Making vasopressors safer
Requirements for **safe** vaspressor use

In an ideal world

1. Knowledge of what constitutes optimal vasopressor dosing

2. A culture of cautiousness regarding vasopressors
What do we know about optimal vasopressor use?

Clinical trial data exists, but they are sparse.
What do we know about optimal vasopressor use?

<table>
<thead>
<tr>
<th>Study</th>
<th>Patients Description</th>
<th>Time Description</th>
</tr>
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<tr>
<td>Suk et al. 2007</td>
<td>16 patients with septic shock</td>
<td>6 hours</td>
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<td>• 28 patients with septic shock – 8 hours</td>
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<td>• Norepinephrine for MAP 65 vs. 85 mmHg</td>
<td>• Norepinephrine for MAP 65 mmHg for 4 hours</td>
<td>• Norepinephrine for MAP 65, 75 and 85 mmHg</td>
</tr>
<tr>
<td></td>
<td>• Then 14 patients received norepinephrine for MAP 85 mmHg for 4 hours</td>
<td>• Assessments at each MAP value lasted 1 hour</td>
</tr>
</tbody>
</table>
What do we know about optimal vasopressor use?

<table>
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<tr>
<th>Study</th>
<th>Patients</th>
<th>Treatment</th>
<th>Duration</th>
<th>Outcome Measures</th>
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<td>Suk et al. 2007</td>
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<td>Before-after comparisons: Increasing blood pressure led to an increase in cardiac index (4.7 to 5.5 L<em>min⁻¹</em>m⁻²) No difference in lactate level, gastric pCO₂ gap and urine output</td>
</tr>
</tbody>
</table>
Any other clinical data?

Observational studies

Outcome of severe sepsis in pediatric oncology patients*
Richard T. Fiser, MD; Nancy K. West, RN, BSN; Andrew J. Bush, PhD; Elaine M. Sillos, MD; Jeffrey E. Schmidt, MD; Robert F. Tamburro, MD, MS


Clinical Characteristics of Patients Developing ARF Due to Sepsis/Systemic Inflammatory Response Syndrome: Results of a Prospective Study
Itir Yegenaga, MD, PhD, Erik Hoste, MD, Wim Van Biesen, MD, PhD, Raymond Vanholder, MD, PhD, Dominique Benoit, MD, Gulcin Kantarcı, MD, PhD, Annemieke D’hondt, MD, PhD, Francis Colardyn, MD, and Norbert Lameire, MD, PhD

American Journal of Kidney Diseases, Vol 43, No 5 (May), 2004: pp 817-824

Adverse cardiac events during catecholamine vasopressor therapy: a prospective observational study


Liberal vs. conservative vasopressor use to maintain mean arterial blood pressure during resuscitation of septic shock: an observational study
Sanjay Subramanian, Murat Yilmaz, Ahmer Rehman, Rolf D. Hubmayr, Bekele Afessa, Ogajen Gajic


Association of arterial blood pressure and vasopressor load with septic shock mortality: a post hoc analysis of a multicenter trial
Martin W Düüsner1, Esko Ruokonen2, Ville Pettitlä3, Hanno Ulmer4, Christian Torgersen5, Christian A Schmittinger5, Stephan Jakob1 and Jukka Takala1

Critical Care 2009, 13:R181
Authors of guidelines have little to rely upon preclinical evidence.

Animal studies suggest that below a mean arterial pressure of 60 mm Hg, autoregulation is compromised in the coronary, renal, and central nervous system vascular beds (24, 25).

So how do we titrate vasopressors?

In a survey of 202 Canadian intensivists on vasopressor use in sepsis, the 153 intensivists who aim for mean arterial pressures use a trigger of 60 mmHg (IQR 60-65) and then target 65 mmHg (IQR 65-65).

Lamontagne et al. Journal of Critical Care 2011; 26:532e1-e7

Russell et al. NEJM 2008
But we also disagree...

On what constitutes optimal vasopressor use

Table 2  Influence of comorbidities on vasopressor use

<table>
<thead>
<tr>
<th>Comorbidities</th>
<th>n (%) who would increase vasopressors</th>
<th>n (%) who would not change vasopressors</th>
<th>n (%) who would decrease vasopressors</th>
<th>n (%) not sure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>176 (88)</td>
<td>18 (9)</td>
<td>0</td>
<td>6 (3)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>51 (25.5)</td>
<td>127 (63.5)</td>
<td>13 (6.5)</td>
<td>9 (4.5)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>8 (4)</td>
<td>106 (53)</td>
<td>70 (35)</td>
<td>16 (8)</td>
</tr>
<tr>
<td>Chronic renal failure</td>
<td>58 (29)</td>
<td>130 (65)</td>
<td>5 (2.5)</td>
<td>7 (3.5)</td>
</tr>
<tr>
<td>Previous stroke or TIA with cerebrovascular disease</td>
<td>118 (59)</td>
<td>64 (32)</td>
<td>5 (2.5)</td>
<td>13 (6.5)</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>28 (14)</td>
<td>140 (70)</td>
<td>18 (9)</td>
<td>14 (7)</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>13 (6.5)</td>
<td>103 (51.5)</td>
<td>68 (34)</td>
<td>16 (8)</td>
</tr>
</tbody>
</table>

n = 200. TIA indicates transient ischemic attack.

Table 3  Influence of acute concurrent illnesses on vasopressor use

<table>
<thead>
<tr>
<th>Illnesses</th>
<th>n (%) who would increase vasopressors</th>
<th>n (%) who would not change vasopressors</th>
<th>n (%) who would decrease vasopressors</th>
<th>n (%) not sure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elevated troponin</td>
<td>9 (4.6)</td>
<td>146 (74.1)</td>
<td>23 (11.7)</td>
<td>19 (9.6)</td>
</tr>
<tr>
<td>Ischemic ECG changes</td>
<td>26 (13.2)</td>
<td>95 (48.2)</td>
<td>45 (22.8)</td>
<td>31 (15.7)</td>
</tr>
<tr>
<td>Pulmonary edema</td>
<td>14 (7.1)</td>
<td>121 (61.4)</td>
<td>37 (18.9)</td>
<td>25 (127)</td>
</tr>
<tr>
<td>Inadequate level of consciousness (without sedation)</td>
<td>32 (16.2)</td>
<td>153 (77.7)</td>
<td>0</td>
<td>12 (6.1)</td>
</tr>
<tr>
<td>Doubling of creatinine</td>
<td>39 (19.8)</td>
<td>131 (66.5)</td>
<td>9 (4.6)</td>
<td>18 (9.1)</td>
</tr>
<tr>
<td>Decreased urine output</td>
<td>64 (32.5)</td>
<td>114 (57.9)</td>
<td>2 (1)</td>
<td>17 (8.6)</td>
</tr>
<tr>
<td>New or worsening lactic acidosis</td>
<td>56 (28.4)</td>
<td>93 (47.2)</td>
<td>18 (9.1)</td>
<td>30 (15.2)</td>
</tr>
<tr>
<td>Digital cyanosis or livedo reticularis</td>
<td>11 (5.6)</td>
<td>72 (36.5)</td>
<td>90 (45.7)</td>
<td>25 (12.7)</td>
</tr>
<tr>
<td>Gastrointestinal bleeding</td>
<td>6 (3)</td>
<td>144 (73.1)</td>
<td>36 (18.3)</td>
<td>13 (6.6)</td>
</tr>
</tbody>
</table>

n = 197.

Lamontagne et al. Journal of Critical Care 2011; 26:532e1-e7
Requirements for safe vaspressor use

In an ideal world

1. Knowledge of what constitutes optimal vasopressor dosing

2. A culture of cautiousness regarding vasopressors
While we wait / hope for clinical trials
Can we learn anything from our mistakes?

Patient of 75 years
Advanced sarcoidosis (neurological involvement) on low-dose steroids (adequate prophylaxis)
Admitted at peripheral hospital 7/03 for fever and pulmonary infiltrates
Deteriorates... Abx broadened... ARDS... intubated 17/03...

Transferred to 3<sup>rd</sup> ICU 19/03 for refractory ARDS (100% FiO₂), agitated and asynchronous
Gas exchange improves with sedation / paralytics (FiO₂ 70%)... but shock becomes apparent
Norepinephrine initiated for **MAP of 65 mmHg** (0.2 mcg/kg/min)
Echo: compliant IVC, mild HK of RV and LV
Moderate ARF (creat. 140), U/O improves with cautious fluids+steroids... MD leaves at 0100

Next morning, the **MAP is right on target but patient had deteriorated**
Norepinephrine 0.65 mcg/kg/min + vasopressin + dobutamine and eventually epinephrine
pH 7.0, anuric, lactates 6.5 mmol/L and then 12 mmol/L
CVVH initiated urgently, but too little too late and **he died**
What had happened?

1. Failure to reassess indication – vasopressors were perhaps no longer what the patient needed when deteriorated

2. Failure to recognize that someone else needed to be called in to help

3. Failure to adhere to prescription – vasopressors had been allowed to increase beyond target MAP
A single-centre intervention quality improvement projet

1- Reassess indication at least daily

2- Recognize the need to call for help

3- Distinguish between target and minimal threshold / exert tighter control on vasopressor use

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Vasopressor prescriptions in the ICU
Quality improvement project

Date: ___________________  Chart #: ___________________  Usual weight: ________ kg

Intensive care unit:
- [ ] StM Fleurimont
- [ ] SIC Fleurimont
- [ ] St Hôtel-Dieu

1.- Which agent(s)?
- [ ] Norepinephrine
- [ ] Dopamine
- [ ] Epinephrine
- [ ] Phenylephrine
- [ ] Vasopressin
- [ ] Other: ___________________

2.- Which indication?
- [ ] Septic shock
- [ ] Hypovolemic shock
- [ ] Cardiogenic shock
- [ ] Obstructive shock
- [ ] Unknown cause shock
- [ ] Other: ___________________

3.- What is the target blood pressure and the tolerated range?

<table>
<thead>
<tr>
<th>Numerical value</th>
<th>Tolerated range</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAP (mmHg):</td>
<td>MIN: MAX: N/A :</td>
</tr>
<tr>
<td>SBP (mmHg):</td>
<td>MIN: MAX: N/A :</td>
</tr>
<tr>
<td>DBP (mmHg):</td>
<td>MIN: MAX: N/A :</td>
</tr>
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</table>

Target blood pressure rationale (optional):

4.- What is the threshold dose that should trigger physician reassessment? (see suggestions below)

Maximum dose should be prescribed in mcg/min and calculated using patient’s usual weight:
- Norepinephrine or epinephrine: > 0.2 mcg/kg/min
- Dopamine: > 20 mcg/kg/min
- Vasopressin: > 0.04 U/min
- Phenylephrine: > 0.75 mcg/kg/min

Example of vasopressor prescription:
Norepinephrine 8mg in 250mL of NS for IV infusion to maintain MAP of 65mmHg (60-70 mmHg). Call MD if the dose reaches 0.2 mcg/kg/min.
A single-centre intervention quality improvement projet

What did we find?

Over 3 weeks, form used for 29 patients receiving vasopressors

Duration of vasopressor therapy ranged from 1 to 5 days

- Shorter in cardiovascular unit where #1 indication was bypass vasoplegia
- Longer in mixed medical-surgical units where #1 indication was sepsis

Indication changed over the course of vasopressor therapy

**In 5 patients**

- Post-sedation to sepsis
- Hemorrhagic to sepsis
- Dialysis-induced to sepsis
- Sepsis to anasarca in need of diuresis
- Post-bypass vasoplegia to cardiogenic shock
A single-centre intervention quality improvement projet

Perception of improved prescription clarity with prescription form

48 members of the team completed a survey at the end of 3-week (Nurses = 30; residents = 8; intensivists = 4; pharmacists = 6)

Proportion who perceived the vasopressor prescriptions were clear
Before implementation of the form: 33%
After implementation of the form: 98%

Sources of confusion
• Blood pressure target and allowed range
• Maximum dose
Requirements for safe vasopressor use

1. Knowledge of optimal vasopressor dosing

There exists an important knowledge gap regarding vasopressor requirements in shock (likely to vary with shock type, patient age, comorbidities, acute concurrent illnesses...)

1. A culture of cautiousness regarding vasopressors

A certain number of simple interventions may help us reduce harm associated with vasopressors

• Clearer communication
• Systematic reassessment of indications
• Automatic triggers to call most responsible physician
Any other clinical data?

Observational studies

Dunser Crit Care 2009