The Drug Box

from *Critical Decisions in Emergency Medicine*

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About the Editor-in-Chief

Dr. LoVecchio has been an emergency physician, medical toxicologist, and an addiction specialist for over 2 decades. He is the medical director of clinical research at Arizona State University. He also works as the principal investigator for studies of the Infectious Disease Network (IDNet), a group of emergency departments funded by the CDC to conduct infectious disease trials. He has served as vice-chair and director of research for the Maricopa Integrated Health System and University of Arizona Department of Emergency Medicine. He is board-certified in four specialties and received his master of public health from The Harvard School of Public Health. He has received more than a dozen research and teaching awards and, in 2022, was recognized as one of the world's top 2% most-cited scientists. Dr. LoVecchio has organized and participated in multiple international medical missions and has been honored locally and nationally as a health care hero and most recently received the Lifetime Achievement Award from the Phoenix Business Journal in 2025. Currently, he is performing research about drug development, drugs of abuse, COVID-19, infectious diseases, wellness, and environmental illness; he has received more than $10 million in research funding as a group.

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2023 GOLD Report for COPD

Introduction

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2023 report emphasizes that patients with chronic obstructive pulmonary disease (COPD) are at an increased risk of other medical conditions, including heart failure, ischemic heart disease, myocardial infarction, pneumonia, and gastroesophageal reflux disease.[1] The GOLD guidelines recommend spirometry, classifying patients with COPD into groups by their symptom and exacerbation history to guide treatment, and increasing therapy in a stepwise approach.

Classification

The 3 classification groups are A, B, and E. Patients in group A are less symptomatic and at a low risk of exacerbations. Patients in groups B and E are more symptomatic and at a high risk of exacerbations.

Groups B and E

Updated pharmacotherapy recommendations state that patients in groups B and E should be started on a combination of long-acting β_2 agonists (LABAs) and long-acting muscarinic antagonists (LAMAs) instead of either alone. The use of LABA and inhaled corticosteroids (ICS) (when ICS are indicated) has been phased out because triple therapy with LABA, LAMA, and ICS has been shown to be superior in reducing all-cause mortality and exacerbations in patients with moderate to severe COPD and a history of exacerbations.

Removing LABA and ICS from COPD recommendations is consistent with the current evidence that ICS are most effective when eosinophilic inflammation is present. Triple therapy is recommended if patients have a blood eosinophil count of 300 cells/µL or greater, concomitant asthma, or 2 or more COPD exacerbations in a year. If patients fall into group B with blood eosinophil counts between 100-300 cells/µL, consider their individual risks and benefits from ICS treatment and decide if this treatment is appropriate based on shared decision-making. ICS are not recommended for patients who have had multiple pneumonia events, blood eosinophil counts <100 cells/µL, or histories of mycobacterial infections.

COPD Defined

GOLD newly defines COPD as a heterogeneous lung condition characterized by chronic respiratory symptoms due to abnormalities of the airways or alveoli that

2023 GOLD Report for COPD (cont.)

cause persistent, often progressive airflow obstruction. GOLD redefines a COPD exacerbation as an event characterized by dyspnea or cough and sputum that worsens over 14 or more days and is caused by airway infection, pollution, or other insults to the airways. Tachypnea or tachycardia may accompany an exacerbation.

Group A

The latest GOLD report also outlines a new classification for exacerbation severity and recommends nonpharmacologic therapies of smoking cessation and flu and pneumococcal vaccinations for patients in group A.

For patients in group A, a long-acting rather than a short-acting bronchodilator alone is recommended (grade 2B). For patients with COPD in groups B and E, initial treatment with dual long-acting bronchodilator therapy is recommended instead of a single long-acting bronchodilator alone (grade 2C).

Reference

1. Agustí A, Celli BR, Criner GJ, et al. Global Initiative for Chronic Obstructive Lung Disease 2023 report: GOLD executive summary. *Am J Respir Crit Care Med.* 2023 Apr 1;207(7):819-837.

Drug Box

Acetaminophen (IV)

Introduction
IV acetaminophen is a nonopioid analgesic that is safe in pediatric and adult patients. The addition of acetaminophen (IV or PO) to morphine following major surgery results in a statistically significant decrease in postoperative morphine use. NSAIDs combined with acetaminophen appears to be more effective than NSAIDs alone for the treatment of postoperative pain. A dose of acetaminophen 100 mg IV costs $10-$40.

Mechanism of Action
Acetaminophen's exact mechanism is unknown; however, its reduction of prostaglandin appears to play a role.

Pharmacokinetics
- ***Onset of effect:*** 5-10 min
- ***Time to peak concentration:*** 15 min
- ***Oral or rectal onset of effect:*** ≥10-60 min

Indications
- Treatment of mild to moderate pain
- Treatment of moderate to severe pain with adjunctive opioid analgesics
- Fever reduction
- Patients in whom oral or rectal administration is not an option

Dosing
- Adults >50 kg (110 lb)
  - 650 mg every 4 hr or 1,000 mg every 6 hr
  - Max single dose of 1,000 mg
  - Should not exceed 4 g/d
- Children >2 yr; adolescents and adults <50 kg (110 lb)
  - 15 mg/kg every 6 hr or 12.5 mg/kg every 4 hr
  - Max single dose of 15 mg/kg
  - Should not exceed 75 mg/kg/d
  - A reduced or modified dose should be used for hepatic insufficiency, chronic alcoholism, malnutrition, or dehydration.
  - For severe renal insufficiency (creatinine clearance ≤30 mL/min), give usual dose <6 hr.

Acetaminophen (IV) (cont.)

Side Effects (IV Acetaminophen vs Placebo)

- Nausea (34% vs 31%), vomiting (12% vs 11%)
- Headache (10% vs 9%), insomnia (7% vs 5%)
- Associated with a transient reduction in blood pressure in the critically ill, although other studies refute clinically relevant adverse events with infusion
- Not linked to an increased risk of nausea, vomiting, and respiratory depression (which can occur with opioids) or platelet dysfunction, gastritis, and renal toxicity (which can occur with NSAIDs).

Contraindications and Precautions

Contraindicated in patients with severe hepatic insufficiency, severe progressive liver disease, and known hypersensitivity to acetaminophen

Drug Box

Acetazolamide

Introduction

Acetazolamide is used to treat glaucoma, epilepsy, and altitude sickness. It may be used long-term for the treatment of open-angle glaucoma and short-term for acute angle-closure glaucoma until surgery can be performed. Acetazolamide is a diuretic and carbonic anhydrase inhibitor. Its main mechanism of action is decreasing the amount of hydrogen ions and bicarbonate in the body.

Historically, acetazolamide has been used to treat periodic paralysis, heart failure, and menstrual-related epilepsy and to relieve symptoms associated with dural ectasia in individuals with Marfan syndrome. It has also been used to prevent methotrexate-induced kidney damage by alkalinizing urine; however, this use of acetazolamide is no longer recommended. Off-label uses are numerous and may include use as a respiratory stimulant in stable hypercapnic chronic obstructive pulmonary disease or use in altitude illness to speed acclimatization if abrupt ascent is unavoidable.

Dosing

- ***Altitude illness:*** 500-1,000 mg/d PO in divided doses every 8-12 hr (immediate-release tablets) or divided every 12-24 hr (extended-release capsules). To reduce side effects, a recommended alternative dose is 125 mg twice daily, beginning either the day before (preferred) or the day of ascent. In situations of rapid ascent (such as rescue or military operations), 1,000 mg/d is recommended, with the addition of dexamethasone. The pediatric dose is 2.5-5 mg/kg/d in divided doses, up to 125 mg, 2 times a day.
- ***Secondary or acute (angle-closure) glaucoma:*** initial dose of 250-500 mg. Maintenance dose of 125-250 mg every 4 hr. Short-term treatment with 250 mg every 12 hr has been effective for some patients.

Side Effects

- Common adverse effects:
  - Paresthesia, fatigue, drowsiness, depression, and decreased libido
  - Bitter or metallic taste (especially when drinking carbonated drinks), nausea, vomiting, abdominal cramps, diarrhea, and black feces
  - Polyuria and kidney stones
  - Metabolic acidosis and electrolyte changes (hypokalemia, hyponatremia)