Diuretics

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Uses

- Prescribed for pts with Htn, CHF, elevated ICP, edema, hemoglobinuria, low intraop UO, hyperkalemia, volume overload, and rhabdomyolysis.
- Mannitol may function as a renal preservative by free radical scavenging and toxin dilution.
- Fenoldopam is a selective dopamine-1 agonist. As a vasodilator, it lowers blood pressure and augments renal blood flow, which improves UO and glomerular filtration rate. It may also serve as a renal protectant. Usual dose begins at 0.03 μg/kg/min titrated to effect.
- HCTZ is used to treat hypercalcemia for kidney stones.

Perioperative Risks

- Hypokalemia
- Hypovolemia
- Low intraop UO
- Hyperkalemia with aldosterone antagonists
- Hypomagnesemia

Worry About

- Hypokalemia and hypovolemia.
- Low intraop UO if preop holds usual diuretics.
- Hypokalemia provoking and/or aggravating digitalis toxicity.
- Deafness with ECA and tinnitus with furosemide.
- End result of diuretic use is increased UO with net loss of H_2O and solutes, especially K^+ and Mg^{2+}.
- Onset of diuresis is within 10 min after IV administration.
- With the exception of an aldosterone antagonist and K^+-sparing diuretics, all others cause K^+ loss.
- Serum K^+ <3.5 mEq/L in 15% of pts and <3.0 mEq/L in up to 10% of diuretic-treated pts.
- Chronic diuretic-induced hypokalemia is less arrhythmogenic than acute, but serum K^+ <3.0 mEq/L is associated with a twofold greater incidence of ventricular arrhythmias than K^+ >3.0 mEq/L.
- Site-specific action associated with additional effect if diuretics from two classes used.
- Mannitol causing brief but appreciable hypervolemia risking CHF and ICP if bolused.
- Mannitol causing hypotension from high osmolar effect if given too rapidly.

Drug Class/Mechanism of Action/Usual Dose

- Diuretics belong to osmotic, carbonic anhydrase inhibition, benzothiadiazide, high-ceiling (loop), K^+-sparing, or aldosterone antagonist class of drugs, based on mechanism of action.
- Only osmotic and loop diuretics are used intraop.
- Osmotic diuretic: Mannitol—ascending loop, limits H_2O reabsorption; onset of action 5–15 min after IV dose: renal clearance
- Usual dose: Mannitol 0.25–2 g/kg (rapid bolus may precipitate hypotension)
- Loop diuretics: Ascending loop, limit NaCl reabsorption; onset of action 5 min after IV dose; $T_{½}$ 1–2 h; duration of action 3–6 h: renal clearance
- Usual IV dose for 70-kg person: Furosemide: 5–40 mg (0.1–1.0 mg/kg); ECA: 25–50 mg (0.5–1 mg/kg); bumetanide: 0.5–1 mg q 2–3 h; max 10 mg/d
- Furosemide PO to IV conversion 2:1

Drug Effects

System	Effect
HEENT	Transient (<24 h) deafness or vertigo may follow IV rapid bolus of ECA; less common after furosemide or bumetanide; rarely permanent. Tinnitus may follow furosemide.
CV	Transient increased in venous capacitance causes hypotension with rapid IV loop diuretic administration; acute transient increase in intravascular volume precedes diuresis with mannitol; vasodilation with fenoldopam.
ENDO	Hypokalemia, metabolic alkalosis
GU	Diuresis
CNS	Mannitol decreased ICP following transient increase; the latter may be mitigated by coadministration of furosemide.

Key References: Bebawy JF, Ramaiah VK, Zeeni C, et al.: The effect of furosemide on intravascular volume status and electrolytes in patients receiving mannitol: an intraoperative safety analysis, *J Neurosurg Anesthesiol* 25(1):51–54, 2013; Kheterpal S, Khodaparast O, Shanks A, et al.: Chronic angiotensin-converting enzyme inhibitor or angiotensin receptor blocker therapy combined with diuretic therapy is associated with increased episodes of hypotension in noncardiac surgery, *J Cardiothorac Vasc Anesth* 22(2):180–186, 2008.

Perioperative Implications/Possible Drug Interactions

Preoperative Concerns

- In chronic hypertensive pts treated with diuretics, a significant intravascular volume contraction may exist, making them more prone to hypotension following induction of anesthesia and any acute blood loss.
- Hypokalemia: Check serum K^+; consider enhanced digitalis toxicity.
- Hypomagnesemia is common in pts treated with loop or thiazide diuretics and predisposes them to ventricular arrhythmias. It should be suspected when hypokalemia is noted. Hypomagnesemia should be corrected prior to repleting K^+.
- Enhanced ototoxicity and nephrotoxicity of loop diuretics are associated with rapid administration of large IV doses and concurrent use of another nephrotoxic drug (e.g., aminoglycoside antibiotic, another loop diuretic, and some cephalosporins, especially cephaloridine).
- It is probably best to continue a chronic dose through the periop period, including day of surgery. (UO will decline if a diuretic not given on day of surgery.) No increase in hypotension will be seen if usual oral diuretics are given preop the day of surgery.

Induction/Maintenance

- Intraop loop diuretic use may significantly decrease serum K^+ level with diuresis.

Adjuvants

- Enhanced renal clearance of other drugs (e.g., neuromuscular-blocking agents) provoked by diuresis is not clinically problematic.

Anticipated Problems/Concerns

- Pts receiving diuretics preop should be considered volume contracted until proven otherwise.
- Hypokalemia associated with diuresis will be aggravated by hyperventilation, which further lowers serum K^+ an additional 0.5 mEq/L for each 10 mm Hg decrease in $PaCO_2$.
- Catecholamine β effect (endogenous and/or exogenous); also lowers serum K^+.
- Low intraop UO in a euvolemic pt if antidiuretic hormone/stress mediated will, in authors' experience, respond to very low dose (e.g., 2–5 mg furosemide) with increased UO.

Epsilon-Aminocaproic Acid (Amicar)

Frank W. Dupont

Uses

- EACA is a hemostatic agent used in the treatment of hyperfibrinolysis associated with excessive bleeding.
- Indications: Fibrinolytic bleeding associated with surgical complications following heart surgery (with or without CPB) and portacaval shunt; surgical hematuria (following prostatectomy and nephrectomy) or nonsurgical hematuria (accompanying polycystic or neoplastic diseases of the GU system); acute and life-threatening abruptio placentae; hepatic cirrhosis; neoplastic disease such as carcinoma of the prostate, lung, stomach, and cervix; hematologic disorders such as amegakaryocytic thrombocytopenia
- Methods of administration: IV solution, oral solution, tablets

Perioperative Risks

- Increased risk of developing thrombosis in pts, who are concurrently treated with factor IX complex or antiinhibitor coagulant complex

Worry About

- EACA should not be used when there is evidence of an active intravascular clotting process. When there is uncertainty as to whether the cause of bleeding is primary fibrinolysis or DIC, this distinction must almost certainly be made before administering EACA. EACA must not be used in the presence of DIC without concomitant heparin.

Overview/Pharmacology

- EACA is an inhibitor of fibrinolysis and enhances hemostasis when fibrinolysis contributes to bleeding.
- Renal excretion is the primary route of elimination: 65% is eliminated unchanged within 12 h; approximately 11% is metabolized; renal clearance is 116 mL/min; and terminal elimination half-life is approximately 2 h.