

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 electrolyte 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.