

MUSCARANIC ANTAGONISTS (ANTICHOLINERGICS)

FLAME LECTURE: 30

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LEARNING OBJECTIVES

- ▶ To understand the use of anticholinergics in the management of Asthma
- ▶ To describe the mechanism of action of anticholinergics
- ▶ Prerequisites:
 - ▶ NONE
- ▶ See also – for closely related topics
 - ▶ FLAME LECTURE 27: SABA IN ASTHMA
 - ▶ FLAME LECTURE 34: ASTHMA EXACERBATION

OVERVIEW

- ▶ While currently not featured in the standard step-wise approach to asthma maintenance management, anticholinergics are primarily used to reduce airway resistance during an acute exacerbation
 - ▶ Bronchodilators (both anticholinergics and beta adrenergic agonists) are effective at reversing airway obstruction that is due to bronchial smooth muscle constriction
 - ▶ While, short-acting inhaled anticholinergics only utilized in exacerbation, long-acting agents can have a role in the management of severe asthma, and may be added to the step-wise management plan in the future

MECHANISM OF ACTION

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

INDICATIONS / BENEFITS

- ▶ A short acting anticholinergic in combination with a SABA in the ED results in fewer hospital admissions during moderate-to-severe exacerbations
- ▶ For those with severe disease, daily use with a long-acting agent, like Tiotropium, can be considered
 - ▶ Show to reduce exacerbations when added to inhaled glucocorticoids in place of a LABA. There is no data showing added on top of a LABA + inhaled glucocorticoids
 - ▶ Tiotropium has selectivity at the M1 and M3 receptors, which in theory may be superior to ipratropium given it does not inhibit M2-mediated bronchodilation

ADVERSE EFFECTS

EASY MNEMONIC

- ▶ Blind as a bat (mydriasis – dilated pupils, blurry vision)
- ▶ Hot as a desert (hyperthermia)
- ▶ Red as a beat (flushed skin)
- ▶ Dry as a bone (dry mouth and urinary retention)
- ▶ Mad as a hatter (confused; especially elderly)
- ▶ And more on the next slide...

ADVERSE EFFECTS

OTHER

- ▶ In addition to tachycardia, there has been some concern for adverse cardiovascular events with use of ipratropium and with 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 needs to 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 intestinal partial/complete obstruction

REFERENCES

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