ANTICHOLINERGICS

FLAME LECTURE:

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LEARNING OBJECTIVES

- To understand the use of anticholinergics in the management of COPD
- To describe the mechanism of action of anticholinergics
- Prerequisites:
  - NONE
- See also – for closely related topics
  - FLAME LECTURE: SABA IN COPD
  - FLAME LECTURE: LABA IN COPD

OVERVIEW

- Goal of therapy in COPD is to reduce airway resistance
  - Bronchodilators (both anticholinergics and beta adrenergic agonists) are effective at reversing airway obstruction that is due to bronchial smooth muscle constriction
  - However, inhaled anticholinergics, *specifically Ipratropium*, are preferred to β_2 agonists for maintenance therapy of COPD due to minimal cardiac stimulating effects
    - Studies have also shown greater effectiveness than either beta-agonists or methylxanthine bronchodilators

MECHANISM OF ACTION

- Inhaled anticholinergics act as antagonists on Muscarinic Receptors in the lungs, which are part of the parasympathetic nervous system
  - M1 receptors are found on peri-bronchial ganglion cells and transmit signals from the preganglionic nerves to the postganglionic nerves
  - M2 receptors are found on the postganglionic nerves
  - M3 receptors are found mainly on smooth muscle
- Inhibition of the M1 and M3 receptors decreases mucous secretions and prevents bronchoconstriction
- M2 receptor activation also prevents bronchoconstriction, so the ideal anticholinergic or antimuscarinic effect would be to inhibit M1 and M3 only (like tiotroprium)

INDICATIONS & BENEFITS

- In pts with mild disease, a short-acting agent (ipratropium) is indicated for use on a PRN basis. It has been shown to reduce symptoms, improve lung function, increase exercise capacity, decrease dyspnea and decrease cough
- In pts with more severe (but stable) disease, daily use with a long-acting agent is beneficial. Tiatropium has been shown to decrease frequency of exacerbation, improve lung function, decrease dynamic hyperinflation, slow the rate of decline in FEV_1 and even improve FEV_1
- Use of anticholinergics in conjunction with beta-agonists has been shown to have an ADDITIVE effect and has been shown to be beneficial during a COPD exacerbation (ex. Duonebs)
- Unfortunately, there has been no documented benefit to mortality in COPD with anticholinergics

ADVERSE EFFECTS

- May cause dry mouth, blurred vision, photophobia, tachycardia, and mental confusion in the elderly
  - "Hot as a hare, red as a beet, dry as a bone, blind as a bat, and mad as a hatter"
- Cardiovascular – there has been some concern for adverse cardiovascular events with use of ipratropium or long-acting muscarinic antagonists (LAMA)
  - No definitive evidence exists, and there is a need for randomized trials with specifically defined cardiovascular endpoints. In the mean time potential cardiac risks must be weighed against known respiratory benefits
- Acute urinary retention or UTI can occur in susceptible patients (BPH, lower urinary tract symptoms). Caution should be used in these patients and renal function and urine output should be monitored
- Bronchitis or exacerbation of COPD symptoms can occur in some patients with use of anticholinergics

CONTRAINDICATIONS

- Hypersensitivity to ipratropium, atropine, or any of its derivatives
- Use with caution in patients with narrow-angle glaucoma as this may increase intraocular pressure
- Also use caution in patients with known bladder outlet obstruction or GI obstruction

REFERENCES

1. Role of Anticholinergic Therapy in COPD

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2. Chronic Obstructive Pulmonary Disease: Diagnosis and Management

(https://www.aafp.org/afp/2017/0401/p433.html)

3. Medications for COPD: A Review of Effectiveness

(https://www.aafp.org/afp/2007/1015/p1141.html)