Impact of body weight on hemodynamic response to fixed dose vasopressin in septic shock

Corissa Piatka
Impact of Body Weight on Hemodynamic Response to Fixed Dose Vasopressin in Septic Shock

Corissa Piatka, PharmD
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Parkview Health

The speaker has no actual or potential conflict of interest in relation to this presentation.
Sepsis and Septic Shock

- Sepsis: uncontrolled inflammatory response secondary to infection
  - Hypotension
  - Acute end organ damage
- Common causes of morbidity and mortality in critically ill
  - Mortality rate for septic shock: 40%
Sepsis and Septic Shock

- Fluid Resuscitation
- Broad Spectrum Antibiotics

Sepsis and Septic Shock

- Fluid Resuscitation
- Broad Spectrum Antibiotics
- Vasopressors

Sepsis and Septic Shock

- Fluid Resuscitation
- Broad Spectrum Antibiotics
- Vasopressors

Sepsis and Septic Shock

Norepinephrine

- Epinephrine, phenylephrine, angiotensin II (Titrated, weight-based dosing)
- Vasopressin (Fixed dose)

Sepsis and Septic Shock

Norepinephrine

Epinephrine, phenylephrine, angiotensin II
  Titrated, weight-based dosing

Vasopressin
  Fixed dose

Sepsis and Septic Shock

Norepinephrine

- Epinephrine, phenylephrine, angiotensin II
  - Titrated, weight-based dosing
- Vasopressin
  - Fixed dose

Assessment Question #1

Based on administration, how does vasopressin differ from other vasopressors?

A. Vasopressin is titrated; other vasopressors are administered at a flat rate.
B. Vasopressin is administered at a flat rate; other vasopressors are titrated.
C. Vasopressin is administered based on weight; other vasopressors are titrated.
D. Vasopressin is administered based on weight; other vasopressors are administered at a flat rate.
Assessment Question #1

Based on administration, how does vasopressin differ from other vasopressors?

A. Vasopressin is titrated; other vasopressors are administered at a flat rate.

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C. Vasopressin is administered based on weight; other vasopressors are titrated.

D. Vasopressin is administered based on weight; other vasopressors are administered at a flat rate.
Assessment Question #2

Which of the following is most likely to occur as a result of vasopressin use in septic shock?

A. Decreased catecholamine requirements
B. Increased cardiac output
C. Renal protective effects
D. Decreased corticosteroid requirements
Assessment Question #2

Which of the following is most likely to occur as a result of vasopressin use in septic shock?

A. Decreased catecholamine requirements
B. Increased cardiac output
C. Renal protective effects
D. Decreased corticosteroid requirements
Sepsis and Septic Shock

Norepinephrine

Epinephrine, phenylephrine, angiotensin II

Titrated, weight-based dosing

Vasopressin

Fixed dose

## Previous Studies

<table>
<thead>
<tr>
<th></th>
<th>Miller et al</th>
<th>Hodge et al</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Study Design</strong></td>
<td>Retrospective cohort</td>
<td>Retrospective cohort</td>
</tr>
<tr>
<td><strong>Primary Endpoint</strong></td>
<td>Relationship of change in catecholamine vasopressor requirements and vasopressin dosing adjusted for body weight</td>
<td>Change in mean arterial pressure 1 hour after vasopressin initiation relative to body weight</td>
</tr>
<tr>
<td><strong>Results</strong></td>
<td>2 hours: $r = -0.36$, $P = 0.03$</td>
<td>Change at 1 hour: $r = -0.071$, $P = 0.84$</td>
</tr>
<tr>
<td></td>
<td>4 hours: $r = -0.46$, $P &lt; 0.001$</td>
<td></td>
</tr>
</tbody>
</table>
Previous Studies

- Torbic et al.
  - Single center, retrospective cohort study of patients with septic shock receiving adjunctive fixed dose vasopressin
  - Primary outcome: association between a weight- or a BMI-adjusted vasopressin dose with a catecholamine-dose change or change in mean arterial pressure
**Previous Studies**

- Torbic et al.

<table>
<thead>
<tr>
<th></th>
<th>BMI &lt; 25 kg/m² (n=238)</th>
<th>BMI 25-30 kg/m² (n=254)</th>
<th>BMI 30-35 kg/m² (n=182)</th>
<th>BMI &gt;35 kg/m² (n=264)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td>62.6 (50.9-71.8)</td>
<td>63.9 (54.6-72.5)</td>
<td>63.3 (53.8-72.1)</td>
<td>60.0 (50.8-69.0)</td>
</tr>
<tr>
<td><strong>Male, n (%)</strong></td>
<td>132 (55)</td>
<td>106 (42)</td>
<td>78 (43)</td>
<td>155 (59)</td>
</tr>
<tr>
<td><strong>Weight (kg)</strong></td>
<td>62.6 (53.6-70.8)</td>
<td>80.0 (72.0-88.3)</td>
<td>94.3 (84.6-104.5)</td>
<td>122.3 (106.0-140.9)</td>
</tr>
<tr>
<td><strong>AVP dose, weight-adjusted (units/kg/min)</strong></td>
<td>0.00049 (0.00042-0.00059)</td>
<td>0.00038 (0.00034-0.00043)</td>
<td>0.00033 (0.00028-0.00038)</td>
<td>0.00026 (0.00022-0.00031)</td>
</tr>
<tr>
<td><strong>SOFA score at AVP initiation</strong></td>
<td>12.5 (10-15)</td>
<td>13 (10-16)</td>
<td>13 (11-15)</td>
<td>12 (10-15)</td>
</tr>
<tr>
<td><strong>Norepinephrine dose at AVP initiation (mcg/min)</strong></td>
<td>22.3 (18-32)</td>
<td>22 (16-35)</td>
<td>24.5 (18-35)</td>
<td>23.7 (18-33.5)</td>
</tr>
</tbody>
</table>

Results presented as median (IQR) unless otherwise specified.
AVP= vasopressin
Previous Studies

• Torbic et al.
  • Results: Weight-adjusted
Previous Studies

- Torbic et al.

- Results: Weight-adjusted

Catecholamine Dose Change

<table>
<thead>
<tr>
<th>Time</th>
<th>Vasopressin Dose (units/kg/min)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 hours</td>
<td>$r = -0.0523$ (-0.111 to 0.016)</td>
<td>0.13</td>
</tr>
<tr>
<td>6 hours</td>
<td>$r = -0.0590$ (-0.111 to 0.020)</td>
<td>0.09</td>
</tr>
<tr>
<td>12 hours</td>
<td>$r = 0.0011$ (-0.066 to 0.077)</td>
<td>0.98</td>
</tr>
</tbody>
</table>
Previous Studies

- Torbic et al.
- Results: Weight-adjusted

<table>
<thead>
<tr>
<th></th>
<th>Catecholamine Dose Change</th>
<th>MAP Change</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Vasopressin Dose</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(units/kg/min)</td>
<td>P-value</td>
</tr>
<tr>
<td>2 hours</td>
<td>( r = -0.0523 )</td>
<td>0.13</td>
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<tr>
<td></td>
<td>(-0.111 to 0.016)</td>
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<td>6 hours</td>
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<td>0.09</td>
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<td></td>
<td>(-0.066 to 0.077)</td>
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</tr>
<tr>
<td></td>
<td>( r = 0.0356 )</td>
<td>0.31</td>
</tr>
<tr>
<td></td>
<td>(-0.215 to 0.111)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>( r = 0.0481 )</td>
<td>0.17</td>
</tr>
<tr>
<td></td>
<td>(-0.033 to 0.092)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>( r = -0.0146 )</td>
<td>0.68</td>
</tr>
<tr>
<td></td>
<td>(-0.115 to 0.016)</td>
<td></td>
</tr>
</tbody>
</table>

Previous Studies

• Torbic et al.
  • Results: BMI-adjusted
Previous Studies

- Torbic et al.
  - Results: BMI-adjusted

**Catecholamine Dose Change**

<table>
<thead>
<tr>
<th>Time</th>
<th>Vasopressin Dose (units/BMI/min)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 hours</td>
<td>$r = -0.0385$ (-0.111 to 0.021)</td>
<td>0.27</td>
</tr>
<tr>
<td>6 hours</td>
<td>$r = -0.0594$ (-0.124 to 0.009)</td>
<td>0.09</td>
</tr>
<tr>
<td>12 hours</td>
<td>$r = -0.0071$ (-0.075 to 0.068)</td>
<td>0.84</td>
</tr>
</tbody>
</table>
### Previous Studies

- **Torbic et al.**
  - **Results:** BMI-adjusted

<table>
<thead>
<tr>
<th></th>
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<th>MAP Change</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Vasopressin Dose</td>
<td>Vasopressin Dose</td>
</tr>
<tr>
<td></td>
<td>(units/BMI/min)</td>
<td>(units/BMI/min)</td>
</tr>
<tr>
<td></td>
<td>P-value</td>
<td>P-value</td>
</tr>
<tr>
<td>2 hours</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>r = -0.0385</td>
<td>r = 0.0515</td>
</tr>
<tr>
<td></td>
<td>(-0.111 to 0.021)</td>
<td>(0.008 to 0.130)</td>
</tr>
<tr>
<td></td>
<td>0.27</td>
<td>0.14</td>
</tr>
<tr>
<td>6 hours</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>r = -0.0594</td>
<td>r = 0.0404</td>
</tr>
<tr>
<td></td>
<td>(-0.124 to 0.009)</td>
<td>(-0.029 to 0.099)</td>
</tr>
<tr>
<td></td>
<td>0.09</td>
<td>0.09</td>
</tr>
<tr>
<td>12 hours</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>r = -0.0071</td>
<td>r = -0.0056</td>
</tr>
<tr>
<td></td>
<td>(-0.075 to 0.068)</td>
<td>(-0.091 to 0.041)</td>
</tr>
<tr>
<td></td>
<td>0.84</td>
<td>0.87</td>
</tr>
</tbody>
</table>
Purpose

• Evaluate effect of body weight on achievement of target mean arterial pressure (MAP) post-initiation of vasopressin in patients with septic shock
Parkview Regional Medical Center

- Parkview Health
- Community hospital
- Level II trauma center
- 460 adult and pediatric inpatient beds
- 6 critical care units
  - Medical ICU (MICU)
  - Surgical Trauma ICU (STICU)
  - Cardiovascular ICU (CVICU)
Parkview Regional Medical Center

- Vasopressor Use
  - Provider preference
    - Norepinephrine
      - Titrated 2-30 mcg/min
      - Titrated 2-50 mcg/min
    - Vasopressin
      - Continuous at 0.03 units/hr
      - Continuous at 0.04 units/hr
Study Design

- Single center
- Retrospective, electronic chart review
- Patients admitted March 2017 through August 2018

Non-Obese: BMI < 30 kg/m²
Obese: BMI ≥ 30 kg/m²

BMI = Body Mass Index
# Inclusion and Exclusion Criteria

## Inclusion
- Age $\geq 18$ years
- Diagnosis of sepsis or septic shock per ICD 10 code
- Admitted to MICU, STICU, CVICU
- Initiated on catecholamine infusion prior to vasopressin infusion

## Exclusion
- Age $< 18$ years
- Indication other than septic shock
- Vasopressin monotherapy
- Catecholamine or vasopressin infusion duration $< 1$ hour
- Baseline MAP $\geq 65$ mmHg at vasopressin initiation
- Transfer from outside ICU
Primary Outcome

- Achievement of target MAP within 4 hours of vasopressin initiation
Definition of Target MAP

Definition of Target MAP

MAP ≥ 65 mmHg

Definition of Target MAP

MAP $\geq$ 65 mmHg
Maintain for 4 hours

Definition of Target MAP

MAP $\geq 65$ mmHg

Maintain for 4 hours

No additional blood pressure support

Secondary Outcomes

• Change in MAP at 4 hours after vasopressin initiation
• Total norepinephrine infusion duration
• Intensive care unit length of stay
• Hospital length of stay
• In-hospital mortality
Statistical Tests

• 324 patients (162 per study arm) for 80% power
  • 15% difference in target MAP achievement
  • A priori α error rate: 0.05

<table>
<thead>
<tr>
<th>Primary Outcome</th>
<th>Secondary Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Chi-square test</td>
<td>• Mann-Whitney rank sum</td>
</tr>
<tr>
<td></td>
<td>• Chi-square test</td>
</tr>
</tbody>
</table>
Study Population

460 patients screened for inclusion

316 Excluded patients
- 170 Baseline MAP > 65 mmHg
- 58 Not in ICU
- 44 Not septic
- 30 Inadequate MAP documentation
- 6 Less than 18 years of age
- 5 Vasopressin infusion less than 1 hour
- 3 Transferred from outside ICU

60 patients in non-obese group

84 patients in obese group
## Results: Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Non-Obese (n=60)</th>
<th>Obese (n=84)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td>69 (61-77)</td>
<td>65 (58-72)</td>
</tr>
<tr>
<td><strong>Male, n (%)</strong></td>
<td>35 (58)</td>
<td>39 (46)</td>
</tr>
<tr>
<td><strong>Weight (kg)</strong></td>
<td>72.4 (62.3-82.6)</td>
<td>104.7 (92.8-121.9)</td>
</tr>
<tr>
<td><strong>Body mass index (kg/m²)</strong></td>
<td>25.0 (21.9-27.5)</td>
<td>37.9 (33.0-44.9)</td>
</tr>
<tr>
<td><strong>AVP dose, weight-adjusted (units/kg/min)</strong></td>
<td>0.000515 (0.00043-0.000577)</td>
<td>0.00033 (0.00027-0.000408)</td>
</tr>
<tr>
<td><strong>SOFA score at AVP initiation</strong></td>
<td>11 (9-13)</td>
<td>12 (9-13)</td>
</tr>
<tr>
<td><strong>Norepinephrine equivalent dose at AVP initiation (mcg/min)</strong></td>
<td>26.5 (20-30)</td>
<td>26 (22-30)</td>
</tr>
<tr>
<td><strong>Norepinephrine duration at AVP initiation (hours)</strong></td>
<td>7.0 (3.8-17.5)</td>
<td>7.2 (3.4-31.5)</td>
</tr>
<tr>
<td><strong>MAP at AVP initiation (mmHg)</strong></td>
<td>58 (52-60)</td>
<td>56 (50-60)</td>
</tr>
</tbody>
</table>

Results presented as median (IQR) unless otherwise specified.

AVP = vasopressin
Results: Primary Outcome

Target MAP Achieved within 4 Hours

<table>
<thead>
<tr>
<th></th>
<th>Proportion of Patients, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Achieved</td>
</tr>
<tr>
<td>Non-Obese</td>
<td>14 (23)</td>
</tr>
<tr>
<td>Obese</td>
<td>20 (24)</td>
</tr>
</tbody>
</table>

P > 0.99
### Results: Secondary Outcomes

<table>
<thead>
<tr>
<th></th>
<th>Non-Obese (n=60)</th>
<th>Obese (n=84)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change in MAP at 4 hours (mmHg), median (IQR)</td>
<td>8 (2-18)</td>
<td>12 (4-19)</td>
<td>0.467</td>
</tr>
<tr>
<td>Norepinephrine infusion duration (hours), median (IQR)</td>
<td>80.2 (50.5-134.6)</td>
<td>119.8 (64.0-181.7)</td>
<td>0.018</td>
</tr>
<tr>
<td>ICU length of stay (days), median (IQR)</td>
<td>5.8 (2.1-10.4)</td>
<td>6.6 (3.3-12.2)</td>
<td>0.159</td>
</tr>
<tr>
<td>Hospital length of stay (days), median (IQR)</td>
<td>8.2 (3.6-16.9)</td>
<td>8.3 (5.8-18.7)</td>
<td>0.477</td>
</tr>
<tr>
<td>In-hospital mortality, n (%)</td>
<td>26 (43)</td>
<td>44 (52)</td>
<td>0.367</td>
</tr>
</tbody>
</table>
Discussion

- Body weight did not impact the achievement of target MAP
  - Consistent with current literature
  - Lack of power
Limitations

- Single center
- Retrospective chart review
  - MAP documentation
    - Timing
    - Arterial line versus cuff
  - Infusion documentation
    - End time accuracy
- BMI criteria
- Mean arterial pressure target as primary outcome
- Strict definition of target MAP
Future Directions

• Redesign to increase patient population
  • Expansion of MICU and intensive care step-down unit
• Evaluation of vasopressin role in septic shock
• Publication
Acknowledgements

- Michael E Todt, PharmD, BCCCP
- Dustin D Linn, PharmD, BCPS, BCCCP
- Sarah Ferrell, PharmD
- Robert Beckett, PharmD, BCPS
References


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