Type 2 Renal Tubular Acidosis

PLAY PICMONIC

Proximal Tubule
P-Rocks Tube
The proximal convoluted tubule is the portion of the nephron between the Bowman capsule and the loop of Henle. In this portion, there is reabsorption of solutes including electrolytes, glucose, amino acids, urea, phosphate, and citrate. In this portion bicarbonate is reabsorbed into the renal tissue and protons are secreted into the filtrate. In renal tubular acidosis type 2, there is a defect in bicarbonate reabsorption in this portion of the nephron.

Pathophysiology

Inability To Reabsorb Bicarbonate
Trapped Bi-Car-Bomb
In RTA type 2 there is an inability of the proximal convoluted tubule cells to reabsorb bicarbonate. Normally, most of the filtered bicarbonate (80-90%) is reabsorbed in the proximal tubule, and the rest is reabsorbed by the intercalated cells of the distal tubule and collecting ducts. Therefore a defect in bicarbonate reabsorption at the level of the proximal tubule leads to significant bicarbonaturia.

ETIOLOGY

Fanconi Syndrome
Fan-Kidney
Fanconi syndrome is a disease of the kidney where a resorption defect in the proximal tubule causes various substrates and electrolytes to be excreted in the urine, such as amino acids, glucose, bicarbonate, and phosphate. It has multiple causes including hereditary causes (cystinosis, Dent's disease, galactosemia) and acquired causes (multiple myeloma, certain drugs). Since it involves impaired reabsorption of bicarbonate, it is a cause or RTA type 2.

Sporadic Type
Sporadic-Spear
Sporadic or idiopathic type 2 RTA usually presents as isolated proximal RTA which means that only bicarbonate reabsorption is impaired. In children, sporadic RTA, ifosfamide therapy (a chemotherapeutic agent) and cystinosis (an inherited disorder that causes Fanconi syndrome) are the most common causes of proximal RTA.

Familial Types
Familial-Family
Isolated proximal RTA can be due to inherited defects in genes involved in the synthesis of transmembrane transporters responsible for proximal acidification. The most common inherited defect is a mutation in the gene SLC4A4 that directs the synthesis of NBCe1, the basolateral sodium bicarbonate transporter. The inheritance pattern of this defect is autosomal recessive which means that to get the disease, the individual must have two copies of the defective gene.

Autosomal Recessive
Recessive-chocolate
The most common inherited defect is the mutation in the gene SLC4A4 that directs the synthesis of NBCe1, the basolateral sodium bicarbonate transporter. This results in autosomal recessive proximal RTA with short stature and ocular abnormalities.

Acetazolamide

A Cheetah-Zorro

Acetazolamide is a carbonic anhydrase inhibitor used to treat altitude sickness, pseudotumor cerebri, glaucoma, among others (refer to Acetazolamide Picmonic for more). Acetazolamide works by inhibiting carbonic anhydrase in the proximal tubule, impairing proximal bicarbonate reabsorption. This impaired reabsorption does not affect the reabsorption of other proximal tubule solutes. Bicarbonate absorption by the proximal tubule is dependent on the activity of carbonic anhydrase which converts bicarbonate to carbon dioxide and water. Therefore its inhibition results in an increased urinary loss of bicarbonate. Another carbonic anhydrase inhibitor that may cause RTA type 2 is topiramate, an anticonvulsant drug.

Characteristics

Decreased Urinary pH

Down-Arrow pH Scale and Urine

In type 2 RTA urine pH is variable but as a general rule, when there have been ongoing losses of bicarbonate, the urinary pH will be low or <5.5. Urine pH can be greater than 5.5 if plasma bicarbonate concentration is normal and serum bicarbonate levels exceed the proximal tubule's reabsorptive threshold. If plasma bicarbonate concentration is already depleted as a result of the ongoing losses, urine pH is <5.5 indicating that bicarbonate is reduced to levels that can be reabsorbed despite defective proximal tubule reabsorption. Therefore, at initial stages, urine pH may be elevated but when there have already been losses of bicarbonate, urine pH is expected to be low.

Hypokalemia

Hippo-banana

Patients with RTA type 2 may present with hypokalemia or low levels of serum potassium due to increased urinary potassium wasting. In RTA type 2 there is an increased rate of urine flow to the distal nephron due to the distal delivery of bicarbonate ions. This increased urinary flow to the distal nephron causes increased urinary potassium wasting. Increased sodium bicarbonate and water delivery to the distal tubule stimulates potassium secretion, which explains potassium wasting in RTA type 2.

Treatments

Treat Underlying Disorder

Underlying Diseased-Guy

Management of proximal RTA depends on the underlying cause. If there is a drug causing the bicarbonate reabsorption impairment, suspension of it must be considered. Patients with Fanconi Syndrome require monitoring for electrolytes abnormalities and correction of phosphate levels in addition to potassium and bicarbonate. In contrast isolated proximal RTA, such as the familial forms and the sporadic form, is not associated with hypophosphatemia and vitamin D deficiency, and therefore there is no need to administer phosphate or vitamin D supplements. In general, in all types, the treatment aims to correct metabolic acidosis and hypokalemia. For correcting the metabolic acidosis the goal of therapy is to achieve a normal serum bicarbonate concentration (between 22 to 24 mEq/L) using alkali therapy.

Alkali Therapy

Elk

For correcting the metabolic acidosis the goal of therapy is to achieve a normal serum bicarbonate concentration (between 22 to 24 mEq/L) using alkali therapy. Alkali is given in divided doses to overcome urinary bicarbonate losses and raise serum levels. The bicarbonaturia generated by the alkali therapy also increases urinary potassium losses so part of the alkali replacement must be given as a potassium salt such as potassium citrate.