



GENITOURINARY SYSTEM

SUBJECT : Pharma tables

LEC NO. : Lec1

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وَقُلْ رَبِّ زِدْنِي عِلْمًا

Thiazide Diuretics

Drug	<p style="text-align: right;">Thiazides: - Chlorothiazides - Hydrochlorothiazide</p> <p style="text-align: right;">Thiazide-like diuretics: - Chlorthalidone · Indapamide - Metolazone</p>						
MOA	Secreted into the proximal tubule by an organic secretory mechanism. (Thiazides compete for the same secretory process by which uric acid is secreted into the proximal tubule). [X] They block the sodium-chloride (Na	They block the sodium-chloride (Na/Cl) channel expressed in the proximal segment of the distal convoluted tubule (DCT), resulting in increased excretion of Na,Cl ions.	Thiazides enhance Ca ²⁺ reabsorption in the distal convoluted tubule, by increasing Na ⁺ /Ca ²⁺ exchange. Thiazide diuretics also reduce the urinary excretion of Ca ²⁺ .	Natriuresis (excretion of sodium in the urine) may be accompanied by some loss of potassium and H ⁺ .			
Uses	Hypertension: 1st line drugs for uncomplicated hypertension. They have low cost and well tolerated An initial reduction in blood pressure results from a decrease in blood volume and, therefore, a decrease in cardiac output. With continued therapy, blood volume returns to baseline. However, antihypertensive effects continue, resulting from reduced total peripheral vascular resistance (unclear mechanism).	Heart failure: Loop diuretics are the diuretics of choice for reducing extracellular volume in heart failure. However, thiazide diuretics can be added to patients with resistance to loop diuretics. It requires careful monitoring of hypokalemia.	Hypercalciuria: used in idiopathic hypercalciuria and calcium oxalate stones in the urinary tract, because they inhibit urinary Ca ²⁺ excretion.	Nephrogenic Diabetes insipidus: caused by the collecting ducts not responding to ADH. Patients present with polyuria (increased urination rate) and polydipsia (increased thirst). The paradoxical effect of diuretics in reducing urine output is not clear. The urine volume of such individuals may drop from 11 to about 3 L/d when treated with thiazides.			
Pharmacokinetics	effective orally with bioavailability of 60%–70%, (except for chlorthiazide is given IV due its low bioavailability (15-30%))	Most thiazides take 1 to 3 weeks to produce a stable reduction in blood pressure	exhibit a prolonged half-life (approximately 10 to 15 hours).	Excretion: unmodified in the urine (except indapamide it undergoes hepatic metabolism and is excreted in both urine and bile)			
Adverse effects	Hypokalemia: the most frequent problem with the thiazide diuretics. serum K ⁺ should be measured periodically (more frequently at the beginning of therapy). Potassium supplementation or combination with a potassium-sparing diuretic may be required. Low-sodium diets blunt the potassium depletion caused by thiazide diuretics.	Hypomagnesemia	Hyponatremia	Hypovolemia: This can cause orthostatic hypotension or light-headedness.	Hyperglycemia possibly due to impaired release of insulin related to hypokalemia. Patients with diabetes still benefit from thiazide therapy, but should monitor glucose to assess the need for an adjustment in diabetes therapy if thiazides are initiated.	Hyperlipidemia: Dyslipidemia can be produced by high doses of thiazides (not typically used). Hyperuricemia, uric acid deposits in the joints and may precipitate a gouty attack in predisposed individuals. Therefore, thiazides should be used with caution in patients with gout or high levels of uric acid.	Hypercalcemia
Notes	Thiazides are the most widely used diuretics because of their antihypertensive effects.	They are sulfonamide related organic acids that do not generally cause hypersensitivity reactions in patients with allergies to sulfonamide antimicrobials	Thiazides have moderate efficacy as diuretics, as 90% of glomerular filtrate has already been reabsorbed. The dose-response curve flattens rapidly				
Drug and diseases that affect thiazides efficacy	Renal failure and heart failure: results in decreased renal blood flow, which reduces the diuretic effects as thiazides must be secreted into the proximal tubule to be effective.	Concomitant use of NSAIDs inhibits the production of prostaglandins, which inhibits renal blood flow	Lithium: thiazide reduces renal clearance of lithium and can cause rapid increase in lithium serum level.				