AACN PCCN Review

Cardiovascular Pharmacology

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# Cardiovascular Pharmacology – Vasoactive & Inotropic Agents

## I. PHYSIOLOGICAL PRINCIPLES

<table>
<thead>
<tr>
<th>Physiology of the Autonomic Nervous System</th>
<th>Sympathetic</th>
<th>Parasympathetic</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Purpose to Regulate Autonomic Function</strong></td>
<td>• Activation: Flight or Fight Responses</td>
<td>• Conservation: Maintain Organ Function and Conserve Energy</td>
</tr>
<tr>
<td><strong>Motor Neurons</strong></td>
<td>• Large and Diffuse Number of Postganglionic Stimulation</td>
<td>• Narrow and Specific Postganglionic Stimulation</td>
</tr>
<tr>
<td><strong>Neurotransmitters</strong></td>
<td>• Norepinephrine</td>
<td>• Acetylcholine</td>
</tr>
</tbody>
</table>
| **Receptors** | • Adrenergic:  
  o Alpha  
  o Beta  
  o Throughout body | • Cholinergic:  
  o Nicotinic  
  o Muscarinic  
  o Specific areas |
| **Innervation** | • Heart, Blood Vessels, Glands, Visceral Organs & Smooth Muscles | • Heart, Glands, & Visceral Organs |

### Autonomic Receptor Stimulation

<table>
<thead>
<tr>
<th>ORGAN</th>
<th>SYMP Receptor</th>
<th>ADRENERGIC Response</th>
<th>PARA Receptor</th>
<th>CHOLINERGIC Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart</td>
<td>Beta 1</td>
<td>• Increase Conduction Velocity (rate) &amp; Increase Contractility</td>
<td>Muscarinic 2</td>
<td>• Decrease Conduction Velocity &amp; Contractility</td>
</tr>
</tbody>
</table>
| Lungs   | Beta 2        | • Bronchial Dilation  
  • Decrease Secretions | Muscarinic 2 | • Bronchial constriction  
  • Increase Secretions |
| Vessels | Alpha 1, Beta 2 | • Constriction  
  • Dilation | Muscarinic 3 | • Relaxes |
| Skeletal Muscle | Beta 2 | • Increase Contractility | | |
| Bladder Sphincter | Alpha 1 | • Contraction | Muscarinic 3 | • Increase  
  • Relax |
| GI: Motility Sphincter | Alpha 1, B2 | • Decrease  
  • Contraction | Muscarinic 3 | | |
| Kidney  | Beta 1        | • Rennin Secreted | | |
| Liver   | Alpha 1, B2   | • Increase Glucose | | |
II. COMMON VASOPRESSOR & INOTROPIC AGENTS

<table>
<thead>
<tr>
<th>Inotropes</th>
<th>Vasopressors</th>
<th>Vasodilators</th>
<th>Beta Agonist &amp; Antagonists</th>
</tr>
</thead>
</table>
| • Digoxin (Lanoxin)  
• Amrinone Lactate (Inocor)  
• Milrinone (Primacor)  
• Dobutamine Hydrochloride (Dobutrex) | • Epinephrine  
• Norepinephrine Bitartrate (Levophed)  
• Dopamine Hydrochloride (Intropin)  
• Phenylephrine (Neosynephrine)  
• Vasopressin | • Sodium Nitroprusside (Nipride)  
• Nitroglycerin  
• Calcium Channel Blockers | • Isoproterenol Hydrochloride (Isuprel)  
• Normodyne (labetalol)  
• Brevibloc (esmolol) |

**Dopamine Hydrochloride (Dopamine)**

**Therapeutic Use**
Naturally occurring catecholamine and precursor to norepinephrine, also serves as a central and peripheral neurotransmitter. First line agent for many types of shocks states. Versatile drug secondary to different actions depending on delivered concentration. The stimulation of dopaminergic receptors is a unique property of this agent.

**Pharmacokinetics**
IV administration only with short half life

**Pharmacodynamics**
- a. Central and peripheral nervous system neurotransmitter and precursor of norepinephrine
- b. Low concentration: vascular D\textsubscript{2} – dopaminergic receptors primarily in renal, mesenteric, coronary and cerebral beds – cause vasodilation. D\textsubscript{1} receptors mediate a mild natriuresis. Current research has demonstrated that even with 1mcg most people will also get some alpha or beta stimulation.
- c. Moderate concentrations: beta\textsubscript{1} adrenergic receptor agonist – positive inotropic effect
- d. High concentrations: alpha\textsubscript{1} adrenergic receptor agonist – potent vasoconstriction

**Hemodynamics (dose dependent)**
- a. Low concentration: increase in UO, maybe some increase in HR or SBP (current research has not shown this to be renally protective)
- b. Moderate concentrations: increase in HR, SBP, CO (mild)
- c. High concentrations: increase in SBP, DBP, SVR

**Mixing and Dosing**
- a. Typical 400mg/250 D5W or NS
- b. Dosed in mcg/kg/min
- c. 1-3mcg/kg/min low dose
- d. 3-5mcg/kg/min mid dose
Norepinephrine Bitartrate (Levophed)

**Therapeutic Use**
Endogenous catecholamine with powerful inotropic and peripheral vasoconstriction effects. Typically not utilized as first line drug due to strong vasoconstrictive properties.

**Pharmacokinetics**
IV administration only with short half life

**Pharmacodynamics:**
- Potent $\alpha_1$ & $\alpha_2$ agonist
- Mild $\beta_1$ agonist
- No effect on $\beta_2$
- Systemic arterial and venous constriction
- Coronary flow increases slightly

**Hemodynamics**
- Increase in SBP & DBP
- Increase in SVR and PVR
- Cardiac output unchanged or decreased (increase in afterload)
- Heart rate may slow from compensatory vagal reflex

**Dosing and Mixing**
- Typical 4mg/250 D5W
- Dosed in mcg/min
- 2-10mcg/min

Epinephrine Hydrochloride

**Therapeutic Use**
Endogenous catecholamine with powerful inotropic, peripheral vasoconstriction effects and inotropic properties. Typically not utilized as first line drug due to profound vasoconstrictive and subsequent side effects.

**Pharmacokinetics**
Short half life with rapid onset

**Pharmacodynamics**
- Alpha and Bata agonist
- Increases myocardial contractility
- Vasoconstriction (all beds)
- Increases myocardial $O_2$ consumption
**Hemodynamics**
a. Increases HR, MAP, CO, SVR, PVR
b. Pro-arrhythmic

**Mixing and Dosing**
a. Typical 2mg/250 D5W or NS up to 8mg/250
b. Dosed in mcg/min
c. 1-4mcg/min

**Vasopressin**

**Therapeutic Use**
Is a naturally occurring antidiuretic hormone. In unnaturally high doses it functions as a non-adrenergic peripheral vasoconstrictor. Major use is as a first line agent in ACLS for pulseless VT/V-fib. Shown to reduce or eliminate the need for catecholamine administration.

**Pharmacokinetics**
a. IV administration only
b. Half life 10-20 min

**Pharmacodynamics**
a. Direct stimulation of smooth muscle V₁ receptors
b. Smooth muscle constriction: pallor of skin, nausea, intestinal cramps, desire to defecate, bronchial constriction, uterine contraction
c. Less constriction of coronary and renal vascular beds and vasodilation of cerebral vasculature
d. No skeletal muscle vasodilation or increased myocardial O₂ consumption during CPR because there is no Beta-adrenergic activity
e. May enhance platelet aggregation in septic shock

**Hemodynamics**
a. Increase in SBP, MAP and SVR
b. Increase UO

**Mixing and Dosing**
a. Typical 200U/250 D5W or NS
b. Dosed in unit/min
c. 0.2-0.9U/min

**Dobutamine**

**Therapeutic Use**
Synthetic catecholamine which has selective beta adrenergic agonist properties. Effective as a positive inotropic for both preload and afterload reduction. Used for its positive inotropic
properties when vasoconstriction is not preferable. Also used commonly as a combination therapy with another catecholamine or vasodilator

**Pharmacokinetics**
- IV administration only  
- half life 2 minutes – rapid onset

**Pharmacodynamics**
- $\beta_1$ adrenergic receptor agonists: increases contractility and stroke volume, increases sinus node automaticity and AV conduction, increases in myocardial oxygen demand  
- Mild $\beta_2$ adrenergic receptor agonist: mild vasodilation, increased perfusion  
- Mild $\alpha_1$ vasoconstriction properties are counter balanced by $\beta_2$ properties  
- Does not cause release of endogenous norepinephrine  
- Infusions of > 72 hrs have shown tolerance to down regulation of $\beta$ adrenergic receptors  
- Less effective in patients receiving $\beta$ blocking agents or with chronic heart failure

**Hemodynamics**
- Increase CO  
- Mild decrease in SVR  
- Mild increase in HR (sometimes more than mild)

**Mixing and Dosing**
- Typical 500mg/250 D5W or NS  
- Dosed in mcg/kg/min  
- 2-10mcg/kg/min

**Milrinone (Primacor)**

**Therapeutic Use**
Synthetic noncatecholamine agent that does not stimulate or block adrenergic receptors. Inhibits the phosphodiesterase III enzyme. Effective as a positive inotrope and vasodilator.

**Pharmacokinetics**
- IV administration only  
- Hepatically cleared  
- Half life 2-3 hours

**Pharmacodynamics**
- Phosphodiesterase III enzyme inhibitor – increases cyclic adenosine monophosphate (cAMP) which enhances calcium entry into the cell and improves myocardial contractility, and inhibiting vasoconstriction (vasodilator).  
- Increased cardiac output by positive inotropic action and reduction in preload and afterload  
- Most effective with patients who have over stimulated sympathetic system  
- Effective in patients with beta receptor down regulation
Hemodynamics
a. Increase in CO
b. Decrease in CVP, SVR, PAOP
c. No significant effect on HR or BP (unless compensatory)

Mixing and Dosing
a. Mix with NS ONLY
b. Dosed in mcg/kg/min
c. Loading dose 50mcg/kg over 10 min
d. 0.375-0.75mcg/kg/min

Review ALL ACLS drugs and algorithms when studying for the PCCN Exam.