ACE Inhibitors

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Uses

- Treatment of essential Htn, CHF, and mitral regurgitation.
- Numerous studies show that ACE-I use improves symptoms and quality of life, as well as reduces mortality rate in elderly with heart failure and decreased LVEF.
- Decreases mortality after myocardial infarction.
- Safe and effective treatment of Htn in diabetics; strong evidence that ACE-I delays the progression of diabetic renal disease.

Perioperative Risks

- Severe and prolonged hypotension in pts undergoing general anesthesia
- May increase insulin sensitivity and hypoglycemia in diabetics
- Conflicting evidence regarding risk of AKI

Worry About

- Decreased GFR and not recommended in pts with renal artery stenosis.
- Life-threatening angioedema involves the swelling of head, neck, and tongue.
- Hyperkalemia because of decreased production of aldosterone.
- Fetal anomalies and fetal and neonatal death.

Overview/Pharmacology/Dose

- A recent systematic review did not find evidence to support that periop ACEIs or ARBs can prevent mortality, morbidity, and complications (hypotension, periop cerebrovascular complications, and cardiac surgery–related renal failure).
- Captopril is available in oral dose and very effective in treating Htn.
- Enalapril has to be converted by esterase in liver to the active metabolite enalaprilat.
- Both captopril and enalapril are renally excreted and should be reduced in pt with renal dysfunction.
- Lisinopril is absorbed as the active form and offered as once-daily dosing.

Characteristic	Captopril	Enalapril	Lisinopril	Benazepril	Fosinopril	Quinapril	Ramipril
Elimination	Renal	Renal	Renal	Renal	50% renal 50% hepatic	61% renal 37% hepatic	Renal
Onset of hypotensive action (h)	0.25	1	1	1	1	1	1–2
Peak hypotensive effects (h)	1–1.5	4–6	6	2–4	2–6	2	3–6
Duration of hypotensive effects (h)	Dose related	24 (18–30)	24 (18–30)	24	24	24	>24 (24–60)
Dose (mg)	25–150, max 450	5–40, max 40	10–40, max 80	20–80, max 80	10–40, max 80	10–80, max 80	2.5–20, max 20

Drug Class

- Affects the renin-angiotensin system by blocking the conversion of angiotensin I to the active angiotensin II and delaying bradykinin breakdown and associated prostaglandins.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Angioedema Bronchospasm	Swelling of face, neck, tongue Dyspnea	Difficulty speaking, swallowing Wheezing	Airway exam
CV	Hypotension	Assess CV response to Rx		
GU	Renal failure Hyperkalemia	Orthopnea, dyspnea	Edema	BUN, Cr, lytes
HEME	Leukopenia, agranulocytosis	Fever	CBC with diff	

Key References: Zou Z, Yuan HB, Yang B, et al.: Perioperative angiotensin-converting enzyme inhibitors or angiotensin II type 1 receptor blockers for preventing mortality and morbidity in adults, *Cochrane Database Syst Rev* (1):CD009210, 2016; Mets B: To stop or not? *Anesth Analg* 120(6):1413–1419, 2015.

Drug Interactions

Preoperative Period

- Assess for evidence of renal insufficiency.
- Monitor for hyperkalemia.
- ACE-I can be continued until the day of surgery because of the potential benefits in reducing mortality and morbidity, but many hold the day of surgery. This issue is controversial.

Induction/Maintenance

- Consider reducing the ACE-I dose so that hypotension can be avoided.
- Severe and refractory hypotension can be resistant to vasopressors such as phenylephrine, ephedrine, and norepinephrine.
- Vasopressin and analogs can be useful to restore BP.
- Use of succinylcholine with elevated K^+ may be associated with cardiac arrhythmia.

Adjuvant/Regional Anesthesia/Reversal

- Hypotensive episodes may be associated with spinal and epidural anesthesia.

Postoperative Period

- Monitor for hypotension.

Acetaminophen

William J. Fawcett

Uses

- Minor analgesic for acute and chronic pain.
- First-line agent in WHO analgesia treatment ladder.
- First-line agent in treatment of pain in pregnancy and compatible with breastfeeding.
- Commonly administered in combination with codeine phosphate (e.g., paracetamol 500-mg and codeine 8-mg or paracetamol 500-mg and codeine 30-mg tablets).
- Commonly used as multimodal analgesic with an opioid-sparing effect.

Risk

- Well tolerated in normal therapeutic doses.
- Overdose associated with hepatotoxicity and nephrotoxicity.
- Unlike NSAIDs, negligible clinical antiinflammatory and antiplatelet effects.

Overview/Pharmacology

- Rapidly absorbed in GI tract, mostly in the small intestine.
- Rectal bioavailability is variable (30–70%).
- IV preparation has been associated with flushing, tachycardia, and hypotension.
- Half-life 1.25–3 h, peak plasma concentration 30–60 min
- 20% is protein-bound.
- Serum therapeutic levels 10–30 μg/mL.
- Analgesic effect lasts for approximately 6 h.
- 25% of dose undergoes first-pass effect in the liver; this is reduced with larger doses as liver's enzymatic capacity is overwhelmed.
- 90% is metabolized by conjugation in the liver via mainly by glucuronidation conjugation (and to a lesser extent sulfate conjugation), forming nontoxic metabolites (saturated at doses >150 mg/kg) and renally excreted (90–100% is recovered in urine within 24 h). Less than 5% is excreted unchanged in the urine.
- 10% undergoes oxidative metabolism via cytochrome P450 isoenzymes CYP2E1, CYP1A2, CYP3A4, and CYP2D6 to form the potentially hepatotoxic and nephrotoxic metabolite N-acetyl-p-benzoquinoneimine NAPQI. This metabolite is readily detoxified by glutathione.