Cholinergic Muscle Stimulants (Parasympathomimetics)

Mechanism of Action:
Cholinergic agents increase acetylcholine’s duration at the cholinergic nicotinic receptor site by inhibiting the hydrolysis of acetylcholine by the enzyme acetylcholinesterase. This facilitates the transmission of impulses at the myoneural junction and enhances muscular strength and response to repetitive nerve stimulation.

Indications for Use:
These agents are indicated for use in the diagnosis and treatment of myasthenia gravis and for reversal of nondepolarizing muscle relaxants.

Contraindications for Use:
Hypersensitivity to these drugs, intestinal and urinary obstructions.

Precautions:
1. Use with extreme caution in pts with asthma, epilepsy, bradycardia, recent coronary occlusion, hyperthyroidism, cardiac arrhythmias, or peptic ulcer disease.
2. Anticholinesterase insensitivity may occur with repeated use of these drugs. Reduce or withhold dosage until the pt again becomes sensitive. Monitor pt for myasthenic crisis.
3. Have atropine sulfate available for possible overdose or when large doses are given, prior injection of atropine is recommended.

Adverse Reactions:
CNS: Convulsions, dysphonia, dizziness, drowsiness, loss of consciousness, headache.
Cardiovascular: Bradycardia, tachycardia, other arrhythmias, decreased cardiac output, hypotension, cardiac arrest, syncope.
Pulmonary: Increased tracheobronchial secretions, laryngospasm, bronchoconstriction, dyspnea, respiratory depression, respiratory arrest.
GI: Increased salivary, gastric and intestinal secretions, nausea, vomiting, dysphagia, increased peristalsis, diarrhea, abdominal cramps.
Misc: Urinary frequency and urgency, diaphoresis, rash, flushing.

Overdosage:
Marked pronouncement of parasympathomimetic actions; arrhythmias, increased GI stimulation, abdominal cramps, diarrhea, vomiting, excessive salivation, blurring of vision, paralysis of voluntary muscles. Treatment consists of discontinuance of all cholinergic meds and administering from 0.5-1.0 mg of atropine IV. A total dose of 5-10 mg of atropine may be needed. Monitor pt for supportive treatment, e.g., assisted ventilation, intubation O₂, etc.

Generic name: Edrophonium Chloride
Brand names: Tensilon, Enlon, Reversol
Indication: Used in the diagnosis of MG; however, due to its short duration, edrophonium is not useful in the maintenance or continued treatment of myasthenic pts. This drug is also used as a nondepolarizing muscle relaxant antagonist.

Onset of action: <1 min IV; 2-10 min IM
Duration: ≈5-20 min IV; ≈10-40 min IM
Dosage form: IV, IM solution: 10 mg/ml
Dosage: For diagnosis:
Adults: Inject 2 mg IV in 15-30 sec; if no reaction occurs, inject 8 mg more. Test may be repeated after 30 min. Myasthenic pts will show an increase in muscle strength in 1-3 min which lasts 5-10 min. If a cholinergic reaction occurs (increased Muscarinic side effects; muscle weakness), discontinue test and administer atropine 0.4-0.5 mg IV.

Children: <34 kg, inject 1 mg. >34 kg, inject 2 mg. If no reaction occurs, an additional dose of up to 5 mg in children <34 kg, and up to 10 mg in children > 34 kg should be given.

For differential diagnosis of myasthenic crisis vs cholinergic crisis:
Adults: inject 1-2 mg; if the crisis is myasthenic, the test will clearly improve respirations. If the crisis is cholinergic (indicating an overdose of the drug), edrophonium will increase secretions and further weaken respiratory muscles. Initiate this test only if assisted ventilation and intubation are immediately available.

Generic name: Neostigmine
Brand names: Prostigmin
Indication: For control and treatment of MG. Corticosteroids may be used as an adjunct in severe cases. Neostigmine is also used as an antidote for nondepolarizing neuromuscular blocking agents.

Onset of action: 4-8 min IV; 20-30 min IM; 45-75 min PO
Duration: 2-4 hrs IV, IM, PO
Dosage form: IV, IM, SC solution: 0.25 mg/ml in 1 ml vials; 0.5 mg/ml in 1 & 10 ml vials; 1 mg/ml in 1 ml vials
PO: 15 mg tablets

Dosage: Adults:
IM, SC: 0.5 mg; adjust dosage according to pt response
IV: 1 mg in 100 ml NaCl infused at 25 ml/hr
PO: Varies from 15-375 mg/day according to pt response. Average dose is 150 mg/day.
Children:
IV, IM, SC: 0.01-0.04 mg/kg q2-4h prn
PO: 2 mg/kg daily, in divided doses

Other drugs used to treat myasthenia gravis:

Ambenonium chloride: Mytelase
Pyridostigmine bromide: Mestinon, Regonol
Physostigmine salicylate: Antilirum