Guanfacine to Aid in Weaning Dexmedetomidine for Sedation in the ICU

Authors: Mary K. Medley, PharmD • Adam L. Wiss, PharmD, BCCCP • J. Brooke Tullos, PharmD

Affiliations: Ascension Saint Thomas Hospital West

The authors have no conflict of interest.

Background:

- Dexmedetomidine is commonly used as sedative in the ICU. Prolonged infusions may lead to withdrawal symptoms upon discontinuation and prohibitive transitioning otherwise stable patients to a lower level of care.
- Clonidine has been utilized to successfully wean dexmedetomidine, but hypotension and bradycardia are often dose-limiting side effects. Conversely, guanfacine, an alpha-2a agonist with increased affinity to alpha-2A receptors and minimal effect on alpha-2B receptors, may provide the desired level of sedation with less hemodynamic side effects.
- The purpose of this study was to analyze guanfacine and dexmedetomidine administration practices for agitation and sedation in the ICU with a focus on safety and efficacy.

Methods:

- This study was an IRB-approved, single-center, retrospective chart review of adult patients admitted to Ascension Saint Thomas Hospital West who were treated with dexmedetomidine and guanfacine for sedation in the ICU between January 2017 and September 2020.
- Patients were excluded if they received less than two doses of guanfacine, received guanfacine prior to initiation of dexmedetomedine, were being treated for alcohol withdrawal or were receiving neuromuscular blocking agents.
- The primary objective was to evaluate the response to guanfacine at 24 hours after initiation in patients on dexmedetomedine. Response to guanfacine was defined as discontinuation of dexmedetomedine within 24 hours of initiating guanfacine without the need for an additional or dose increase of existing ancillary psychoactive medications for sedation.
- Secondary objectives included rates of hypotension and bradycardia.

Results:

- Baseline Characteristics:
  - Responder: n=21
  - Nonresponder: n=27
  - p-value:

<table>
<thead>
<tr>
<th>Baseline Characteristics</th>
<th>Responder</th>
<th>Nonresponder</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex, n (%)</td>
<td>16 (76)</td>
<td>16 (59)</td>
<td>0.22</td>
</tr>
<tr>
<td>Age, yr, median (IQR)</td>
<td>63 (46-77)</td>
<td>59 (45-74)</td>
<td>0.40</td>
</tr>
<tr>
<td>BMI (kg/m²), median (IQR)</td>
<td>27 (24-33)</td>
<td>31 (26-38)</td>
<td>0.16</td>
</tr>
</tbody>
</table>

- Medical History, n (%):
  - Coronary artery disease | 9 (43) |
  - Congestive heart failure | 7 (33) |
  - Anxiety/depression | 4 (19) |
  - IV drug abuse | 3 (14) |
  - Alcohol abuse | 3 (14) |

- Primary Illness, n (%):
  - Neurologic | 10 (48) |
  - Cardiac | 8 (38) |
  - Pulmonary | 1 (5) |
  - Other | 2 (10) |

- APACHE II Score, median (IQR):
  - 23 (19-27) |
  - 24 (20-29) |
  - 0.77 |

- Mechanical Ventilation, n (%):
  - 6 (29) |
  - 15 (56) |
  - 0.06 |

- Baseline CAM-Positive, n (%):
  - 12 (57) |
  - 22 (82) |
  - 0.08 |

- Baseline RASS Score, n (%):
  - +2 | 4 (19) |
  - 1 | 6 (29) |
  - 0 | 6 (29) |
  - -1 | 4 (19) |
  - -2 | 5 (19) |

- Outcomes:
  - ICU LOS (days), median (IQR) | 14 (7-24) |
  - Hospital LOS (days), median (IQR) | 24 (14-39) |
  - 18 (11-29) |
  - 19 (13-36) |
  - 0.35 |
  - 0.41 |

- Discharge disposition, n (%):
  - Facility | 15 (71) |
  - Deceased | 3 (14) |
  - Home | 3 (14) |
  - 15 (71) |
  - 7 (26) |
  - 6 (22) |
  - 0.38 |

- Dex characteristics, median (IQR):
  - Time on dex prior to T-0 (hr) | 59 (45-82) |
  - Dose at T-0 (mcg/kg/hr) | 0.2 (0.0-0.4) |
  - Dose at T-24 (mcg/kg/hr) | 0.6 (0.2-0.9) |
  - Time to dex discontinuation (hr) | 0.01 |
  - 73 (30-111) |

- Guanfacine regimen, n (%):
  - 1mg daily | 6 (29) |
  - 2mg twice daily | 13 (62) |
  - 3 (11) |
  - 0.14 |

- CAM-Positive ICU Days %, median (IQR) | 50 (0-81) |
  - 63 (40-100) |
  - 0.08 |

- Safety outcomes, n (%):
  - Hypotension (SBP < 90 mmHg) | 3 (14) |
  - Required treatment | 3 (11) |
  - 0.09 |
  - Bradycardia (HR < 60 bpm) | 2 (6.7) |
  - Required treatment | 1 (4) |
  - 0.14 |

Discussion:

- Overall, 44% of patients were successfully weaned off of dexmedetomidine within 24 hours after the initiation of guanfacine. In nonresponders, the median time to dexmedetomedine discontinuation was 73 hours.
- Mechanical ventilation, time on dexmedetomedine prior to guanfacine initiation and discontinuation of guanfacine appears to play a role in response to guanfacine.
- Guanfacine appears to have a favorable safety profile.

Conclusion:

Guanfacine may be a safe and effective strategy to assist in transitioning patients off of prolonged dexmedetomidine infusions.

References: