Hemodynamic Effects of Dexmedetomidine Compared to Propofol in Critically Ill Adults

Beaumont

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Introduction

- Sedation is used in the intensive care unit (ICU) to facilitate mechanical ventilation and is associated with decrease in:[1-3]
  - Delirium
  - Ventilator dependent days
  - Morbidity and mortality
- The Society of Critical Care Medicine's (SCCM) 2013 Clinical Practice Guidelines for the Management of Pain, Agitation, and Delirium recommend maintaining light levels of sedation for improved clinical outcomes[4]
- SCCM recommends using the Richmond Agitation-Sedation Scale (RASS) to monitor sedation levels
  - Target RASS of 0 to -2 *(Table 1)*[4]

***Table 1. Richmond Agitation-Sedation Scale*[4]**

Depth of Sedation*	RASS Score
Agitated	+1 to +4
Awake and Calm	0
Lightly Sedated	-1 to -2
Deeply Sedated	-3 to -5

**Modified from SCCM guidelines*[4]

- Propofol and dexmedetomidine are the recommended first line agents due to their desirable pharmacokinetic properties *(Table 2)*[4]

***Table 2. Propofol and Dexmedetomidine Pharmacokinetics*[7,8]**

	Propofol	Dexmedetomidine
Mechanism	Sedative hypnotic GABA agonist	Centrally acting α-2 adrenergic receptor agonist
Dosing	5 – 50 µg/kg/min	0.2 – 0.7 µg/kg/hr
Onset	1 – 2 minutes	5 – 10 minutes
Duration	3 – 10 minutes	60 – 120 minutes

- Both agents have been associated with hemodynamic instability including hypotension and bradycardia which may result in:[1,5,6]
  - Reduced cardiac output
  - Decreased organ perfusion
  - Increased mortality

Rationale

- Studies have shown conflicting data on the rates of hemodynamic instability between the recommended agents
  - Wide ranges of hypotension (23–98%) and bradycardia (3–42%) have been reported[1,6]
  - Recent studies in specific ICU populations (medical and neurocritical) report similar rates of hypotension and bradycardia between agents[1,2]
- This study will compare the rate of hemodynamic effects of propofol and dexmedetomidine in a large mixed ICU population

Objectives

- Primary
  - Compare the hemodynamic effects associated with dexmedetomidine versus propofol during the first 24 hours of infusion
- Secondary
  - Evaluate the efficacy of first line sedative agents for sedation in critically ill patients
  - Characterize interventions utilized in treatment of sedative-induced hypotension and bradycardia

Methods

STUDY DESIGN

- Single center, retrospective, observational chart review
- This study was approved by the Institutional Review Board at Beaumont Health
- A convenience sample of patients administered propofol or dexmedetomidine between July 1, 2013 and July 1, 2015 will be reviewed for eligibility *(Figure 1)*
- Data will be collected from the electronic medical record

Figure 1. Eligibility Criteria

Inclusion Criteria	Exclusion Criteria
• Mechanically ventilated, critically ill patients • Age ≥ 18 years old • Continuous intravenous sedation with either propofol or dexmedetomidine infusion for ≥ 4 hours • Target RASS of 0 to -2	• Procedural sedation • Use of ≥ 2 concurrent continuous infusions of sedatives • Use of vasopressor or inotrope within 1 hour prior to sedation initiation • Treatment for active seizures or alcohol withdrawal • Use of continuous infusion neuromuscular blocking agents • Blood product transfusion or paracentesis

Table 3. Data Collection

Baseline Data	Primary Endpoints	Secondary Endpoints
Demographic information	Frequency of severe hypotension and bradycardia events • Severe hypotension ▫ MAP < 60 or a decrease in SBP of 40 mmHg or more from baseline • Severe bradycardia ▫ HR < 50 bpm	Time to target RASS
ICU type and admission diagnosis		Percent time spent within target RASS range
Acute Physiology and Chronic Health Evaluation (APACHE) II Score		ICU type and admission diagnosis
Hemodynamics (averaged 6 hours prior to sedative administration) • Heart rate (HR) • Systolic blood pressure (SBP) • Diastolic blood pressure (DBP) • Mean arterial pressure (MAP)		Treatment of hemodynamic events • Sedative dosing ▫ Dose titration • Vasopressor or inotrope use ▫ Dose titration
Use of analgesics and antihypertensives	Hemodynamics (during sedation period)	

Methods (Cont.)

DATA COLLECTION ENDPOINTS

Data collection will conclude at the 24 hour time point or earlier if:

- The patient is extubated, undergoes cardiopulmonary resuscitation (CPR), or expires
- Renal replacement therapy is initiated
- Sedatives are discontinued

Statistical Analysis

- Data analysis will be performed with Statistical Analysis Software® (SAS) for Windows® version 9.3 and R for Windows® version 2.15.1
  - Descriptive statistics
  - Parametric variables:
    - Student's t-test, Pearson chi-square test, and Fisher's exact test
  - Non-parametric variables:
    - Wilcoxon signed-rank test, Wilcoxon two-sample rank-sum test
- P-value ≤ 0.05 will be considered statistically significant

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Disclosures

Authors of this presentation have the following to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation:

- All authors have nothing to disclose.

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