St George's University of London | UNIVERSITY OF NICOSIA

Medical Programme

THIAZIDES AND LOOP DIURETICS

Stay in the loop

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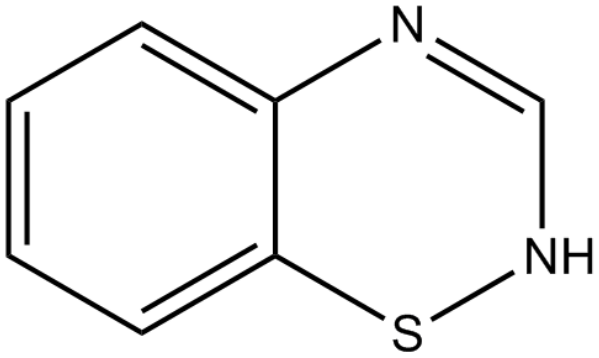
Sheba Student Presentation series

Definition

- **Diuretics** is a term that generally refers to substances that induce diuresis. While diuresis refers to the production and or excretion of urine. It plays a major role in fluid balance.

- Diuretics are used in a wide variety of cases; clinically in treatment of disease states, extreme dieters (slimming) to dopping by boxers and weightlifters amongst other sports.

Thiazides



- **Thiazide diuretics** are a particular class of diuretics that are traditionally named by virtue of their parent chemical structure. Eg. cholorothiazide
- However, this has also come to include newer drugs that are thought to share a similar mechinism of action. Eg. chlorthalidone

Indications

- Hypertension
- Congestive heart failure (CHF)
- Oedema
- Nephrotic syndromes
- Hepatic cirrhosis

Pharmacokinetics

- Thiazides have a much slower onset of action; 2 hours (for diuresis)
- They also have longer half lives than loop diuretics; between 5 hours and to 15 hours.
- Minimally metabolized by the liver
- Excreted in urine.
- Oedema
- Nephrotic syndromes
- Hepatic cirrhosis

Administration & Dosing chlortalidone (Hygroton)

- Normally given PO
- Oedema [up to 50mg daily]
- Hypertension [25mg daily in the morning, increased to 50mg prn]
- Heart failure [25 to 50mg daily in the morning, increased to 100 to 200mg prn]

- Thiazides are inneffective if eGFR <30ml/min/1.73m^2

Mechanism of Action

- Thiazides act on the sodium / chloride co-transporters at the distal convoluted tubules and collecting ducts and prevents the channels from functioning properly. (Thus sodium is not retained and water follows salt).
- Over time it will cause vasodilation as well. (the exact reason for this is yet to be understood.
- Longer acting than loop diuretics, but not as effective

Side effects

- Nocturia and polyuria
- Impotence
- Hyperlipidaemia

- Confusion, dizziness
- Anorexia
- Epigastric distress

Adverse drug reactions

- Thiazides can prevent up to 8% of K^+ re-absoprtion.
- Hypokalaemia,
- Hypercalcaemia (unlike loop diuretics!),
- Hypokalaemia (this in turn can cause glucose intolerance as glucose is taken up into cells with potassium!)

- Agranulocytosis,
- Thrombocytopenia.

Adverse drug reactions: Hypokalaemia

- It is common for a patient on diuretics to become hypokalaemic.
- This is dangerous because it predisposes to arrhythmias. It may also precipitate encephalopathy in those with liver failure.
- You can reduce the risk by taking potassium chloride supplements, or by taking potassium sparing diuretics.
- The KCl supplements have to be taken in large quantities, which irritates the stomach.

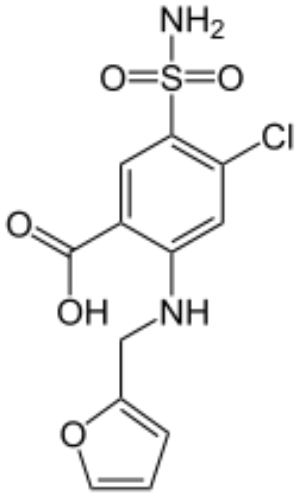
Contraindications

- Patients with documented hypersensitivity to thiazides or sulfa medications.
- Addison's disease.

Use with caution in patients with concomitant;

- Diabetes mellitus,
- Gout,
- Hypercholesterolaemia,
- Systemic Lupus Erythematosus

Loop Diuretics



Furosemide

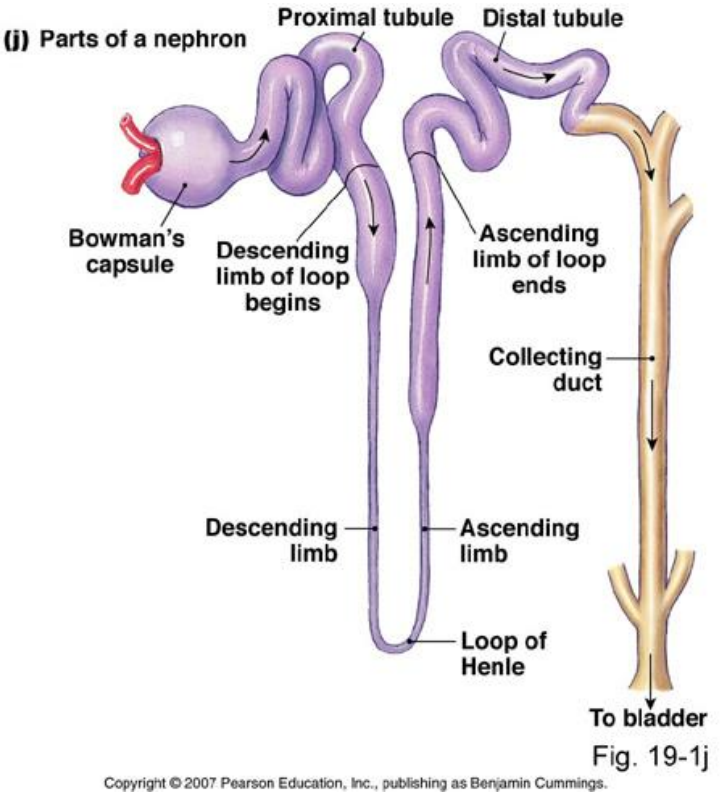


Fig. 19-1j

- Furosemide (Lasix®); these are so called loop diuretics because of their site of action (loop of Henle).

Indications

- Hypertension
- Congestive heart failure (CHF)
- Pulmonary Oedema due to LVF
- Nephrotic syndromes
- Hepatic cirrhosis

Pharmacokinetics

- Rapid onset 5mins when given IV up to 30 mins (IM), up to 1hr (PO)
- Relatively short half life ranging 30 to 120mins but can be up to 9 hours in patients with end stage renal disease.
- Mainly cleared in urine

Administration & Dosing

- Can be given either; PO, IV ot IM.

- Oedema [40mg loading dose then 20 to 40mg maintenance and up to 120mg if proving to be resistant]
- Resistant hypertension [40 to 80mg daily]

- **Injection**
- 20 to 50mg initially, increased if necessary 20mg every 2 hours.
- Doses >50mg is by IV only.

- Can be used in patients with Renal failure (but would require higher doses).

Mechanism of action

- Loop diuretics act on the thick ascending loop of Henle as well as proximal and distal renal tubules.
- It prevents sodium and chloride ion re-absorption by binding to the sodium / potassium / chloride channel thus preventing it from functioning properly, thus these ions remain in the filtrate.
- When given intravenously, these drugs have a venodilating effect that cause pooling of blood and can be useful in left ventricular failure.

Side effects

- Cochlear damage and ototoxicity (can be seen in renal damage as the drug is not cleared quickly)
- Hypotension (excess salt and water loss)
- Renal impairment
- Bone marrow suppression, thrombocytopenia
- Muscle cramps
- Use with caution during pregnancy as it is excreted in breast milk.

Adverse drug reactions

- Loop diuretics prevent re-absorption of up to 25% of K^+. Highly effective at reducing BP and increasing sodium and water excretion.
- When the drug is stopped there is rebound sodium retention. (due to short half life)
- Excreted by the kidney. Can cause; renal failure (as a result of massive drop in BP), hyponatraemia, hypokalaemia, chochlear damage, hypocalcaemia, hypomagnesaemia.

Adverse drug reactions

- Hyperuricaemia,
- hyponatraemia,
- hypokalaemia,
- hypocalcaemia,
- hypomagnesaemia.

Contraindications

- Patients with documented hypersensitivity either to sulfa medications or furosemide specifically.

Use with caution in patients with concomitant;

- Diabetes mellitus,
- Systemic Lupus Erythematosus,
- Liver disease.

References

1. http://emedicine.medscape.com/article/331037-overview#showall
2. http://reference.medscape.com/drug/lasix-furosemide-342423
3. http://reference.medscape.com/drug/microzide-hydrodiuril-hydrochlorothiazide-342412

Bibliography & Further Reading

•British National Fomulary (BNF)

Thank you for listening