

Clinical Case Conference: Acid-base disorders

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How do you “measure” renal new bicarbonate generation?

- Two things increase new bicarbonate generation, titratable acids and ammonia
- One thing decreases new bicarbonate generation, failure to reabsorb luminal bicarbonate
- Net acid excretion (NAE) = urinary titratable acids + urinary ammonia – urinary bicarbonate
 - $NAE = U_{TA}V + U_{Amm}V - U_{HCO_3}V$

Case 1

- A patient presents with metabolic acidosis with a pH 7.20, HCO_3^- 12 and pCO_2 32 mmHg.
- How can you tell if this is results from:
 - Renal failure to generate “new” bicarbonate, or
 - Bicarbonate losses from diarrhea?

Case 1 – Answer

- Major component of NAE (new bicarbonate formation) is:
 - Ammonia metabolism and excretion.
- Glutamine metabolism:
 - With urinary ammonia excretion
 - 1 mmol new HCO_3^- per mmol of ammonia excreted
 - Without urinary ammonia excretion
 - Glutamine converted to urea



Case 1 – answer

- How do you measure urinary ammonia?
 - Bad news ...
 - Lab can, but won't
 - Trick,
 - Urine doesn't cause lightning
 - Urinary cations = urinary anions
- Urinary cations – Na^+ , K^+ , and NH_4^+
- Urinary anions – Cl^- and HCO_3^-
 - If urine $\text{pH} \leq 6.5$, urinary HCO_3^- inconsequential
- Lab will measure urinary Na^+ , K^+ , and Cl^-
- If urinary $\text{Na}^+ + \text{K}^+ \approx \text{Cl}^-$, then minimal NH_4^+
 - Renal tubular acidosis
- If urinary $\text{Na}^+ + \text{K}^+ \gg \text{Cl}^-$, then substantial NH_4^+
 - Diarrhea



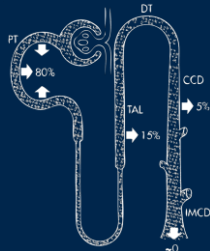
Case 2

- A 4 year-old child presents for “failure-to-thrive.” His serum bicarbonate is 12 mmol/L and K^+ is 2.8 mmol/L. His urine pH is 6.1, and the urine does not contain glucose or amino acids.
- What is the diagnosis?
 - Proximal RTA (renal tubular acidosis)



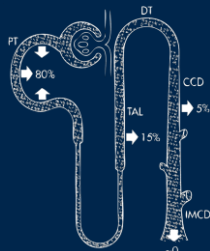
Proximal renal tubular acidosis (Type II)

- Proximal tubule unable to reabsorb normal amounts of filtered bicarbonate
- At normal serum bicarbonate, TAL and collecting duct unable to reabsorb all the bicarbonate that “escapes” the proximal tubule
- Alkaline urine and progressive urinary bicarbonate losses
- Eventually serum bicarbonate levels decrease, which decreases filtered bicarbonate



Proximal renal tubular acidosis (Type II)

- With decreased filtered bicarbonate, proximal tubule able to reabsorb “enough” bicarbonate
- When bicarbonate delivered to TAL and collecting duct normal the collecting duct is able to acidify the urine
- Key features:
 - Alkaline urine pH when serum bicarbonate normal
 - Acid urine pH when serum bicarbonate low



Case 2

- A 4 year-old child has “failure-to-thrive.” His serum bicarbonate is 12 mmol/L and K^+ is 2.8 mmol/L. His urine pH is 6.1, and the urine does not contain glucose or amino acids.
- What is the diagnosis?
 - Proximal RTA
- Why is he not growing normally?

Metabolic acidosis and the skeleton

- Substantial alkali load in skeleton as alkali salts
- Metabolic acidosis
 - Stimulates osteoclast bone resorption
 - Inhibits osteoblast bone formation



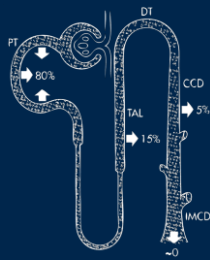
Case 2

- A 4 year-old child has “failure-to-thrive.” His serum bicarbonate is 12 mmol/L and K^+ is 2.8 mmol/L. His urine pH is 6.1, and the urine does not contain glucose or amino acids.
 - What is the diagnosis?
 - Why is he not growing normally?
 - Why is his serum K^+ low?



Proximal RTA and potassium

- Bicarbonate excreted in urine must be balanced by cation
 - Na^+ or K^+
 - Initially both lost
 - With Na^+ depletion comes intravascular volume depletion
 - Stimulation of aldosterone release
 - Stimulation of principal cell-mediated Na^+ reabsorption and K^+ secretion
 - Eventually substantial total body K^+ losses, and hypokalemia



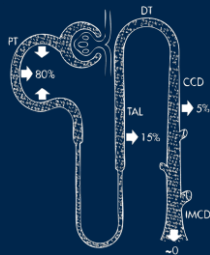
Case 2

- A 4 year-old child has "failure-to-thrive." His serum bicarbonate is 12 mmol/L and K^+ is 2.8 mmol/L. His urine pH is 6.1, and the urine does not contain glucose or amino acids.
 - What is the diagnosis?
 - Why is he not growing normally?
 - Why is his serum K^+ low?
 - What will happen to his urine pH if you give him oral alkali therapy?



Therapy of proximal RTA

- Alkali therapy raises serum bicarbonate
 - Raises filtered bicarbonate
 - Above level that proximal tubule can transport
 - Excessive bicarbonate delivery to TAL and collecting duct
 - Urinary bicarbonate losses
 - Alkaline urine



Case 2

- A 4 year-old child has "failure-to-thrive." His serum bicarbonate is 12 mmol/L and K^+ is 2.8 mmol/L. His urine pH is 6.1, and the urine does not contain glucose or amino acids.
 - What is the diagnosis?
 - Why is he not growing normally?
 - Why is his serum K^+ low?
 - What will happen to his urine pH if you give him oral alkali therapy?
 - Will he/she need a little (~1 mmol/kg/d) or lot (10-15 mmol/kg/d) of oral alkali therapy?



Therapy of proximal RTA

- As serum bicarbonate increases, urinary bicarbonate losses increase
- Need 10-15 mmol/kg/d
 - Replace bicarbonate deficit
 - Replace ongoing, and worsening, urinary bicarbonate losses
 - 50% as Na⁺ salt and 50% as K⁺ salt

Case 3

- 23 yo ♂ presents with chief complaint of "I keep having kidney stones and they hurt!!!!"
- Laboratory studies show acidemia with primary metabolic acidosis
- [HCO₃⁻] is 4 mmol/L, [K⁺] is 2.1 mmol/L, and urine pH is 7.5
- What is the diagnosis?

Case 3

- Key data: acidemic with metabolic acidosis but alkaline urine
- Where does urine pH decrease?
- Collecting duct
 - Distal renal tubular acidosis (type I)

Case 3

- 23 yo ♂ presents with chief complaint of "I keep having kidney stones and they hurt!!!!"
- Laboratory studies show acidemia with primary metabolic acidosis
- $[HCO_3^-]$ is 4 mmol/L, $[K^+]$ is 2.1 mmol/L, and urine pH is 7.5
- Why is the acidosis so much worse than the last case?

Case 3

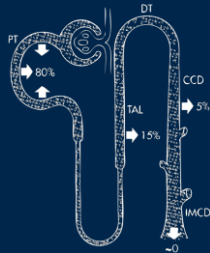
- 23 yo ♂ presents with chief complaint of "I keep having kidney stones and they hurt!!!!"
- Laboratory studies show acidemia with primary metabolic acidosis
- Why is the acidosis so much worse than the last case?
 - Ongoing renal HCO_3^- losses, plus inability to generate titratable acids and to excrete ammonia

Case 3

- 23 yo ♂ presents with chief complaint of "I keep having kidney stones and they hurt!!!!"
- Laboratory studies show acidemia with primary metabolic acidosis
- Why is K^+ low?
 - Ongoing renal HCO_3^- losses need to be balanced by cation excretion

Case 3

- 23 yo ♂ presents with chief complaint of "I keep having kidney stones and they hurt!!!!"
- Diagnosis: Distal RTA
- Distal RTA causes kidney stones, but proximal RTA does not. Why?
 - Both cause Ca^{2+} salt resorption from bone, excreted in urine
 - Ca-PO_4 solubility is pH-dependent.
 - ↓ when U_{pH} is high
 - ↑ when U_{pH} is low

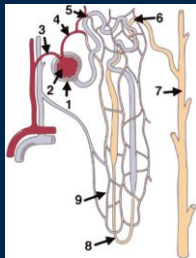


Case 4

- 64 year old with diabetes mellitus, chronic kidney disease is acidemic with a primary metabolic acidosis
 - The patient has osteoporosis, so you are worried
 - Evaluation shows the serum $[\text{K}^+]$ is 6.1 mmol/L (normal is 4-5.5)
 - Urine pH is 5.8
- Why does your patient have metabolic acidosis and what should you do to treat him/her?

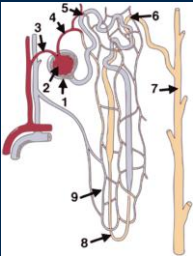
Case 4 - answer

- Serum K^+ regulates renal ammonia metabolism
- Why?
 - Long-term serum K^+ is regulated by renal K^+ excretion
 - Occurs in collecting duct
 - How does the collecting duct "know" what the serum K^+ is?



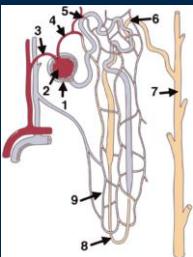
Case 4 - answer

- Serum K^+ regulates renal ammonia metabolism
- Hypokalemia:
 - Increases proximal tubule ammonia production
 - Increases ammonia reabsorption in TAL
- Ammonia regulates collecting duct K^+ transport
 - Inhibits K^+ secretion
 - Stimulates $H^+-K^+-ATPase$



Case 4 - answer

- Serum K^+ regulates renal ammonia metabolism
- Hyperkalemia
 - Inhibits renal ammonia metabolism
 - Decreases ammonia-mediated "new" bicarbonate generation
 - Causes metabolic acidosis



Case 4

- 64 year old with diabetes mellitus, chronic kidney disease is acidemic with a primary metabolic acidosis
 - The patient has osteoporosis, so you are worried
 - Evaluation shows the serum $[K^+]$ is 6.1 mmol/L (normal is 4-5.5)
 - Urine pH is 5.8
- Why does your patient have metabolic acidosis?
 - Hyperkalemia, resulting from diabetes mellitus and chronic kidney disease
 - Decreases renal ammonia excretion
 - Decreases net acid excretion
 - Results in chronic metabolic acidosis
- What should you do to treat him/her?
 - Treat the hyperkalemia
 - Diuretics as first-line therapy

