King Saud University
College of Medicine
1st Year, 5th Block

Potassium Sparing Diuretics 5

Renal Block

Objectives :

1	Understand sites of action of potassium sparing diuretics on nephron.
2	know molecular target of actions of potassium sparing diuretics.
3	Understand the pharmacokinetics and pharmacodynamics of potassium sparing diuretics.
4	Discuss the clinical applications of potassium sparing diuretics.
5	Know what are the major adverse effects of potassium sparing diuretics.

Classification of K-sparing diuretics

Steroids

"Aldosterone antagonists"
e.g. Spironolactone (mimic the structures of aldestrone)

Non-steroids

"Na^+ channels inhibitors" (in DCT and collecting duct.)
e.g. Amiloride, Triamterene

Potassium-Sparing Diuretics

Mechanism of Action

Act in collecting tubules and ducts by inhibiting Na re-absorption and K & H excretion **(K-sparing effect)** by either:

- Inhibition of Na influx through Na channels in the luminal membrane (**triamterene** – **amiloride**).
- **Spironolactone**: by antagonizing cytoplasmic aldosterone receptors.

Pharmaco-dynamics

↑ urinary Na+ excretion
↓ urinary K+ excretion **Hyperkalemia**.
↓ H+ excretion (**acidosis**).

Therapeutic Uses

- Drug of choice for patients with hepatic cirrhosis "they have elevated aldestrone --> increase in ECF --> decrease in oncotic pressure --> ascites --> they will have hypovolemia --> activation of RAAS --> worsening of edema"
- Secondary hyperaldosteronism. (CHF, hepatic cirrhosis, nephrotic syndrome)
- Treatment of hypertension (combined with thiazide or loop diuretics to correct for hypokalemia).

Adverse Effects

- Hyperkalaemia.
- Metabolic acidosis.
- Gynaecomastia "because the testosterone has the same nucleus (steroied) it will cause inhibition of testosterone secretion. "
- GIT upset and peptic ulcer.

Contra-indications

- **Hyperkalaemia**: as in chronic renal failure, K+ supplementation, β-blockers or ACE inhibitors.
- **liver disease** (dose adjustment is needed).

Summary for all the diuretics

Diuretics	Mechanism of action	Effects	Uses	ADRs
CA inhibitors Acetohexamide Dorzolamide	Inhibition of NaHCO3 reabsorption in PCT	↑ Urinary Na HCO3, K Urinary alkalosis Metabolic acidosis	Glaucoma, epilepsy Mountain sickness Alkalosis Phosphatemia	Metabolic acidosis , Urinary alkalosis Hypokalemia
Osmotic diuretic Mannitol	Osmotic effect in PCT	↑Urine excretion ↑ Little Na	-Cerebral edema, glaucoma -Acute renal failure, drug toxicities.	Extracellular water expansion Dehydration Hypernatremia
Loop diuretics Furosemide	Na/K/2Cl transporter in TAL the most effective	↑Urinary Na, K, Ca, Mg	**Acute pulmonary edema** (Drug of choice) Heart failure Hyperkalemia, Hypercalcemia	Hypokalemia, hypovolemia, hyponatremia, hypomagnesemia, **hypocalcemia** Precipitate gout, alkalosis
Thiazide diuretics hydrochlorothiazide	Na and Cl cotransporter in DCT	↑Urinary Na, K, Mg BUT↓ urinary Ca (hypercalcemia) Metabolic alkalosis	**Commonly used** Hypertension, mild heart failure, nephrolithiasis, diabetes inspidus	Hypokalemia, hyponatremia, hypovolemia, hypomagnesemia, **hypercalcemia** Alkalosis, precipitate gout Hyperlipidemia, hyperglycemia
K-sparing diuretic Spironolactone	competitive antagonist of aldosterone in CCT	↑ Urinary Na ↓ K, H secretion Metabolic acidosis	**Hepatic cirrhosis** (Drug of choice)	Gynaecomastia **Hyperkalaemia**, Metabolic acidosis. GIT upset and peptic ulcer

Therapeutic Applications of Diuretics

Medical condition	Thiazides Diuretic	Loop Diuretics	Notes
1. Treatment of hypertension:	used alone or in combination with beta-blockers at low-dose (fewer side effects)	Used in presence of renal failure.	
2. Edema States	Used in mild edema with normal renal function.	Used in cases with impaired renal function.	
3. Congestive Heart failure	Used in only mild cases with well-preserved renal function	Much more preferred in severe cases especially when GF is lowered.	In life-threatening acute pulmonary edema, Furosemide (loop duretic) is given IV.
4. Renal failure	Used till GFR ≥ 40-50 ml/ min	Are used below given values, with increasing the dose with as GFR goes down.	
5. Diabetes inspidus	Reduces urine volume		Large volume(>10 L/day) of dilute urine in diabetes inspidus.
6. Hepatic cirrhosis with ascites			Spironolactone (K-sparing diuretic) is the drug of choice.

MCQs

1- K+ sparing Diuretics cause metabolic acidosis in which mechanism :
A) Increase excretion of bicarbonate.
B) Decrease excretion of Ca++
C) Decrease excretion of K+
D)Decrease Reabsorption

2- Which of the following cause Gynaecomastia :
A) Amiloride.
B) Triamterene.
C) Spironolactone.
D) Dorzolamide.

3- Which of the following condition needs dose adjustment of K+ sparing Diuretics:
A)ACE inhibitors.
B) β-blockers.
C) chronic renal failure.
D) liver disease.

4- A patient uses Digoxin and we need to give him a diuretic. Which of the following is the appropriate one:
A) Spironolactone
B) Mannitol
C)hydrochlorothiazide
D) Furosemide

5- Which of the following has a weak diuretic action and never use alone :
A) Triamterene
B) Hydrochlorothiazide.
C) Furosemide.
D) Mannitol

1-C 2-C 3-D 4-A 5-A 6-D 7-D 8-D 9-D 10-D

6-Which of the following has a diuretic effect in Inhibition of Na influx through Na channels in the luminal membrane :
A) Acetazolamide.
B) Indapamid.
C) Furosemide.
D) Amiloride

7- The drug that needs aldosterone to be present in order to be effective is:
a) Hydrochlorothiazide (HydroDiuril)
b) Amiloride (Midamor)
c) Both of the above
d) None of the above

8- The drug that has a steroid-like structure which is responsible for its anti-androgenic effect is:
a) Amiloride (Midamor)
b) Furosemide (Lasix)
c) Hydrochlorothiazide (HydroDiuril)
d) Spironolactone (Aldactone)

9-Which one of the following drugs is the least potent diuretic:
a) Osmotic diuretics
b) Loop diuretics
c) Thiazide diuretics
d) Potassium-sparing diuretics

10- Amiloride (Midamone) acts on which site of nephron :
a) Proximal convoluted tubule
b) Ascending thick limb of the loop of Henle
c) Distal convoluted tubule
d) Collecting duct

PHARMACOLOGY 433

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We hope that we made this lecture easier for you

Good Luck !