Diuretics: MOA, Types, Uses, Side Effects and more

Diuretics are among the most commonly used antihypertensive medications They are classified into three main classes. In this article, we shall be looking at each class, their mode of action, examples and specific indications.

Diuretics are drugs causing a net loss of sodium and water in urine.

How do they work?

Diuretics initially work on the kidneys by increasing diuresis (water loss) and depletion of sodium and body fluid volume. This decrease in body fluids causes a decrease in cardiac output. Subsequently, after 4 to 6 weeks, sodium balance and cardiac output is regained by 95%, but blood pressure remains low!

Maybe you are asking yourself Why?

The Answer is: Reduction in total peripheral resistance (TPR) due to a deficit or little amount of sodium ions and water causes vascular stiffness. A similar effect is seen with sodium restriction (low sodium diet).

These drugs are classified to:

- 1. Thiazides
- 2. Potassium-sparing
- 3. Loop Diuretics

Potassium Sparing

Potassium Sparing include: Spironolactone, Amiloride, Triamterene

They are called K+-sparing diuretics because they do not produce hypokalemia like the loop and thiazide diuretics.

By inhibiting aldosterone-sensitive sodium reabsorption, fewer potassium ions and hydrogen ion are exchanged for sodium ions by this transporter mechanism and therefore fewer potassium ions and hydrogen are lost to the urine.

Other K-sparing diuretics work by inhibiting Na channels associated with the aldosterone-sensitive sodium pump.

Their mechanism depends on renal prostaglandin production. Because this class of diuretic has relatively weak effects on overall sodium balance, they are often used in conjunction with thiazide or loop diuretics to help prevent hypokalemia.

Thiazides

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Thiazides include Hydrochlorothiazide, Chlorthalidone, Metolazone, Indapamide.

Thiazides exert their effects by inhibiting the sodium-chloride transporter in the distal renal tubule. Because the sodium-chloride transporter only reabsorbs about five percent of filtered sodium, thiazides are less effective than loop diuretics in producing diuresis and natriuresis(sodium loss in the urine).

Because loop and thiazide diuretics increase Na transport into the distal renal tubule, this increases potassium loss because the stimulation of aldosterone-sensitive sodium pump making it increase sodium reabsorption. In exchange, potassium and hydrogen ion are lost to the urine.

The increased hydrogen ion loss can lead to metabolic alkalosis. Part of the loss of potassium and hydrogen ion by loop and thiazide diuretics results from activation of the <u>renin-angiotensin-aldosterone system</u> that occurs because of reduced blood volume and arterial pressure. Increased aldosterone hormone levels stimulate Na reabsorption and increase urinary potassium and hydrogen loss.

Loop diuretics

Loop diuretics include : Furosemide ,Bumetanide ,Torsemide

Loop diuretics inhibit the sodium-potassium-chloride cotransporter in the thick ascending limb. Sodium potassium chloride transporter reabsorbs about 25% of the sodium load in a normal person with normal functioning kidneys; therefore, inhibiting this pump can cause a significant increase in the distal tubular concentration of Na, reduced hypertonicity of the surrounding interstitium, and less water reabsorption in the collecting duct of the nephron.

This disturbed sodium and water handling lead to both diuresis and natriuresis. Loop diuretics are very powerful diuretics and the reason for this is by the fact that they act on the thick ascending loop of Henle. This ascending limb handles a significant fraction of sodium reabsorption.

Loop diuretics are known to induce renal synthesis of prostaglandins. This contributes to their renal action including the increase in kidney blood flow and redistribution of blood flow to the renal cortex.

Specific Indications.

Apart from hypertension, These drugs are also indicated for:

- Congestive heart failure,
- Edematous states,
- African-American patients;
- And obviously, sometimes they are used because they are the least expensive.

Major Side Effects associated are.

- Decreases in potassium (Sudden cardiac death torsades de pointes),
- Decreased magnesium;
- · Increases in calcium,

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- Increased uric acid levels (Hyperuricemia: inhibition of urate excretion),
- Increased glucose levels-Inhibition of insulin release due to K+ depletion (proinsulin to insulin) precipitating <u>diabetes</u>
- Increases LDL-cholesterol;
- Gynecomastia.

Relative Contraindications.

- Contraindicated in <u>Diabetes</u>,... You know why? Let us know in the comment section below
- Gout,
- Hyperlipidemia.-rise in total LDL level increases the risk of stroke.

JNC recommendation on diuretics:

JNC recommends a low dose of thiazide therapy (12.5 - 25 mg per day) in essential hypertension. Preferably these thiazides should be used with a potassium-sparing diuretic as the first choice in old patients.

If therapy fails, introduce another antihypertensive but does not increase the dose of thiazide diuretics.

Loop diuretics are prescribed in severe hypertension associated with body fluid retention.