Glycopyrrolate

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Ariel Gallanosa, Joshua B. Stevens, Joseph Maxwell Hendrix, Judy Quick

Continuing Education Activity

Glycopyrrolate is a muscarinic receptor antagonist and an essential anticholinergic agent in perioperative care and various medical settings. Clinicians use this medication to inhibit salivary and respiratory secretions, achieve antisialagogue effects, and prevent reflex bradycardia during surgical procedures. By targeting muscarinic receptors, glycopyrrolate provides critical support in maintaining physiological stability and optimizing conditions for surgical interventions.

A detailed understanding of glycopyrrolate's mechanism of action, dosing strategies, and adverse effect profile is crucial for ensuring safe and effective administration. Clinical applications include tailoring dosing adjustments based on patient-specific factors, recognizing contraindications, and implementing appropriate monitoring protocols. Collaboration among anesthesiologists, surgeons, nurses, and pharmacists enhances the safe use of glycopyrrolate, promotes effective management of complications, and supports optimal patient outcomes in diverse clinical scenarios.

Objectives:

- Determine the mechanism of action of glycopyrrolate.
- Identify the indications for glycopyrrolate therapy.
- Determine the monitoring necessary during glycopyrrolate therapy.
- Implement interprofessional team strategies for improving care coordination and communication to improve outcomes for patients receiving glycopyrrolate therapy.

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Indications

Glycopyrrolate, also known as glycopyrronium, is an anticholinergic medication. This drug is a synthetically created quaternary amine with pyridine and a cyclopentane moiety within the compound's structure. Glycopyrrolate has been widely used as a preoperative medication to inhibit salivary gland and respiratory secretions. Anticholinergics are typically administered to produce an antisialagogue, sedative, or amnesic effect and to prevent reflex bradycardia. These drugs are not predictably effective in increasing gastric fluid pH or decreasing gastric fluid volume. Glycopyrrolate is among the most commonly used anticholinergic medications.

- Glycopyrrolate is used perioperatively as a muscarinic receptor antagonist.[2][3]
- The topical formulation of glycopyrrolate is indicated to treat primary axillary hyperhidrosis in patients 9 and older.[4]
- Glycopyrrolate is also helpful in reducing severe or chronic drooling in pediatric patients with neurologic conditions, such as cerebral palsy. The intravenous formulation of glycopyrrolate classically reverses vagal reflexes and bradycardia intraoperatively and reverses the muscarinic effects of cholinergic agents such as neostigmine or pyridostigmine.[5]
- Glycopyrrolate may be administered to reverse the neuromuscular blockade due to nondepolarizing muscle relaxants postoperatively and is frequently used in conjunction with neostigmine, a cholinesterase inhibitor.[6]
- Various oral inhalation formulations of glycopyrrolate are indicated for the long-term maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD).[7][8]

Other commonly used anticholinergics include atropine and scopolamine. Most frequently, clinicians use glycopyrrolate to reduce pharyngeal, tracheal, bronchial, and sialagogue effects preoperatively; decreased secretions are the desired effect during anesthesia when a tracheal tube is in place. A blockade of reflexive vagal cardiac inhibition reflexes may also occur during intubation and anesthetic induction.

Mechanism of Action

Glycopyrrolate's primary mechanism of action is the blockage of acetylcholine's effects at the parasympathetic sites in various tissues. This blockage primarily occurs in the central nervous system, smooth muscle, and secretory glands. Glycopyrrolate also reduces the rate of salivation by preventing the stimulation of the acetylcholine receptors themselves. Glycopyrrolate does not cross the blood-brain barrier or the placenta and has a slower diffusion rate than other anticholinergic drugs, such as atropine and scopolamine.

Pharmacokinetics

Absorption: Glycopyrrolate exhibits onset of action within 1 minute when given intravenously. This drug is a quaternary amine with cyclopentane and pyridine moieties in the compound, making it different from atropine.

Metabolism: Glycopyrrolate has a 2 to 4-hour duration of action after intravenous administration, while atropine has 30 minutes. Glycopyrrolate exhibits an elimination half-life of approximately 50 minutes.

Elimination: Glycopyrrolate undergoes urinary excretion and elimination.

Administration

Available Forms, Dosage, and Strengths

Glycopyrrolate may be administered intravenously, intramuscularly, orally, topically, or by inhalation.

Injection: Glycopyrrolate comes packaged as a 0.2 mg/mL solution for injection. Before intravenous administration, the syringe should be inspected to ensure no particulate matter. Intramuscular or intravenous administration requires no dilution and should be at 0.2 mg over 1 to 2 minutes. Additionally, it may be administered via the tubing of a running intravenous infusion of a compatible solution. The drug should be stored in a cool, dry area protected from light before administration. Any unused solution should be discarded as it is unstable at a pH greater than 6. Glycopyrrolate dosing ranges from a premedication dose of 0.005 to 0.01 mg/kg up to 0.2 to 0.3 mg in adults and is typically half that of atropine.

Oral: Glycopyrrolate tablets are available in 1 mg, 1.5 mg, and 2 mg strengths. The oral solution is available in a 1 mg/5 mL formulation. The starting dose is 1 to 2 mg twice daily and gradually titrated upward based on the patient's response.

Topical: The topical formulation is available as a single-use cloth pre-moistened with a 2.4% glycopyrronium solution. This cloth is used only once every 24 hours on both underarms.

Inhaled: Glycopyrrolate is available as a capsule containing 15.6 µg of dry powder that may be inhaled twice daily and as a vial containing 25 µg of nebulization solution inhaled twice daily.

Specific Patient Populations

Pregnancy considerations: Typical glycopyrrolate doses do not influence the fetal heart rate or fetal heart rate variability to a significant extent. After parenteral administration, there is a low concentration of glycopyrrolate in umbilical venous and arterial blood and the amniotic fluid. Glycopyrrolate does not appear to penetrate through the placental barrier significantly. As animal reproduction studies are not consistently predictive of human response, this drug should be used during pregnancy only if needed. Because of limited data in human pregnancy studies, both atropine and glycopyrrolate are considered acceptable anticholinergics, and usage varies based on the clinician's preference.

Breastfeeding considerations: Glycopyrrolate is a quaternary ammonium compound; it is not likely to be absorbed and reach the infant's bloodstream, particularly when inhaled or applied topically on the skin. Long-term oral use of glycopyrrolate might reduce milk production or milk letdown, but a single dose is unlikely to interfere with breastfeeding. Clinicians should observe for signs of decreased lactation (eg, insatiety or poor weight gain).

Renal impairment: According to product labeling, dose adjustments may be necessary. Clinicians should exercise caution when administering glycopyrrolate to patients with impaired renal function.

Hepatic impairment: The product labeling does not provide information about patients with impaired liver function. Clinicians should exercise caution when administering glycopyrrolate to these patients.

Pediatric patients: Glycopyrrolate should generally be avoided in neonates. Patients receiving higher than recommended dosages can potentially experience a hyperexcitability reaction.

Adverse Effects

Potential adverse reactions associated with glycopyrrolate administration include anticholinergic symptoms such as mydriasis, hyperthermia, tachycardia, and cardiac arrhythmia. They may also include blurred vision, constipation, cycloplegia, dry mouth, dry skin, flushing, photophobia, urinary retention, and xerophthalmia.

Glycopyrrolate may affect the patient's ability to perform tasks requiring mental alertness. For example, patients may not be able to operate heavy machinery safely. Additionally, the medication may induce drowsiness or blurred vision, which is exacerbated by the consumption of alcohol.

Use with discretion in patients with autonomic neuropathy or hyperthyroidism. Heat prostration can occur in the presence of fever, high ambient temperature, or physical exercise. Clinicians should limit or discontinue this medication for patients who exercise or in situations involving elevated ambient temperatures.

Patients younger than 12 with pediatric spastic paralysis are more likely to exhibit an increased anticholinergic response, which elevates the risk of adverse effects.

Contraindications

Glycopyrrolate is contraindicated for patients with hypersensitivity to glycopyrronium, excipients, or other ingredients in the anticholinergic class. The following is a list of medical conditions that would preclude the use of anticholinergic therapy, categorized by the system:

- **Ophthalmic:** angle-closure glaucoma [20]
- **Cardiovascular:** mitral stenosis and cardiovascular instability in patients with acute hemorrhage [21]
- **Gastrointestinal:** hiatal hernia, gastrointestinal obstruction, paralytic ileus, reflux esophagitis, severe ulcerative colitis, toxic megacolon, intestinal atony in older or debilitated patients [22][23]
- **Neuromuscular:** myasthenia gravis [24]
- **Urologic:** obstructive uropathy [25]

Additionally, patients receiving solid oral potassium chloride formulations require close monitoring if coadministering with glycopyrrolate.

Monitoring

Glycopyrronium reduces the body's ability to sweat. Therefore, it may cause hyperthermia and heat stroke in hot environments. Other potential adverse effects include dry mouth, difficulty urinating, headaches, diarrhea, and constipation. Clinicians should monitor heart rate and maintain adequate hydration in patients receiving this drug.

A dose adjustment may be necessary if urinary retention occurs. Existing renal impairment may be further complicated. In the general population, administration of this medication may increase the risk of confusion, hallucinations, and anticholinergic effects.

Clinicians should administer glycopyrrolate cautiously in patients with a hiatal hernia and reflux esophagitis. This drug can worsen prostatic hyperplasia symptoms or bladder neck destruction and increase the risk of urinary retention. In patients with ulcerative colitis, a high dose may inhibit intestinal motility and worsen toxic megacolon or ileus symptoms. Glycopyrrolate administration is contraindicated for patients with ulcerative colitis. Since gastrointestinal motility may decline, constipation or intestinal pseudo-obstruction may occur. If the latter condition arises, it may result in painful abdominal distention, nausea, or vomiting. If intestinal obstruction of any type is suspected, it is imperative to discontinue use and simultaneously reevaluate. Symptoms such as diarrhea, particularly in patients who have undergone bowel resections of the ileum or colon, warrant a lower threshold for clinical suspicion. When an obstruction is suspected, or if the patient has diarrhea, promptly discontinue treatment.

Because of its quaternary structure, glycopyrrolate cannot cross the blood-brain barrier and is almost devoid of the central nervous system and ophthalmic activity. Potent inhibition of salivary gland and respiratory tract secretions is the primary rationale for using glycopyrrolate as a premedication. Heart rate usually increases after intravenous administration but not intramuscular.

Toxicity

Acute toxicity with glycopyrrolate is secondary to an extension of the pharmacologic effects on the muscarinic cholinergic receptors. Muscarinic receptor sites are located in the brain's cerebral cortex, thalamus, hippocampus, and reticular activating system. They are also present in the postganglionic parasympathetic nervous system and other sites like sweat glands. Anticholinergic agents block the effects of acetylcholine by competitively binding and blocking muscarinic receptors.

Central Nervous System Toxicity

CNS toxicity as a result of glycopyrrolate administration may also called central anticholinergic syndrome, as central nervous system toxicity can be an undesirable side effect of any anticholinergic medication. This condition manifests as delirium or prolonged somnolence after anesthesia. While this is more likely to occur with scopolamine than atropine, the incidence should

be low with proper dosages. However, older patients may be more susceptible. Glycopyrrolate is less likely to cause this condition than other anticholinergic medications because it does not cross the blood-brain barrier.

Tachycardia

The most likely response after intramuscular administration of atropine, glycopyrrolate, or scopolamine for premedication is an increase in heart rate, indicating a weak cholinergic antagonist effect of these drugs.

Treatment

According to product labeling, a quaternary ammonium anticholinesterase such as neostigmine (which does not cross the blood-brain barrier) can be given to combat peripheral anticholinergic effects parenterally in increments of 0.25 mg in adults. This may be repeated every 5 to 10 minutes until anticholinergic overactivity is reversed or up to a maximum of 2.5 mg. If CNS symptoms (eg, restlessness, excitement, psychotic behavior, convulsions) are present, physostigmine (which does cross the blood-brain barrier) should be administered. Physostigmine in doses of 0.5 to 2 mg can be administered intravenously and repeated up to 5 mg in adults. To combat hypotension, IV fluids, pressor agents, and supportive care are administered.

Enhancing Healthcare Team Outcomes

Glycopyrrolate is a medication frequently prescribed by nurse practitioners, primary care providers, anesthesiologists, and internists. All providers prescribing this agent should be aware of its potential adverse effects. Glycopyrronium may cause hyperthermia and heat stroke in hot environments as it reduces the body's ability to sweat. Clinicians should monitor liver function tests in patients with hepatic impairment. Nursing staff should monitor and inform the prescriber if urinary retention occurs or if existing renal impairment worsens. The use of glycopyrrolate in the general population may increase the risk of confusion, hallucinations, and other anticholinergic effects. Before administering glycopyrrolate therapy, nurses should counsel patients for common adverse effects like dry mouth, difficulty urinating, headaches, diarrhea, and constipation. Pharmacists should verify the dose and possible drug-disease interactions. Pharmacists should warn the patient that the medication may induce drowsiness or blurred vision, which is exacerbated by alcohol consumption. As healthcare team members, all MDs, DOs, PAs, NPs, nursing staff, and pharmacists should collaborate to improve care coordination and communicate to advance better outcomes using glycopyrrolate when indicated.

Review Questions

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