

Diuretics

Chandan Shrestha, PhD

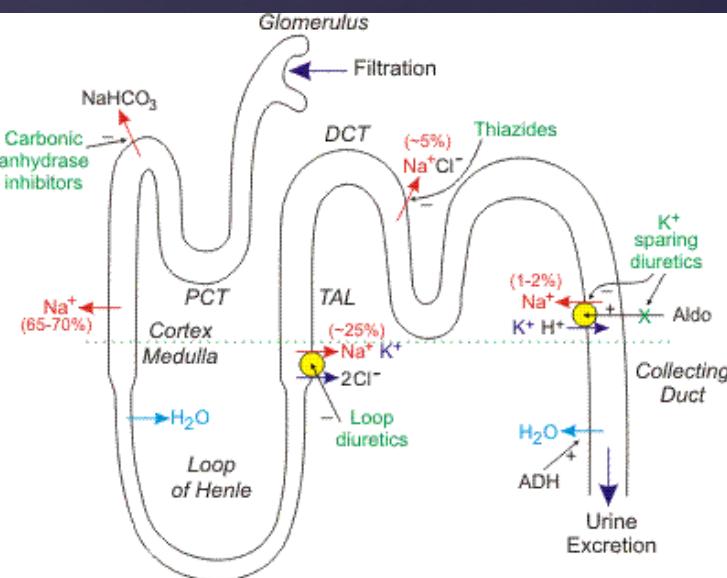
Introduction

- Diuretics are drugs which increase sodium and water excretion by the kidney.
- "diuresis" means increased urine flow
- "natriuresis" means increased urinary sodium excretion
- Management of hypertension
- Edema

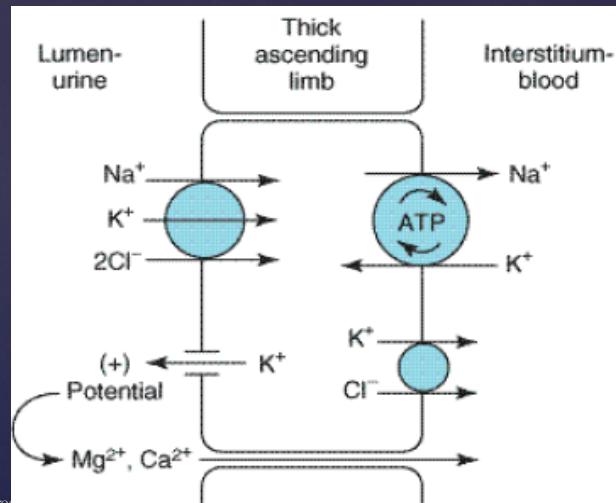
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Diuretics Drugs

1. Thiazide and thiazide-like diuretics: hydrochlorothiazide, chlorthalidone Indapamide
2. Loop diuretics or the high ceiling diuretics: furosemide, torsemide, bumetamide, ethacrynic acid
3. K⁺ sparing
 - Na channel inhibitors: amiloride, triamterene
 - Aldosterone receptor antagonists: spironolactone, eplerenone
4. Osmotic diuretics: mannitol, glycerine, isosorbide
5. Carbonic anhydrase inhibitors: acetazolamide



Loop Diuretics



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High Ceiling (Loop) Diuretics Furosemide

- Act on thick ascending limb of the loop of Henle
- Inhibits $\text{Na}^+-\text{K}^+-\text{Cl}^-$ transporter thus prevents the reabsorption of Na^+
- Inhibits the reabsorption of Ca^{++} and Mg^{++}
- Increases the excretion of Na^+ , Cl^- , K^+ , H_2O , Ca^{++} and Mg^{++}
- Maximal natriuretic effect than others

Clinical Indication

1. Edema
2. HTN
3. Forced Diuresis
4. Hyperkalemia
5. Acute Renal Failure

High Ceiling (Loop) Diuretics

Furosemide

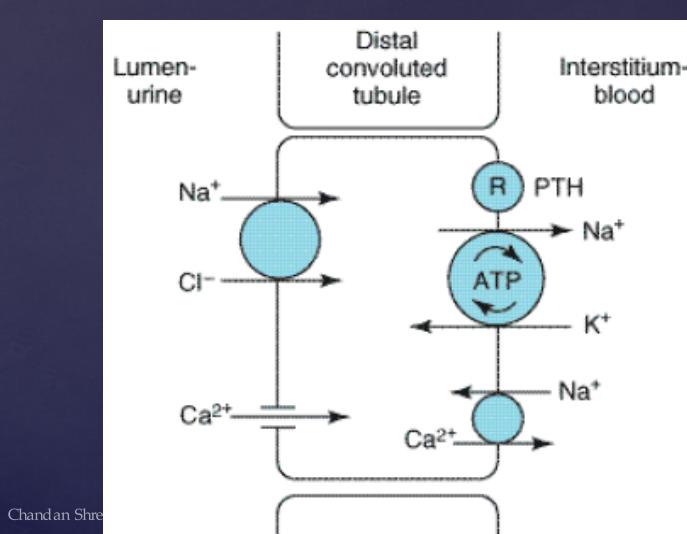
A/E

- Hypokalemic metabolic alkalosis (increased excretion of K^+)
- Hyponatremia, Hypomagnesemia
- Hyperuricemia (compete with uric acid secretion)
- Ototoxicity
- Allergic reactions (sulfonamide derivatives)

C/I

- Cross reactivity in patients who are sensitive to sulfonamide
- Overzealous use of any diuretics is danger in Hepatic cirrhosis, borderline renal failure or heart failure
- Concurrent use of lithium

Thiazide like diuretics



Thiazides

Hydrochlorothiazide

- Act on distal convoluted tubules
- Inhibits $\text{Na}^+ - \text{Cl}^-$ transporter thus prevents the reabsorption of Na^+
- Increases the excretion of Na^+ , Cl^- , K^+ and H_2O
- Long term use: increase excretion of Mg^{++} but decreases Ca^{++}

Clinical Indication

1. HTN
2. Heart Failure
3. Nephrolithiasis due to idiopathic hypercalciuria
4. Diabetes insipidus
5. Edema

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Thiazides

Hydrochlorothiazide

A/E

- Hypokalemic Metabolic Alkalosis
- Hyperuricemia
- Hyperlipidemia and hyperglycaemia
- Hypercalcemia
- Hyponatremia
- Allergic reaction
- Others: weakness, fatigability and paresthesias

C/I

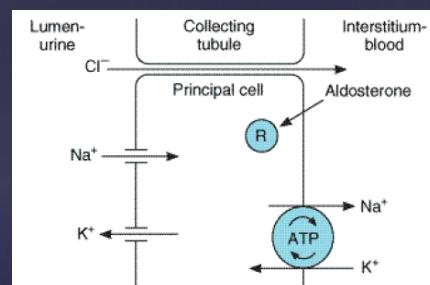
- Excessive use of any diuretics is dangerous in Hepatic cirrhosis, borderline Renal failure or heart failure

Diuretics:

- Prevents Na^+ reabsorption either by inhibiting enzymes or transporter
- increases the urine volume; thereby decreasing blood volume.
- Promoting the excretion of K^+
- Hypokalemia (Muscle weakness, paralysis; sudden risk of HF)

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Potassium sparing Drugs



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Potassium Sparing Drugs

- Decrease the reabsorption of Na^+ but prevent excretion of K^+ .
- Used in combination with other diuretics.
- Act on Late distal convoluted tubules and collecting duct.

Types

1. Aldosterone Antagonist
2. Epithelial Na^+ channel (ENaC) blocker

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Aldosterone Antagonist Spironolactone

Aldosterone

- Steroid hormone Secreted by Adrenal gland
- Aldosterone binds with its receptor (inside the cell) → increases the synthesis Na^+ channel and Na^+/K^+ ATPase transporter → Promote the reabsorption of Na^+ but K^+ secretion
- **Spironolactone** binds to aldosterone receptor and prevents binding of aldosterone to its receptor and thus inhibit the action of aldosterone on principal cells → decrease the expression of the transporter → decreases Na uptake and K loss from the tubular cells.
- Loss of Na in the urine leads to mild diuresis.
- Eplerenone (^{Chandan Shrestha, PhD} greater selectivity)

ENaC blocker Amiloride and Triamterene

- Non steroid
- Do not block aldosterone receptor but inhibit epithelial Na channel at late DT and CD.
- decreases Na uptake and K loss from the tubular cells.
- Loss of Na in the urine leads to mild diuresis.
- Amiloride is more potent than Triamterene

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Potassium Sparing Drugs

Clinical Indication

- Edema
- HTN
- Hypokalemia
- CHF

A/E

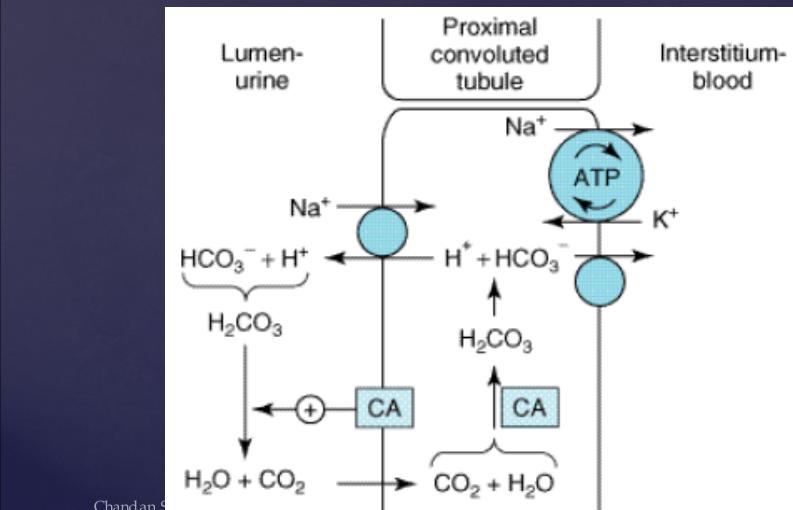
- Hyperkalemia
- Gynaecomastia
- Acidosis

C/I

Chronic renal insufficiency

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Carbonic anhydrase inhibitors



Carbonic Anhydrase inhibitors Acetazolamide

- Act on proximal convoluted tubules.
- Carbonic anhydrase is the enzymes involved in the breakdown of carbonic acid; critical step in the reabsorption of bicarbonate.
- By blocking CA, inhibitors block sodium bicarbonate reabsorption and cause diuresis.

Clinical Indication

1. Glaucoma (\downarrow aqueous humor formation $\rightarrow \downarrow$ IOP)
2. Mountain sickness (Weakness, dizziness, insomnia, headache and nausea $> 3000\text{m}$)
3. Urinary Alkalization (promote the excretion of acidic drug)
4. Epilepsy
5. Periodic paralysis

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Carbonic Acid inhibitors

Acetazolamide

A/E

- Renal Stones
- Renal Potassium Wasting
- Hypercholeremic Metabolic Acidosis
- *Others:* Drowsiness and paresthesias
hypersensitivity reactions (sulfonamide derivatives: fever, rashes)

C/I

Cirrhosis (due to hyperammonia and hepatic encephalopathy)

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Administration: orally

Osmotic Diuretics

Mannitol

- Act at proximal convoluted tubules and descending loop of henle.
- filtered through the glomerulus but cannot be reabsorbed → increases the osmolality of the filtrate → water is retained in the tubules.
- Increase the excretion of sodium, potassium, Chloride, magnesium, bicarbonate and hydrogen phosphate and water.

Clinical Indication

- To increase urine volume
- To reduce intracranial and intraocular pressure

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Osmotic Diuretics Mannitol

A/E

- Extracellular Volume Expansion
- Dehydration and **Hyponatremia**

C/I

- Acute tubular necrosis
- Pulmonary Edema
- CHF
- Acute left ventricular failure

Administration

- Chandan Shrestha, PhD
- i.v. as 10 -20% solution (Not absorbed orally)

Nursing Consideration

Dehydration and electrolyte imbalance

- Monitor serum electrolyte (K^+)
- Maintain I/O

Administer drug in the morning