Nitroglycerin

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Uses

- Therapy for pts with angina.
- CHF
- In MI, can reduce infarct size.
- Prinzmetal angina.
- Can be given as a patch, paste, or pill taken sublingually as needed.
- Uterine relaxation for retained placenta, although a systematic review did not demonstrate the efficacy of NTG used alone.
- May be beneficial in reducing postop morphine usage for pain management.

Perioperative Risks

- Development of hypotension
- Drug rash (rare)

Worry About

- Severe hypotension, especially with regional anesthesia

Overview/Pharmacology

- Used for both chronic treatment and acute management.
- Prophylactic NTG has not been shown to reduce the incidence of intraop MI.
- Tolerance to drug from prolonged IV infusion or continuous patch can occur.
- Metabolized by reductive hydrolysis in liver.
- Rapidity of onset and duration of action are directly related to method of administration.
  - Sublingual: Onset within 1–2 min, duration less than 1 h
  - Oral: Peak effect within 60–90 min, duration 3–6 h
  - Paste: Onset within 60 min, duration 4–8 h
  - Patch: Duration up to 24 h
- Prolonged use can lead to tolerance and reduced effectiveness.
- NTG paste and/or patch may be absorbed unevenly intraop.

Drug Class/Mechanism of Action/Usual Dose

- Organic nitrate
- Activates guanylate cyclase; increases levels of cGMP in smooth muscle and other tissues; increases NO.
- Usual dosage
  - Sublingual: 0.4 mg as needed
  - Paste: 1/2–1 inch
  - Isosorbide dinitrate (Isordil): 5–30 mg every 6 h
  - IV: 0.5–2 μg/kg per min
- Bolus for uterine relaxation (slow 50 μg; may repeat once with caution if RA is actively causing sympathectomy).

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Vasodilation of veins moreso than arteries Redistribution of coronary blood flow	Relief of angina	BP	PCWP
RESP	Decreased pulm vascular resistance			PCWP
GU	Uterine (smooth muscle) relaxation			
CNS	Dilation of meningeal arterial vessels	Headache		

Key References: Zvara DA, Groban L, Rogers AT, et al.: Prophylactic nitroglycerin did not reduce myocardial ischemia during accelerated recovery management of coronary artery bypass graft surgery patients, *J Cardiothorac Vasc Anesth* 14(5):571–575, 2000; Abdel-Aleem H, Abdel-Aleem MA, Shaaban OM: Nitroglycerin for management of retained placenta, *Cochrane Database Syst Rev* (11):CD007708, 2015.

Perioperative Implications

Preoperative Concerns

- Assess volume status
- Consider monitoring
  - BP (arterial cath)
  - PA cath (may give useful information if nitroglycerin infusion is used)

Induction/Maintenance

- May interact with other induction agents to cause hypotension.
- Ideally should be given IV because of uneven absorption intraop (binding sites on tubing).
- Effective means of alleviating myocardial ischemia intraop.
- Has been used prophylactically as bolus during induction.
- Anesthetic agents may mimic beneficial effects of nitroglycerin.

Adjuvants/Regional Anesthesia/Reversal

- Agents that can result in hypotension may be exacerbated by NTG.

Postoperative Period

- Pts on chronic NTG may benefit from resumption of the drug.
- Can be given as patch or paste after pt has been rewarmed.

Anticipated Problems/Concerns

- Tolerance to NTG manifests by reduced hemodynamic effects, a function of dose and frequency of administration.
- Many inhalational agents and opiates have some of the hemodynamic effects of NTG (e.g., venodilation, reduced demand for oxygen).

Nonstatin Hypolipidemic Agents

Michael G. Irwin

Uses

- Primary indications include
  - Hyperlipidemia: Hydroxymethylglutaryl coenzyme-A (HMG-CoA) reductase inhibitors (statins) are the major hypolipidemic drugs. Nonstatin drugs are used in pts with side-effects or those not responding well to statin therapy. Evolocumab also has an indication specifically for the treatment of homozygous familial hypercholesterolemia.
  - Primary and secondary prevention of CV disease: CV benefits (reduction in myocardial infarction and stroke) in pts with hypercholesterolemia and mixed dyslipidemia.

Overview/Pharmacology

- Selective cholesterol absorption inhibitors: Ezetimibe
  - Inhibits cholesterol absorption from the small intestine by blocking a critical mediator of cholesterol absorption, the Niemann-Pick C1–like 1 (NPC1L1) protein on the GI tract's epithelial cells as well as in hepatocytes.
  - Metabolized in the liver and small intestine via glucuronide conjugation with subsequent renal and biliary excretion. Half-life around 22 h. No significant inhibitor or inducer effects on cytochrome P-450 isoenzymes. Significant medication interactions with cyclosporine and fibrates other than fenofibrate.
  - Common adverse drug reactions (≥1% of pts) include headache and/or diarrhea (steatorrhea). Infrequent adverse effects (0.1–1% of pts) include myalgia and/or raised liver function test (ALT/AST) results.
- Niacin (also known as vitamin B3, or nicotinic acid)
  - Decreases synthesis of apoB-containing lipoproteins via inhibition of DGAT2, a key enzyme for triglyceride synthesis, binding to HCAR2, thereby decreasing lipolysis and FFA flux to the liver for triglyceride synthesis and increased apoB catabolism. HDL levels are increased through direct and indirect pathways.
  - Common adverse effects are flushing, headache, pain, abd pain, diarrhea, dyspepsia, nausea, vomiting, rhinitis, pruritus, and rash. High doses may reduce blood pressure as a result of acute vasodilation. Cardiac arrhythmias, increased PT and decreased platelet count have been reported.
  - Contraindicated in active liver disease, persistent elevated serum transaminases, active peptic ulcer disease, or bleeding.
- Fibrates (fibric acid derivatives): Gemfibrozil, fenofibrate, clofibrate
  - Reduce insulin resistance when dyslipidemia is associated with other features of the metabolic syndrome
  - Activate peroxisome proliferator-activated receptors (PPARs). Mechanism of action: Induction of lipoprotein lipolysis; increased hepatic FA uptake and reduction of TG production; induction of the β-oxidation pathway, causing a decrease in FA synthesis; increased removal of LDL particles; increase in HDL production; inhibition of cholesterol 7 alpha hydroxylase