Gitelman Syndrome

PLAY PICMONIC

Pathophysiology

Autosomal Recessive

Recessive-chocolate

Gitelman syndrome is typically inherited in an autosomal recessive pattern as a result of mutations in genes coding for thiazide-sensitive sodium-chloride cotransport (NCC) channels in the distal tubule.

Defective Sodium-Chloride Cotransporter in Distal Tubule

Bouncer blocking Na-CL salt shaker from entering

The underlying mechanism in Gitelman syndrome is caused by defective sodium-chloride cotransport channels in the distal tubule. This defect leads to decreased absorption of sodium and chloride, as well as water, leading to volume loss. This volume loss then leads to subsequent compensation by the renin-angiotensin-aldosterone system, leading to several of the electrolyte abnormalities seen in Gitelman syndrome.

Mechanism Mimics Thiazide Diuretics

Tarzan-die-rocket

Gitelman syndrome is thought to be caused by defective sodium-chloride cotransporters. This mimics the mechanism of thiazide diuretics, which reduce blood pressure by inhibiting these same cotransporters and therefore decreasing absorption of free water.

Clinical Presentation

Cramping and Tetany

Clamps-titanic

The subjective symptoms of Gitelman syndrome are variable and often non-specific. One of the most common symptoms is cramping and tetany. This is caused by the hypokalemia and hypomagnesemia characteristic of Gitelman syndrome.

Severe Fatigue

Sleepy guy

Severe fatigue may also be seen in Gitelman syndrome. This is seen as a result of electrolyte abnormalities as well as volume loss and resulting decreased blood pressure.

Polyuria

Polly-urinates

Polyuria is commonly seen in Gitelman syndrome as a result of the diuretic-like effect caused by defective sodium-chloride cotransporters, which mimics the effect of thiazide diuretics. This results in decreased sodium absorption at the distal tubule, leading subsequently to decreased absorption of water, which is then lost in the urine.

Diagnosis

Hypokalemia

Hippo-banana

Hypokalemia is seen in Gitelman syndrome as a result of increased action of the renin-angiotensin-aldosterone system (RAAS). Recall that aldosterone acts in the collecting ducts to cause absorption of sodium in exchange for excretion of potassium. It does so by increasing action of the basolateral sodium-potassium exchange pumps and by increasing expression of ENaC and ROMK channels, which absorb sodium and excrete potassium respectively. In Gitelman syndrome, aldosterone is increased in order to compensate for volume loss, leading to increased action at the sodium-potassium exchange, thereby decreasing serum potassium.

Metabolic Alkalosis

Metal-ball Elk-loser

Metabolic alkalosis is commonly seen in Gitelman syndrome as a result of volume contraction caused by increased action of the renin-angiotensin-aldosterone system. Recall that one of the actions of aldosterone is to increase action of the H+/ATPase in the intercalated cells of the collecting duct. Therefore increased aldosterone as compensation for volume loss leads to increased excretion of H+ in the urine.

High Urine Chloride

up-arrow-chlorine-urine

High urine chloride is a characteristic finding seen in Gitelman syndrome. This is important in parsing out Gitelman syndrome from other potential causes of metabolic alkalosis, such as primary hyper-aldosteronism, in which urine chloride excretion is low. Of note, thiazide diuretics can also cause increased urine chloride excretion, however this should already have been made obvious when taking a patient's history if they are taking thiazide diuretics.

Treatment

Electrolyte Supplements

electric lights

All patients with Gitelman syndrome should be treated with supplements for electrolytes that may be depleted, namely potassium, magnesium (when hypomagnesemia is present), and sodium-chloride to promote volume retention.

Spironolactone

Spiral-of-milk

Spironolactone (or any potassium-sparing diuretic) is often used in the treatment of Gitelman syndrome. It aids in treatment by blocking many of the actions of aldosterone that lead to the electrolyte abnormalities seen in Gitelman syndrome.