이뇨제
Diuretics

이종호
한림의대 약리학교실

이뇨제

- 개념
- Normal regulation of fluid and electrolytes by the kidneys
- Kidney function in disease
- Thiazides and related agents
- Loop or high-ceiling diuretics
- Potassium-sparing diuretics
- Carbonic anhydrase inhibitors
- Osmotic diuretics

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- 개념
- Normal regulation of fluid and electrolytes by the kidneys
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- Carbonic anhydrase inhibitors
- Osmotic diuretics

1. Proximal convoluted tubule
2. Descending loop of Henle
3. Ascending loop of Henle
4. Distal convoluted tubule
5. Collecting tubule and duct

이뇨제

- 개념
- Normal regulation of fluid and electrolytes by the kidneys
- Kidney function in disease
- agents
- diuretics
  1. Edematous states
  2. Nonedematous states
- Potassium-sparing diuretics
- Carbonic anhydrase inhibitors
- Osmotic diuretics

Nonedematous states

- Hypertension
  - Thiazides
- Kidney stones
  - Calcium phosphate, calcium oxalate
  - Thiazides
- Hypercalcemia
  - Loop diuretics with normal saline intravenously
- Diabetes insipidus
  - Thiazides
- Prophylaxis of renal failure

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- 개념
- Normal regulation of fluid and electrolytes by the kidneys
- Kidney function in disease
- Thiazides and related agents
  - 1. Chlorothiazide and hydrochlorothiazide
  - 2. Thiazide-like analogs
- Carbonic anhydrase inhibitors
- Osmotic diuretics

작용기전

- By blocking the **Na^+/Cl^- transporter (NCC)** on the luminal membrane of the distal convoluted tubule.

임상적 이용

- Hypertension
  - Mild to moderate
- Heart failure
- Renal stones due to hypercalciuria
- Nephrogenic diabetes insipidus
  - ADH insensitivity – decreased water permeability

부작용

- Hypokalemic metabolic alkalosis and hyperuricemia
- Impaired carbohydrate tolerance
- Hyperlipidemia
- Hyponatremia
- Allergic reactions
- Contraindications
  - Hepatic cirrhosis, borderline renal failure, heart failure

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- 개념
- Normal regulation of fluid and electrolytes by the kidneys
- Kidney function in disease
- Thiazides and related agents
- Loop or high-ceiling diuretics
  - 1. Bumetanide, furosemide, torsemide and ethacrynic acid
- Carbonic anhydrase inhibitors
- Osmotic diuretics

작용기전

- Inhibit the **$Na^+/K^+/2Cl^-$ transporter(NKCC2)** in the luminal membrane in the thick ascending limb of Henle's loop.

임상적 이용

- **Acute pulmonary edema** in heart failure
- **Acute hypercalcemia** in malignancy
  - Loop agents with administration of saline solution
- Hyperkalemia
- Acute renal failure
  - Loop agents can increase the rate of urine flow
- Anion overdose
  - Bromide, fluoride, iodide
  - Loop agents with administration of saline solution

부작용

- Hypokalemic metabolic alkalosis
- Ototoxicity
- Hyperuricemia
  - Hypovolemia-associated enhancement of uric acid reabsorption in the proximal tubule
- Hypomagnesemia
- Allergic reactions
  - Skin rash, eosinophilia, interstitial nephritis
- Contraindications
  - Hepatic cirrhosis, borderline renal failure, heart failure

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- Potassium-sparing diuretics
- bitors
- 1. Spironolactone
- 2. Triamterene and amiloride

Spironolactone의 작용기전

- Antagonize aldosterone at intracellular receptor sites.
  - Active metabolite; canrenone
  - Prevents
    - Na^+ reabsorption
      - By inhibiting expression of Na^+ channels and Na^+/K^+-ATPase
    - K^+, H^+ secretion
- Not effective in Addison disease (primary adrenal insufficiency)

Triamterene과 amiloride의 작용기전

- Directly block **epithelial Na^+ channels (ENaC)**
  - Decrease in Na^+/K^+ exchange

Potassium-sparing diuretics

- 작용
  - Excretion of Na^+
  - Retention of K^+

임상적 이용

- Hyperaldosteronism
  - Primary hypersecretion
  - Secondary hyperaldosteronism

부작용

- Hyperkalemia
  - Should **never** be given with potassium supplements
  - Combinations of potassium-sparing and thiazide diuretics
- Hyperchloremic metabolic acidosis
- Gynecomastia
  - Spironolactone
- Acute renal failure
  - Triamterene with indomethacin
- Kidney stones
  - Triamterene

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- Normal regulation of fluid and electrolytes by the kidneys
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- Loop or high-ceiling diuretics
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- Carbonic anhydrase inhibitors
- 1. Acetazolamide cs

작용기전

- Inhibits carbonic anhydrase located intracellularly and on the apical membrane of the proximal tubular epithelium
  - Decreased exchange Na^+ for H^+ results in a mild diuresis.

작용

- Loss of HCO_3^-
  - Hyperchloremic metabolic acidosis
- Increased phosphate excretion

임상적 이용

- Chronic glaucoma
  - To decrease intraocular pressure
    - Decreased production of the aqueous humor by inhibiting carbonic anhydrase in the ciliary body of the eye.
  - Topical agents
    - Dorzolamide, brinzolamide
- Urinary alkalinization
- Metabolic alkalosis
- Acute mountain sickness
  - Acidosis in the CNS results in hyperventilation

부작용

- Hyperchloremic metabolic acidosis
- Renal stone
  - Alkalinization of the urine causes precipitation of calcium salts
- Renal potassium wasting
- Other toxicities
  - Drowsiness, paresthesia
  - Hypersensitivity reactions
- Contraindications
  - Liver cirrhosis
    - Alkalinization of the urine -> decreased urinary excretion of NH_4^+ -> hyperammonemia -> hepatic encephalopathy

삼투성 이뇨제

- 임상적 이용
  - Not useful for treating Na^+ retention
  - To increase urine volume
    - Acute renal failure due to shock, drug toxicities, and trauma (hemolysis, rhabdomyolysis)
  - Reduction of intracranial and intraocular pressure
- 부작용
  - Expansion of extracellular water and hyponatremia
  - Dehydration, hyperkalemia and hypernatremia