Titrating Vasoactive Drugs
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Rules for Use of Vasoactive Drugs

Titrating Vasoactive Drips

- Vasoactive medications are indicated when the SBP has a decrease of > 30mmHg from the baseline or a MAP < 60mmHg and when either condition results in end-organ dysfunction due to hypoperfusion.
- The correction of hypovolemia should be corrected prior to initiating vasopressors.
smaller combined doses of inotropes and vasopressors may be advantageous over a single agent used at higher doses to avoid dose-related adverse effects.

the use of vasopressin at low to moderate doses may allow catecholamine sparing. may be particularly useful in settings of catecholamine hyposensitivity and after prolonged critical illness.

In cardiogenic shock complicating AMI, recommend dopamine or dobutamine as first-line agents with moderate hypotension (systolic blood pressure 70 to 100 mm Hg). Norepinephrine as the preferred therapy for severe hypotension (SBP 70 mm Hg).
• routine inotropic use is not recommended for end-stage HF
• when use is essential, every effort should be made to either reinstitute stable oral therapy as quickly as possible or use destination therapy such as cardiac transplantation or LV assist device support

Titrating Vasoactive Drips

• One vasoactive medication can stimulate more than one receptor.
• dobutamine increases cardiac output by activating the beta-1 adrenergic receptors;
• it also activates the beta-2 adrenergic receptors and causes vasodilation and may cause hypotension

Titrating Vasoactive Drips

• Some vasoactive medications have dose dependent response.
• dopamine stimulates beta-1 adrenergic receptors at doses of 2 to 10 mcg/kg/min
• at doses greater than 10mcg/kg/min, stimulates the alpha adrenergic receptors
Other vasoactive medications can affect MAP both by direct actions on adrenergic receptors and by reflex actions triggered by the pharmacologic response. Norepinephrine stimulates the beta-1 adrenergic receptors, normally this would cause tachycardia. The elevated MAP from norepinephrine's alpha adrenergic receptor-induced vasoconstriction results in a reflex decrease in heart rate.

**Titrating Vasoactive Drips**

- Fluid Resuscitation
  - Adequate intravascular volume should be repleted prior to initiating vasopressors.
  - Fluids may be held in hypotensive patients with pulmonary edema or CHF.
  - Most patients with septic shock require at least 2 liters of IV fluid in order for vasopressors to be maximally effective.

- The initial vasopressor should be based upon the suspected underlying cause of shock.
- Dose should be titrated up to achieve effective blood pressure or end organ perfusion as evidenced by such criteria as urine output or mentation.
Titrating Vasoactive Drips

• if the first agent is at the maximum dose and the response is inadequate a second agent should be added in ADDITION to the first.
• in certain situations, such as refractory septic shock, the addition of a second agent may remain to be ineffective and a third agent may be added.

Titrating Vasoactive Drips

• responsiveness to vasoactive medications may decrease over time due to tachyphylaxis, which is a decrease in the response due to previous exposure.
• patients in critical care also receive subcutaneously injected medications, such as heparin and insulin.
  - bioavailability of these medications may be reduced during treatment with vasoactive medications due to cutaneous vasoconstriction.

Titrating Vasoactive Drips

• frequently re-evaluate the critically ill patient
• the dosage of a vasoactive medication should not simply be titrated up because of persistent or worsening hypotension without reconsideration of the patient's clinical situation and the appropriateness of the current treatment plan.
Titrating Vasoactive Drips

- Alpha adrenergic: Alpha-1 adrenergic receptors are located in the vascular walls. Stimulation causes vasoconstriction.
- Alpha-1 adrenergic receptors are also found in the heart and can increase the duration of contraction without increasing chronotropy (heart rate).
**Beta adrenergic:**
- Beta-1 adrenergic receptors are found in the heart. When initiated they cause an increase in inotropy (force of contraction) and chronotropy (heart rate) with minimal vasoconstriction.
- Beta-2 receptors are found in blood vessels and in the lungs. When stimulated they cause vasodilation and bronchodilation.

**Dopaminergic:**
- Dopamine receptors are found in the renal, mesenteric, and cerebral vascular beds.
- Stimulation causes vasodilation.
- subtype of dopamine receptors that cause vasoconstriction by inducing norepinephrine release.

**Titrating Vasoactive Drips**

<table>
<thead>
<tr>
<th>Vasopressor</th>
<th>Receptor</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenyphrine (Neo-Synephrine)</td>
<td>Alpha</td>
<td>Increases MAP, PAOP, CPP, E FP, SVR</td>
</tr>
</tbody>
</table>
### Titrating Vasoactive Drips

<table>
<thead>
<tr>
<th>Vasopressor</th>
<th>Receptor</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epinephrine (Adrenalin)</td>
<td>Potent Beta-1, Moderate Beta-2, Alpha-1</td>
<td>Increases HR, MAP, PAP, PAOP, CVP, CO Increase/decrease SVR, SV</td>
</tr>
<tr>
<td>Norepinephrine (Levophed)</td>
<td>Alpha-1 and Beta-2</td>
<td>Increases MAP, PAP, PAOP, CVP, SVR Increase/decreases HR, SV, CO</td>
</tr>
<tr>
<td>Dopamine (Inotropin)</td>
<td>dopamine-1 receptors Beta-1 Alpha</td>
<td>Vasodilation renal, mesenteric, cerebral Increases CO, SV, variable HR Vasodilation increases SVR</td>
</tr>
</tbody>
</table>

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### Titrating Vasoactive Drips

<table>
<thead>
<tr>
<th>Inotrope</th>
<th>Receptor</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dobutamine (Dobutrex)</td>
<td>Beta-1 with minimal alpha and beta-2</td>
<td>Net effect increases CO, SV with or without a small decrease in BP</td>
</tr>
<tr>
<td>Isoproterenol (Isuprel)</td>
<td>Beta-1 and Beta-2</td>
<td>Increases HR, MAP, PAP, SV, CO May decrease PAOP, CVP, SVR</td>
</tr>
<tr>
<td>Vasopressin (anti diuretic hormone)</td>
<td>Vasopressin receptors (V1) Nonadrenergic mechanism</td>
<td>Vasorestriction due to stimulation of V1 receptors located in the vascular smooth muscle</td>
</tr>
</tbody>
</table>
**Inotrope Receptor Action**

<table>
<thead>
<tr>
<th>Inotrope</th>
<th>Receptor</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milrinone</td>
<td>PDE-I (Type 3)</td>
<td>Nonadrenergic mechanism</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Weak inotrope; inappropriate monotherapy for shock</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Increases SV, CI</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Decreases CVP, PAOP, SVR</td>
</tr>
<tr>
<td></td>
<td></td>
<td>May increase HR &amp; dysrhythmias</td>
</tr>
</tbody>
</table>

**Titrating Vasoactive Drips**

**Common Vasodilators**

<table>
<thead>
<tr>
<th>Agent</th>
<th>Onset</th>
<th>Duration</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitroprusside</td>
<td>Immediate</td>
<td>1-2 min</td>
<td>Potent, Titratable</td>
<td>Cyanide, Thioptarmine</td>
</tr>
<tr>
<td>Nitroglycerin</td>
<td>2-5 min</td>
<td>3-5 min</td>
<td>Coronary Perfusion</td>
<td>Tolerance, Variable Efficacy</td>
</tr>
<tr>
<td>Fenoldopam</td>
<td>&lt;5 min</td>
<td>5-10 min</td>
<td>Renal Perfusion</td>
<td>Increased IOP</td>
</tr>
<tr>
<td>Hydralazine</td>
<td>10-20 min</td>
<td>3-8 hrs</td>
<td>Edema, Praxis</td>
<td>Tachycardia, Headache</td>
</tr>
<tr>
<td>Nicardipine</td>
<td>5-15 min</td>
<td>1-4 hrs</td>
<td>CNS Protection</td>
<td>Avoid in CHF or Cardiac Ischemia</td>
</tr>
<tr>
<td>Enalaprilat</td>
<td>15-30 min</td>
<td>6 hr</td>
<td>CHF, Acute LV Failure</td>
<td>Avoid in MI</td>
</tr>
</tbody>
</table>

Modified from the 6th Joint National Commission Reports, NIH, 1997

**Adrenergic Antagonists**

<table>
<thead>
<tr>
<th>Agent</th>
<th>Onset</th>
<th>Duration</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Labetalol</td>
<td>5-10 min</td>
<td>3-6 hrs</td>
<td>Combines Beta Blockade with Vasodilation</td>
<td>Beta Blocker Effects Heart Block, Acute CHF</td>
</tr>
<tr>
<td>Phentolamine</td>
<td>1-2 min</td>
<td>3-10 min</td>
<td>Catecholamine Excess</td>
<td>Tachycardia</td>
</tr>
<tr>
<td>Esmolol</td>
<td>2 min</td>
<td>10-20 min</td>
<td>Aortic Dissection, Perioperative</td>
<td>Beta Blocker Effects Heart Block, Acute CHF</td>
</tr>
</tbody>
</table>

Modified from the 6th Joint National Commission Reports, NIH, 1997
### Titrating Vasoactive Drips

<table>
<thead>
<tr>
<th>Drug</th>
<th>Concentration</th>
<th>Initial Dose</th>
<th>Titration</th>
<th>Goal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardizem</td>
<td>125mg/250cc</td>
<td>Bolus 0.25mg/kg max repeat w/ 0.25mg/kg &amp; 0.25mcg/kg</td>
<td>0.15mg/kg</td>
<td>Titrate to HR and BP parameter</td>
</tr>
<tr>
<td>Dobutamine</td>
<td>50mg/250cc</td>
<td>1.5-2.5mcg/kg</td>
<td>None</td>
<td>Titrate to CI</td>
</tr>
<tr>
<td>Dopamine</td>
<td>50mg/250cc</td>
<td>2.5-5mcg/kg</td>
<td>None</td>
<td>Titrate to CI(2)</td>
</tr>
<tr>
<td>Epinephrine</td>
<td>8mg/250cc</td>
<td>Start at 1mcg/kg/hr</td>
<td>5-10mcg/kg/hr</td>
<td>Titrate to HR or as ordered</td>
</tr>
<tr>
<td>Labetalol</td>
<td>1000mg/250cc</td>
<td>20mg bolus over 5 mins start gtt at 2mg/hr</td>
<td>2mg/min</td>
<td>Titrate to HR and BP per order</td>
</tr>
<tr>
<td>Natrecor (Nestiritide)</td>
<td>1.5 g/250cc</td>
<td>Bolus 2mcg/kg over 1 min then 0.01 mcg/kg/min</td>
<td>0.005 mcg/kg/min</td>
<td>Titrate to CI or as ordered</td>
</tr>
<tr>
<td>Nicardipine</td>
<td>25mg/250cc</td>
<td>5mg/hr</td>
<td>2.5mg/hr</td>
<td>15 min up to 15mg/hr</td>
</tr>
<tr>
<td>Nitroglycerin</td>
<td>50mg/250cc</td>
<td>5-10mcg/min</td>
<td>5-10mcg/min q 3-5 min up to 200mcg/min</td>
<td>Titrate to CP relief or ordered</td>
</tr>
<tr>
<td>Nipride (Nitroprusside)</td>
<td>50mg/250cc</td>
<td>0.3mcg/kg/min</td>
<td>0.5mcg/kg/min q 5-15 minutes</td>
<td>Titrate to MAP or as ordered</td>
</tr>
<tr>
<td>Levophed (Norepinephrine)</td>
<td>8mg/250cc</td>
<td>2mcg/min</td>
<td>1mcg/min q 5 mins up to 30mcg/min</td>
<td>Titrate to MAP or as ordered</td>
</tr>
<tr>
<td>Neo-Synephrine (Phenylephrine)</td>
<td>50mg/250cc</td>
<td>10mcg/min</td>
<td>10mcg/min</td>
<td>10 mcg/min or 30 mcg/min</td>
</tr>
<tr>
<td>Diprivan (Propofol)</td>
<td>1g/100cc</td>
<td>2mg/kg/min</td>
<td>5-10mcg/kg/min</td>
<td>15 min up to 15mcg/kg</td>
</tr>
<tr>
<td>Vasopressin</td>
<td>20 units/200cc</td>
<td>0.01 units</td>
<td>0.01 units up to 0.1 units/hr</td>
<td>Titrate to MAP or as ordered</td>
</tr>
</tbody>
</table>
Case Study I

- 68 year old male admitted following AAA repair
- History – CAD, PVD, CABG 3 years ago
- Arrives lethargic but arousable; ventilated with warming blanket; arterial line, PA catheter; large abdominal dressing dry & intact
- Sinus rhythm with occasional PVCs

Titrating Vasoactive Drips

Case Study I (continued)

Temperature 96°F
HR 116 beats/min
RR 12 beats/min
BP 158/86 mmHg

Why is the patient hypertensive?
What is the priority for this patient

Titrating Vasoactive Drips
Titrating Vasoactive Drips
Case Study I (continued)
• 2 hours after arrival he becomes cool and clammy, hypotensive, and tachycardic
  Temperature  98.8°F
  HR  122 beats/min
  RR  16 breaths/min
  BP  92/50 mmHg

What is causing hypotensive state?
What intervention(s) is appropriate?
Case Study I (continued)

- He is given 500 mL of NS and 500 mL albumin; his PAOP increases to 16 and BP 138/78
- 30 minutes later, his BP again declines and another 500 mL of NS and 250 mL of albumin are administered
- Later he becomes hypotensive again, he shows tachycardia with frequent PVCs and one sustained burst of V tach

Temperature 98°F
HR 124 beats/min
RR 24 breaths/min
BP 88/68 mmHg

CVP 12 mmHg
PAOP 22 mmHg
PAP 44/24 mmHg
CO 3.0 L/min
CI 1.8 L/min/m²
SVR 1680

Is this too much fluid for a patient with heart disease?
What do you interpret to be the etiology of this hypotensive state?
Case Study I (continued)

- ST segment depression and T wave inversion are noted in lead V3.
- A stat 12 lead, serum troponin, and BNP level are obtained
- ECG confirms ST depression in V2-V6, a normal troponin level rules out non-ST-elevation MI

Titrating Vasoactive Drips

Case Study I (continued)

- BNP is elevated @ 580 pg/mL, confirming ventricular dysfunction and a diagnosis of anterior wall ischemia and failure is made
- What therapy is recommended at this time?

Titrating Vasoactive Drips

Case Study I (continued)

- Patient stabilizes, remains sedated through night; weaning is postponed
- On POD 2 he spikes a temp of 102°F
- What is the suspected problem?
- What are the priority interventions?
- He becomes hypotensive again.
Titrating Vasoactive Drips

Case Study I (continued)

- Temperature: 101.3°F
- HR: 128 beats/min
- RR: 30 breaths/min
- BP: 80/40 mmHg

What is the source of the hypotension?
What therapy is necessary?

Titrating Vasoactive Drips

Case Study I (continued)

- CVP: 8 mmHg
- PAOP: 14 mmHg
- PAP: 30/15 mmHg
- CO: 5.3 L/min
- CI: 3.2 L/min/m²
- SVR: 709

Titrating Vasoactive Drips

Case Study I (continued)

- Temperature: 100.3°F
- HR: 124 beats/min
- RR: 28 breaths/min
- BP: 92/48 mmHg
Titrating Vasoactive Drips

Case Study I (continued)

CVP 12 mmHg
PAOP 15 mmHg
PAP 40/24 mmHg
CO 4.7 L/min
CI 2.8 L/min/m²
SVR 868
SvO₂ 60%
Lactate 5.5

What is the interpretation of these findings?
What interventions are appropriate?

Case Study II

A 73-year-old woman is in the unit with the diagnosis of HF. She presently is alert and oriented but complains of severe shortness of breath. Her pulse oximeter reveals a value of 89% on (FiO₂) of 50% via a high-humidity face mask. She has crackles throughout both lungs and has 3+ pitting edema of both lower legs. She has a PA catheter inserted to aid in the interpretation of the situation.

Temperature 37.6°C
HR 74 beats/min
RR 34 breaths/min
BP 202/114 mmHg
Case Study II (continued)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CVP</td>
<td>13 mmHg</td>
</tr>
<tr>
<td>PAOP</td>
<td>21 mmHg</td>
</tr>
<tr>
<td>PAP</td>
<td>43/24 mmHg</td>
</tr>
<tr>
<td>CO</td>
<td>3.9 L/min</td>
</tr>
<tr>
<td>CI</td>
<td>1.9 L/min/m²</td>
</tr>
<tr>
<td>SVR</td>
<td>2674 dynes/sec/cm²</td>
</tr>
<tr>
<td>SvO₂</td>
<td>52%</td>
</tr>
<tr>
<td>PVR</td>
<td>191</td>
</tr>
</tbody>
</table>

What are the signs & symptoms of heart failure in this patient?
What is the best choice for management of this patient?

Case Study III

A 35-year-old woman with pancreatitis and ARDS experiences a progressively worsening oxygenation status. The care team decided to replace her PA catheter with an SvO₂ catheter to better monitor and manage the patient. Once the SvO₂ catheter was in place and calibrated, it was noted that her SvO₂ was only 55%.

Case Study III (continued)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hct</td>
<td>22%</td>
</tr>
<tr>
<td>CO</td>
<td>6 L/min</td>
</tr>
<tr>
<td>PAOP</td>
<td>18 mm Hg</td>
</tr>
<tr>
<td>So₂O₂</td>
<td>91% on an FiO₂ of 0.6, PEEP of 15 cm H₂O</td>
</tr>
</tbody>
</table>

Would this patient benefit from fluid resuscitation?
Case Study III (continued)
On day 6, she became increasingly agitated and her SvO\textsubscript{2} decreased to 60%. She was febrile and her sputum was noted to be purulent appearing. Sputum cultures were obtained and other reasons the agitation were also considered. A STAT chest radiograph was obtained to rule out pneumothorax (it was ruled out), and an arterial blood gas was obtained. ABG revealed a PaCO\textsubscript{2} of 45 mm Hg, and a PaO\textsubscript{2} of 55 mm Hg. Her ventilator settings were SIMV of 12/min (spontaneous rate was 10 above the ventilation), FiO\textsubscript{2} of 0.45, PEEP of 5 cm H\textsubscript{2}O, Hct of 29%, and CO of 6 L/min.

Case Study IV
A 76-year-old man is admitted to the unit with the diagnosis of acute inferior wall myocardial infarction and a history of COPD. During the shift he begins to complain of shortness of breath. He has crackles one-third the way up his posterior lobes along with expiratory wheezing. He has an S\textsubscript{3} (gallop) and a II/VI systolic murmur.

Case Study IV (continued)
CVP 13 mmHg
PAOP 21 mmHg
PAP 38/23 mmHg
CO 4.6 L/min
CI 1.9 L/min/m\textsuperscript{2}
SvO\textsubscript{2} 49%
BP 100/58 mmHg
What are the treatment priorities for this patient?
Case Study V
A 71-year-old man is admitted to the ICU with hypotension of unknown origin. He presently has a fiberoptic PA catheter in place to determine the origin of the hypotension. He is unresponsive with a Glasgow coma scale of 4. The hemodynamic parameters are as follows:

- CVP: 12 mmHg
- PAOP: 18 mmHg
- PAP: 42/22 mmHg
- CO: 3.9 L/min
- CI: 2.3 L/min/m²
- SvO₂: 51%
- BP: 102/68 mmHg
- HR: 101 beats/min

What are the treatment priorities for this patient?

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Case Study V (continued)

- CVP: 13 mmHg
- PAOP: 14 mmHg
- PAP: 40/20 mmHg
- CO: 4.4 L/min
- CI: 2.6 L/min/m²
- SvO₂: 57%
- BP: 104/66 mmHg
- HR: 106 beats/min

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Case Study V (continued)

- CVP: 12 mmHg
- PAOP: 18 mmHg
- PAP: 42/22 mmHg
- CO: 3.9 L/min
- CI: 2.3 L/min/m²
- SvO₂: 51%
- BP: 102/68 mmHg
- HR: 101 beats/min

What are the treatment priorities for this patient?