Adrenergic and anti-adrenergic drugs

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Sympathetic nervous system

Fight or flight response results in:
1. Increased BP
2. Increased blood flow to brain, heart and skeletal muscles
3. Increased muscle glycogen for energy
4. Increased rate of coagulation
5. Pupil dilation
Adrenergic receptors

- Alpha—A1 and A2
- Beta—B1, B2, B3
- Dopamine—subsets D1-5
Review of functions of sympathetic nervous system receptors

- Alpha 1—smooth muscle contraction
- Alpha 2—negative feedback causes less norepinephrine to be released so BP is reduced
- Beta 1—increased heart rate
- Beta 2—bronchodilation
- Beta 3—actual site for lipolysis
Mechanisms of action and effects of adrenergic drugs

• Direct adrenergic drug action
• Affects postsynaptic alpha 1 and beta receptors on target effector organs
• Examples: epinephrine, Isuprel, norepinephrine, phenylephrine
Mechanisms of action cont.

• 2. Indirect adrenergic drug action occurs by stimulation of postsynaptic alpha 1, beta 1 and beta 2 receptors. Cause release of norepinephrine into the synapse of nerve endings or prevent reuptake of norepinephrine.

• Examples include cocaine and TCAs
Mechanisms of action cont.

• 3. mixed action. Combination of direct and indirect receptor stimulation

• Examples are ephedrine and pseudoephedrine
Mechanisms of action cont.

- Stimulation of alpha 2 receptors in CNS is useful in decreasing BP
- Most body tissues have both alpha and beta receptors
- Effect occurs secondary to receptor activated and number of receptors in the particular body tissue
• Some drugs act on both receptors--dopamine
• Some are selective--Isuprel
Indications for use

- Emergency drugs in treatment of acute cardiovascular, respiratory and allergic disorders
- In children, epinephrine may be used to treat bronchospasm due to asthma or allergic reactions
- Phenylephrine may be used to treat sinus congestion
Indications of adrenergics cont.

- Stokes Adams
- Shock
- Inhibition of uterine contractions
- For vasoconstrictive and hemostatic purposes
Contraindications to use of adrenergics

- Cardiac dysrhythmias, angina pectoris
- Hypertension
- Hyperthyroidism
- Cerebrovascular disease
- Distal areas with a single blood supply such as fingers, toes, nose and ears
- Renal impairment use caution
Individual adrenergic drugs

• *Epinephrine*—prototype

• Effects include: increased BP, increased heart rate, relaxation of bronchial smooth muscle, vasoconstriction in peripheral blood vessels
epinephrine

- Increased glucose, lactate, and fatty acids in the blood due to metabolic effects
- Increased leukocyte and increased coagulation
- Inhibition of insulin secretion
epinephrine

- Affects both alpha and beta receptors
- Usual doses, beta adrenergic effects on heart and vascular smooth muscle will predominate, high doses, alpha adrenergic effects will predominate
- Drug of choice for bronchospasm and laryngeal edema of anaphylaxis
epinephrine

- Excellent for cardiac stimulant and vasoconstrictive effects in cardiac arrest
- Added to local anesthetic
- May be given IV, inhalation, topically
- Not P.O
epinephrine

- Physiologic antagonist to histamine
- Those on beta blockers may need larger doses
- Drug of choice in PEA. Vasopressin has now become drug of choice in ventricular tachycardia
- Single dose of Vasopressin, 40 units IV
Other adrenergics

• Ephedrine is a mixed acting adrenergic drug. Stimulates alpha and beta receptors. Longer lasting than epinephrine.
• See in Primatene mist
Pseudophedrine

- Used for bronchodilating and nasal decongestant effects
isuprel (Isoproterenol)

- Synthetic catecholamine that acts on beta 1 and 2 receptors
- Stimulates heart, dilates blood vessels in skeletal muscle and causes bronchodilation
- No alpha stimulation
- Used in heart blocks (when pacemaker not available) and as a bronchodilator
Neosynephrine (Phenylephrine)

- Pure alpha
- Decreases CO and renal perfusion
- No B1 or B2 effects
- Longer lasting than epinephrine
- Can cause a reflex bradycardia
- Useful as a mydriatic
Toxicity of adrenergics in critically ill patients

- Affects renal perfusion
- Can induce cardiac dysrhythmias
- Increases myocardial oxygen consumption
- May decrease perfusion of liver
- Tissue necrosis with extravasation
Anti-adrenergics

- Sympatholytic
- Block or decrease the effects of sympathetic nerve stimulation, endogenous catecholamines and adrenergic drugs
Antiadrenergic s—mechanisms of action and effects

- Can occur by blocking alpha 1 receptors postsynaptically
- Or by stimulation presynaptic alpha 2 receptors. Results in return of norepinephrine to presynaptic site. Activates alpha 2 resulting in negative feedback. Decreases release of additional norepinephrine.
Alpha-Adrenergic Agonists and blocking agents

• Alpha 2 agonists inhibit release of norepinephrine in brain; thus, decrease effects on entire body
• Results in decrease of BP
• Also affects pancreatic islet cells, thus some suppression of insulin secretion
Alpha 1 adrenergic blocking agents

- Act on skin, mucosa, intestines, lungs and kidneys to prevent vasoconstriction
- Effects: dilation of arterioles and veins, decreased blood pressure, pupillary constriction, and increased motility of GI tract
Alpha 1 adrenergic blocking agents

• May activate reflexes that oppose fall in BP such as fluid retention and increased heart rate

• Can prevent alpha medicated contraction of smooth muscle in nonvascular tissues

• Thus, useful in treating BPH as inhibit contraction of muscles in prostate and bladder
Alpha 1 antagonists

- Minipress (prazosin)—prototype.
- Hytrin (terazosin) and Cardura (doxazosin)—both are longer acting than Minipress.
Alpha 1 antagonists cont.

- **Flomax (tamsulosin).** Used in BPH. Produces smooth muscle relaxation of prostate gland and bladder neck. Minimal orthostatic hypotension.

- **Priscoline (tolaxoline).** Used for vasospastic disorders. Pulmonary hypertension in newborns. Can be given sub Q, IM or IV.
Alpha 2 agonists

- Catapres (clonidine). PO or patch.
- Tenex (guanfacine)
- Aldomet (methyldopa). Can give IV. Caution in renal and hepatic impairment.
Beta adrenergic blocking medications

• Prevent receptors from responding to sympathetic nerve impulses, catecholamines and beta adrenergic drugs.
Effects of beta blocking drugs

- Decreased heart rate
- Decreased force of contraction
- Decreased CO
- Slow cardiac conduction
- Decreased automaticity of ectopic pacemakers
Effects of beta blocking drugs

- Decreased renin secretion from kidneys
- Decreased BP
- Bronchoconstriction
- Less effective metabolism of glucose. May result in more pronounced hypoglycemia and early s/s of hypoglycemia may be blocker (tachycardia)
Effects of beta blocking agents

- Decreased production of aqueous humor in eye
- May increase VLDL and decrease HDL
- Diminished portal pressure in clients with cirrhosis
Indications for use

- Alpha 1 blocking agents are used for tx of hypertension, BPH, in vasospastic disorders, and in persistent pulmonary hypertension in the newborn
- May be useful in treating pheochromocytoma
- May be used in Raynaud’s or frostbite to enhance blood flow
Regitine (phentolamine)

- Used for extravasation of potent vasoconstrictors (dopamine, norepinephrine) into subcutaneous tissues
Indications for use

- Alpha 2 agonists are used for hypertension—Catapres
- Epidural route for severe pain in cancer
- Investigationally for anger management, alcohol withdrawal, postmenopausal hot flashes, ADHD, in opioid withdrawal and as adjunct in anesthesia
Beta blocking medications

• Mainly for cardiovascular disorders (angina, dysrhythmias, hypertension, MI and glaucoma)
• In angina, beta blockers decrease myocardial oxygen consumption by decreasing rate, BP and contractility. Slow conduction both in SA node and AV node.
Beta blockers

- Possibly work by inhibition of renin, decreasing cardiac output and by decreasing sympathetic stimulation
- May worsen condition of heart failure as are negative inotropes
- May reduce risk of “sudden death”
Beta blockers

• Decrease remodeling seen in heart failure
• In glaucoma, reduce intraocular pressure by binding to beta-adrenergic receptors in ciliary body, thus decrease formation of aqueous humor
Beta blockers

- Inderal (propranolol) is prototype
- Useful in treatment of hypertension, dysrhythmias, angina pectoris, MI
- Useful in pheochromocytoma in conjunction with alpha blockers (counter catecholamine release)
- migraines
Beta Blockers

• In cirrhosis, Inderal may decrease the incidence of bleeding esophageal varices
• Used to be contraindicated in heart failure, now are standard
• Known to reduce sudden death
• Often given with ACEIs
• Indications include: htn, angina, prevention of MI