Distal Renal Tubular Acidosis (Type I)



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Pathophysiology

Distal Tube
Disco-tube
The distal tubule is the segment of the nephron located between the ascending loop of Henle and the connecting tubule and collecting duct. Type I renal tubular acidosis is due to the inability of the intercalated cells of the distal tubule to secrete H+.

Defect in H+ Secretion
Defective hydrogen-pump
RTA type I is due to the Inability of ?-intercalated cells to secrete H+, no new bicarbonate (HCO3-) is generated leading to metabolic acidosis. The alpha intercalated cells are a type of epithelial cell found in the late distal convoluted tubule and are responsible for secreting protons (H+) into the urine through H+ ATPase and through H+/K+ ATPase. The buildup of hydrogen in those cells leads to a buildup of hydrogen in the blood and to acidosis. Remember that bicarbonate (HCO3-) reabsoprtion occurs primarily, 80-90%, in the proximal tubules. In RTA type I HCO3? reabsorption is mostly quantitatively normal; however, as a consequence of the elevated urine pH, a certain degree of bicarbonaturia may be obligatorily present (<5% of the filtered load). The beta intercalated cells are the cells in charge of HCO3- secretion.

Labs

Increased Urinary pH
Up-arrow pH scale and urine
Since there is a defect in renal secretion of H+, the urinary pH is elevated.

Urinary pH >5.5
2 High 5 hands in the air with dot in the middle
In type I RTA urine pH is >5.5. This is due to impaired distal acidification and is characterized by the inability to lower urinary pH maximally (<5.5) under the stimulus of systemic acidemia.

Hypokalemia
Hippo-banana
In type I RTA the serum K+ is decreased. Hypokalemia occurs because of renal potassium wasting as a result of impaired hydrogen secretion. The most common form of RTA type I is due to selective failure of activity of the H+ ATPase. leading to urine acidification and a reduction in the electrical dissipation of the membrane potential. This alteration in membrane potential has been thought to be a driving force for potassium secretion and eventual potassium wasting.

Causes

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Amphotericin B Toxicity

Amphibian-terminator-bee

Impaired renal function is a relatively common complication of amphotericin B, including urinary potassium wasting and hypokalemia, urinary magnesium wasting and hypomagnesemia, and metabolic acidosis due to RTA type 1. This is reversible with the suspension of the drug. The mechanism of RTA type I induced by amphotericin is due to an increase in membrane permeability caused by the drug which results in the reduction of ion concentration gradients between the cytoplasm of distal tubule cells and the tubule lumen. In this context, potassium leaks from the cytoplasm down a favorable concentration gradient into the lumen (causing hypokalemia due to increased urinary loss) and hydrogen ions diffuse down their gradient from the lumen into the cytoplasm of distal tubule cells. Therefore it can be said that the defect in acid excretion induced by amphotericin b is due to back-diffusion of secreted hydrogen ions.

Autoimmune Disease

Auto-in-moon

The mechanism of RTA type I in autoimmune diseases is mainly due to autoantibodies against the transporters in the intercalated cells. For example, in primary Sjogren's syndrome, renal involvement is one of the extraglandular manifestations and in most cases, it affects the renal tubules through tubular interstitial nephritis and occasionally autoantibodies against a certain transporter. All segments of the nephron can be involved but distal RTA is the most frequent tubular dysfunction in Sjogren's syndrome. A similar mechanism is involved in other autoimmune diseases.

Lithium

Lithium-Battery

Drugs causing type I RTA include: lithium, amphotericin B, NSAIDs, Ifosfamide. The mechanism of RTA type I induced by lithium is similar to the mechanism mentioned for amphotericin b. It is possible that lithium administration induces distal renal tubular acidosis by allowing excessive back-diffusion of acid.

Obstruction Of The Urinary Tract

Obstructed kidney with tuba

In obstructive uropathy, there has been shown to be a transport defect in the distal nephron, characterized by impaired sodium reabsorption and decreased secretion of hydrogen and potassium leading to distal tubular acidosis. Note that in obstructive uropathy there would be hyperkalemia and not hypokalemia. In the other causes of RTA type I there is hypokalemia.

Complication

Kidney Stones

Kidney-throwing Stones

Calcium stones are formed because calcium tends to precipitate in an alkaline solution. Other factors contribute to calcium stone formations such as reduced urinary citrate since acidemia enhances proximal citrate reabsorption. Additionally, the acidemia present in RTA causes increased calcium phosphate release from bone during bone buffering of retained acid. This increased bone turnover is also associated with an increased risk of calcium stones. Calcium phosphate stones may be seen bilaterally and this should raise suspicion for RTA type I. Patients with recurrent calcium stones (particularly calcium phosphate stones) and a urine pH that is persistently 5.5 or higher should be evaluated for distal RTA.

Treatment

Bicarbonate

Bi-car-bombs

Treatment consists of correcting metabolic acidosis with Alkali therapy with sodium bicarbonate or sodium citrate (Shohl's solution). If hypokalemia persists despite the correction of the acidosis, serum bicarbonate potassium citrate alone or combined with sodium citrate is indicated.

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