Primarily metabolized in the liver and renally excreted

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- No dosing guidelines for usage in the ESKD
- No data on dialysis clearance.
- Two prior reports describing Bethanecol toxicity in dialysis patients.

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Report 1

- 65 y/o male admitted with acute urinary obstruction and urinary retention and a Cr of 11.3 mg/dl. He underwent catheterization and Bethanecol was initiated. After four days of Bethanecol treatment he developed profuse sweating, hypersialorrhea, polydipsia, and hypernatremia (147mmol/l).
- **All signs and symptoms normalized after stopping Bethanecol**

Belmin J et al , Muscarinic poisoning induced by Bethanecol in renal insufficiency. Presse Med.1988 Feb 13;17(5):213. French

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Report 2

- 59-y/o female hemodialysis patient with diabetic nephropathy with residual renal function who developed urinary retention after an acute myocardial infarction. Bethanecol was initiated and over the next 2-3 days when she developed signs of muscarinic intoxication including profuse sweating, hypersialorrhea, and gastrointestinal distress. **Within 24 hours of discontinuing the Bethanecol her symptoms resolved**.

Renard E et al ,Acute muscarinic syndrome induced by Bethanecol in a diabetic woman with chronic kidney failure]. Presse Med. 1989 May 27;18(21):1080. French

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Summary

- Bethanecol – common used medication thought to be "**Benign"**
- Given these prior reports and our recent experience we would recommend avoiding this medication if at all possible in patients with ESKD.
- Any medications started in ESKD patients should be carefully considered.

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