ANTICHOLINERGICS

Physiology

- Anticholinergics reversibly antagonize the action of acetylcholine.

- Two major subtypes of cholinergic receptors: muscarinic receptors and nicotinic receptors.

Muscarinic receptors

- G protein-coupled
- found on
  - autonomic effector cells innervated by peripheral postganglionic parasympathetic nerves,
  - ganglia
  - brain

Muscarinic receptors

M1

- Found in autonomic ganglia, the brain, salivary glands, and stomach. Stimulation decreases activity in autonomic ganglia but increases secretion of saliva and gastric acid, from the salivary glands and stomach, respectively.

M2

- Found mainly in the heart. Stimulation decreases the sinus node rate, slowing conduction through the AV node, and decreases the force of atrial contraction, and possibly ventricular contraction.

M3

- Found on smooth muscle, endocrine and exocrine glands, and the iris. Stimulation produces bronchospasm, causes mild vasodilation, increases saliva and gastric acid production, and constricts the pupil.

M4 & M5

- M4 is found in the central nervous system where stimulation of the receptor subtype produces a diversity of actions; Parkinson Disease, Schizophrenia and Neuropathic pain. M5 may be involved in schizophrenia and drug dependence.

Nicotinic Receptors

- Complex structure of several subunits encoded by multiple genes.
- Combined into four main families of nicotinic receptors
- - the muscle-type- neuromuscular junction
- - the ganglion-type, autonomic ganglia;
- - two brain-types, CNS
- * Roles in neuronal development, learning and memory formation, and reward

Anticholinergics

- ***Anticholinergic* generally refers to drugs and plant toxins that act as muscarinic receptor antagonists**
- Muscarinic receptor antagonists block of acetylcholine binding
- Effects from antagonism of the nicotinic cholinergic system is not a component of Anticholinergic Syndrome/ Toxidrome.

Classification of Anticholinergics

- Natural alkaloids
  - Atropine (from the plant Atropa belladonna/ Deadly nightshade)
  - Hyoscine (Scopolamine) (from Hyoscyamus niger/ henbane)

    Datura stramonium (plant- Jimson weed/ Angel's Trumpet)

- Semi synthetic derivatives
  - Homatropine – eye drops
  - Tiotropium bromide- Spiriva

Classification of Anticholinergics

a) Mydriatics

Tropicamide – eye drops

b) Antisecretory -antispasmodics

Quaternary compounds

- Glycopyrrolate Tertiary amines
- Oxybutynin

c) Antiparkinsonian drugs

- Benzhexol
- Benztropine

Classification of Anticholinergics

- Miscellaneous
  - Tricyclic antidepressants

  e.g. Amitriptyline

  - Phenothiazines

  e.g. Prochlorperazine

  - Antihistamines e.g. Cyclizine

  - Neuroleptics e.g. Olanzapine

Anticholinergic Syndrome

Most common causes are

- Antihistamines
- Anticholinergic drugs including
  - atropine
  - benztropine
  - benzhexol
  - procyclidine
  - orphenadrine
- Tricyclic antidepressants (TCAs)
- Neuroleptics (in particular thioridazine and chlorpromazine)
- Carbamazepine
- Anticholinergic plants
  - Datura (Brugmansia) stramonium (Angel's trumpet)
  - Atropa belladonna (Deadly Nightshade)

Anticholinergic toxicity

- Toxidrome may be caused by
  - intentional overdose,
  - inadvertent ingestion,
  - medical noncompliance, and
  - polypharmacy.

  - Systemic effects have also resulted from topical eye drops.

Anticholinergic toxicity

- The range of toxicity is highly variable and unpredictable. in healthy adults

- Rate of absorption varies depending on the drug and the route of exposure

  -e.g. the duration of toxic effects in benztropine intoxication may last for 2–3 days

- Onset usually within 30 mins to 2 hours. Symptoms are dose-dependant,

  - usually last between 2 to 7 days (up to 1month)

Clinical Presentation

Central anticholinergic syndrome

- central effects of muscarinic receptor antagonism predominate, with fever, agitation, delirium, and coma.

Peripheral anticholinergic syndrome

- peripheral effects such as tachycardia, flushed dry skin, dry mouth, ileus, and urinary retention.

Management

- - Majority of cases require only supportive care.
- - Initial management should follow the same approach regardless of the poison involved:

  - A B C D Es

- <u>Airway</u>

  Protect airway early in patients with severe intoxication (e.g. seizures, severe delirium).

- Hypoactive gut increases risk of aspiration.

Management

- Breathing

Should be assessed by Observation

- Pulse Oximetry
- ABGs (arterial blood gases)
- (1) Hypoxia may result in brain damage, cardiac arrhythmias, and cardiac arrest.
- (2) Hypercarbia results in acidosis, which may contribute to arrhythmias, especially in patients with salicylate or tricyclic antidepressant overdoses.
- Patients with respiratory insufficiency should be intubated and mechanically ventilated.

Management

- Circulation
- IV access should be secured
- Continuous monitoring of
  - pulse rate,
  - blood pressure
  - urinary output, and
  - evaluation of peripheral perfusion.

- Obtain an ECG and institute continuous cardiac monitoring in patients with moderate to severe toxicity (e.g, agitation, delirium, seizures, coma and hypotension).