Effect of adjunct midodrine on length of stay in vasopressor-dependent adult ICU patients

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IRB status - received
Disclosure Statement

• Carlo Balmes
• Conflict of interests: none
• Sponsorship: none
• Proprietary information or results of ongoing research may be subject to different interpretations
• Speaker’s presentation is educational in nature and in agreement to non-commercial guidelines
Learning Objectives

- Summarize evidence for the potential benefit of midodrine use for persistent hypotension in the ICU

- Apply findings from this evaluation to describe patients who would most likely benefit from midodrine for persistent hypotension
Providence Alaska Medical Center

- 402 bed tertiary community medical care center
- 62 emergency department beds
- 37 adult ICU beds
- Level II trauma center
Assessment Questions

1. Midodrine addition results in reductions in which of the following parameters as suggested by existing literature? (Select all that apply)
   A. vasopressor requirements
   B. ICU length of stay
   C. mortality
   D. time on mechanical ventilation

2. Which is considered a low-dose vasopressor?
   A. Epinephrine infusing at 4 mcg/min
   B. Phenylephrine infusing at 120 mcg/min
   C. Norepinephrine infusing at 12 mcg/min
   D. None of the above

3. Which of the following patients would most likely benefit from midodrine addition?
   A. A patient with shock secondary to an UGIB with an LVEF of 15%
   B. A patient admitted for septic shock with persistent hypotension requiring norepinephrine 4 mcg/min
   C. A patient admitted for bowel ischemia
   D. A patient with sick sinus syndrome
Background

- Persistent hypotension requiring vasopressors is a barrier to ICU discharge
- Upward titrating vasoactive infusions are not allowed outside of the ICU at PAMC
- Midodrine, an oral prodrug with selective $\alpha$-adrenergic activity, may have benefit in shock-refractory patients
- Existing evidence has demonstrated midodrine may decrease vasopressor requirements and ICU LOS
- Prescribing practices of midodrine vary across intensivists
- Optimal target patient population is unclear
Study Objectives

• Evaluate the benefit of midodrine addition to low-dose vasopressors in shock-refractory ICU patients

Primary Outcome:
• Time from start of low-dose vasopressor infusion to ICU discharge

Secondary Outcome:
• Duration of low-dose vasopressor use
Methodology

• 2-arm retrospective study

• Patients to be screened were identified through electronic report of ICU patients who received greater than 24 hours of vasopressors

**Key data points collected**

• SOFA score
• concurrent administration of steroids
• administration of a fluid bolus prior to midodrine initiation
• midodrine dose
• initial ICU admission diagnosis
• occurrence of bradycardia within 24 hours of midodrine initiation
• occurrence of bowel ischemia
Methodology

- Low-dose vasopressors defined as a continuous infusion of norepinephrine at a rate of less than 8 mcg/min or other vasopressor equivalence.

**Conversion Formulas:**

- \[ \text{dopamine} \, \frac{\mu g/kg/min}{2} = \text{norepinephrine} \, \mu g/min \]
- \[ \text{epinephrine} \, \mu g/min = \text{norepinephrine} \, \mu g/min \]
- \[ \text{phenylephrine} \, \frac{\mu g/min}{10} = \text{norepinephrine} \, \mu g/min \]
- \[ \text{vasopressin} \, u/hr \times 8.33 = \text{norepinephrine} \, \mu g/min \]
Methodology

**Inclusion Criteria:**
- Patients ≥ 18 years-of-age
- ICU admission
- Required at least 24 hours of IV vasopressors
- Required low-dose vasopressors at any time for treatment of persistent hypotension

**Exclusion Criteria:**
- NPO
- Pregnant
- Incarcerated
- Midodrine or droxidopa use prior to admission
- Pheochromocytoma
- Thyrotoxicosis
- Hypovolemic shock
- Bradycardia (HR < 50 BPM)
- Severe heart disease (EF < 30%)
- Adrenal insufficiency based on medical history or diagnosis per ICU H&P
- Hypersensitivity to midodrine
Methodology

Statistical Analysis

- Sample size and power: 80 patients in each arm required to achieve a power of 80% to detect a difference of 24 hours with an alpha of 0.05.
- One sided t-test used to analyze primary and secondary outcomes

*Statistical analysis pending completion of data collection*
Population

- 248 charts reviewed
- 199 patients excluded
- Midodrine arm (n = 26)
- Control arm (n = 23)

199 patients excluded
- < 24 hours pressors = 72
- deceased prior to ICU discharge = 29
- hypovolemic shock = 26
- EF < 30% = 25
- Midodrine PTA = 15
- Outside study period = 12
- Bradycardia = 6
- Outside facility = 5
- Adrenal insufficiency = 3
- Pressors ordered, not given = 2
- NPO = 2
- Midodrine ordered, not given = 1
- House convenience = 1
## Preliminary Results – Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Treatment arm (n = 26)</th>
<th>Control arm (n = 23)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age</td>
<td>60.4 (35 – 80)</td>
<td>62.5 (40 – 79)</td>
</tr>
<tr>
<td>Sex</td>
<td>Male – 14 Female – 12</td>
<td>Male – 15 Female – 8</td>
</tr>
<tr>
<td>ICU admit diagnosis</td>
<td>Septic shock – 17</td>
<td>Septic shock – 15</td>
</tr>
<tr>
<td></td>
<td>Post-op hypotension – 7</td>
<td>Post-op hypotension – 6</td>
</tr>
<tr>
<td></td>
<td>Cardiogenic shock – 1</td>
<td>Cardiogenic shock - 2</td>
</tr>
<tr>
<td></td>
<td>Distributive shock – 1</td>
<td></td>
</tr>
<tr>
<td>Median SOFA score at admit</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Median SOFA score at LD-pressor initiation</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>SD steroids administered</td>
<td>10 (38.5%)</td>
<td>10 (43.5%)</td>
</tr>
</tbody>
</table>
# Preliminary Results – Outcomes

<table>
<thead>
<tr>
<th>Overall population</th>
<th>Treatment arm (n = 26)</th>
<th>Control arm (n = 23)</th>
<th>Mean difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ICU LOS, hrs</td>
<td>111.87</td>
<td>123.38</td>
<td>-9.84</td>
</tr>
<tr>
<td>Mean low-dose vasopressor duration, hrs</td>
<td>55.3</td>
<td>40.25</td>
<td>+15.05</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Septic shock patients</th>
<th>Treatment arm (n = 17)</th>
<th>Control arm (n = 15)</th>
<th>Mean difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ICU LOS, hrs</td>
<td>108.53</td>
<td>138.77</td>
<td>-30.24</td>
</tr>
<tr>
<td>Mean low-dose vasopressor duration, hrs</td>
<td>59.55</td>
<td>44.22</td>
<td>+15.36</td>
</tr>
</tbody>
</table>
Midodrine Usage Patterns

Vasopressor start

Immediate addition (n = 3)

Vasopressors off

Vasopressors off < 12 hours (n = 3)

Delayed overlap (n = 18)

Vasopressors off > 24 hours (n = 2)
Discussion

- Limited by retrospective nature and small sample size
- EHR limitations
- Preliminary results of study trend towards benefit from midodrine addition in subgroup of septic shock patients
- Variation in prescribing practices was confirmed
  - Subjective addition of midodrine
  - Midodrine as weaning tool vs. midodrine to prevent pressor restart
Conclusion

• Trend towards no difference in ICU LOS in the total population
• Trend towards no difference in duration of low-dose vasopressors
• Trend towards shorter ICU LOS in midodrine treated septic shock patients
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Acknowledgements

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References


Questions?