Diuretics and Drugs Affecting Renal Function, Water, and Electrolyte Metabolism

Subcommittee:

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<table>
<tr><th colspan="3">Diuretics</th></tr>
<tr><td colspan="3">Recommended Curriculum Equivalent: 2 hrs</td></tr>
<tr><td colspan="3">Drug Classes and Drugs to Consider</td></tr>
<tr><td>Carbonic Anhydrase Inhibitor</td><td>Osmotic Diuretic</td><td>Loop Diuretics</td></tr>
<tr><td>acetazolamide</td><td>mannitol</td><td>FUROSEMIDE
bumetanide</td></tr>
<tr><td colspan="2">Distal tubule Diuretics</td><td>K-sparing Diuretics</td></tr>
<tr><td colspan="2">CHLORTHALIDONE
HYDROCHLOROTHIAZIDE
metolazone</td><td>AMILORIDE
SPIRONOLACTONE
TRIAMTERENE
eplerenone</td></tr>
<tr><td colspan="3">Learning Objectives</td></tr>
<tr><td colspan="3">Physiology and Pathophysiology
Describe the location and function of major ion transporters and channels on renal epithelial membranes.
Explain how sodium transport influences the reabsorption of other ions and water in the kidney.
Explain how abnormal renal function can cause hypertension or edema.</td></tr>
<tr><td colspan="3">Mechanism of Action
Describe the changes that occur with electrolyte transport, water reabsorption and hemodynamics when specific diuretics inhibit kidney function.</td></tr>
<tr><td colspan="3">Actions on organ systems
Describe the hemodynamic, ion transport and excretory effects of different classes of diuretic drugs.</td></tr>
<tr><td colspan="3">Pharmacokinetics
Explain the importance of the organic anion transporters and protein binding to the renal action of diuretics.
Provide examples of how other drugs or diseases can interfere with the effects of diuretics.</td></tr>
<tr><td colspan="3">Adverse effects, drug interactions and contraindications</td></tr>
</table>

Explain how thiazides and loop diuretics can cause a metabolic alkalosis.
Explain how diuretic therapy can lead to hyponatremia.
Describe the metabolic imbalances with diuretic therapy on glucose, urate, lipids, calcium, magnesium and potassium. Explain the underlying mechanisms involved.
Describe the clinical consequences of interactions between diuretics and drugs such as cardiac glycosides, oral hypoglycemics, uricosurics, aminoglycosides, amphotericin, NSAIDs and angiotensin inhibitors.
Describe why reduced renal perfusion can limit the use of thiazide diuretics.

Therapeutic uses

Explain the renal and extra-renal mechanisms by which diuretics are useful in treating hypertension and edema.
Explain how osmotic drugs can reduce toxic nephropathy.

Clinical Pharmacology

In salicylate overdose, failure of urine alkalinization with intravenous bicarbonate then allows for the use of a carbonic anhydrase inhibitor to increase urine pH and allow for increased urinary clearance of salicylic acid in the absence of access to dialysis. Hydrochlorothiazide can be used in a 12.5 mg dose (1/2 tablet) to counteract the increase in circulating aldosterone secondary to use of an ACE inhibitor for the management of hypertension. Hydrochlorothiazide is indicated as the only diuretic that spares calcium in patients with osteopenia. Furosemide is the only effective oral diuretic in patients with a creatinine clearance less than 60 ml/min. Potassium-sparing diuretics are relatively contraindicated in patients receiving ACE inhibitor therapy due to the increased potential for hyperkalemia. Caution with interaction between thiazide diuretics and concurrent acute NSAIDs due to increased potential for interstitial nephritis.

Relevance

USMLE topic	**Principles of therapeutics**
Cardiovascular System-Abnormal Processes- Metabolic and Regulatory Disorders & Vascular Disorders- Principles of Therapeutics: Antihypertensive Drugs. Renal/Urinary System-Abnormal Processes	Diuretics, antidiuretic drugs
AAMC Medical School Objectives Project Report X Patient Safety - Table 1	**Topic C:** Drug treatment of common conditions

Notes

Objectives for diuretics as antihypertensive drugs are covered in Cardiovascular Drugs.
Objectives for renin inhibitors, ACE inhibitors and angiotensin-receptor blockers are covered in Cardiovascular drugs.
Objectives for drugs used in renal transplantation and some renal diseases are covered in Immunosuppressive Drugs.

Agents Affecting the Renal Conservation of Water	
Recommended Curriculum Equivalent: 1 hr.	
Drug Classes and Drugs to Consider	
Vasopressin Agonists	**Vasopressin Antagonists**
DESMOPRESSIN (V_2) vasopressin (V_1, V_2)	conivaptan ($V_{1a}R$, V_2R) tolvaptan (V_2R)
Learning Objectives	
Physiology and Pathophysiology Explain the mechanisms by which the kidney makes a concentrated or dilute urine. Describe the roles of vasopressin, aquaporins, V_1 and V_2 receptors, cyclic AMP and prostaglandins in regulating renal epithelial water permeability.	
Mechanisms of Action Describe how drugs can mimic or interfere with the cellular mechanisms of vasopressin.	
Actions on organ systems Compare and contrast the renal and extrarenal effects of vasopressin and desmopressin.	
Pharmacokinetics Explain how altering the structure of vasopressin affects its pharmacokinetics and pharmacodynamics.	
Adverse effects, drug interactions and contraindications Explain the mechanism of vasoconstriction produced by vasopressin. Explain how NSAIDs and clonidine can alter water reabsorption by the kidney. Describe the hazards of correcting hyponatremia with vasopressin antagonists too rapidly. Explain how drugs such as clonidine, chlorpropamide, demeclocycline, lithium, and NSAIDs can modify the action of vasopressin. Explain how blocking the V_1 receptor can alter ACTH secretion.	
Therapeutic uses Compare and contrast the therapy of central and nephrogenic diabetes insipidus. Describe the pharmacological treatment of the syndrome of inappropriate ADH secretion. Explain the mechanism of lithium carbonate interference with renal water reabsorption.	
Clinical Pharmacology Caution in use of conivaptan and tolvaptan concurrently with drugs inhibiting CYP3A or P-gp due to increased risk of toxicity associated with overly rapid correction of hyponatremia.	
Relevance	

USMLE topic Renal/Urinary System	**Principles of therapeutics** Drugs and fluids used to treat volume, electrolyte, and acid-base disorders
AAMC Medical School Objectives Project Report X Patient Safety - Table 1	**Topic D** Management of less common but severe medical conditions and emergencies
Notes Objectives for desmopressin-enhanced clotting factor release are covered in Hematological Drugs.	