Creating A 21st Century Precision Medicine Intensive Care Unit

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INTRODUCTION

The management of sedation is a major challenge in the care of critically ill patients on mechanical ventilation (MV). During the first 48 hours in the ICU, healthcare providers often make multiple adjustments to find the correct drug or dose. In addition to alterations in organ function, fluid status and other comorbidities, we are interested in determining if genetics plays an important role in sedative response. It is expected that patients with deleterious genetic variants will not achieve the target Richmond Agitation Sedation Score (RASS) between 0 to -2 within the first 48 hours in the ICU. It is also expected that patients with deleterious genetic variants will have longer length of stay (LOS), longer time on MV, more adverse drug reactions (ADRs), and higher mortality.

OBJECTIVES

- **The primary objective** of this study is to define the actionable genetic variants in patients on MV in the ICU who have a target RASS between 0 to -2.
- **The secondary objective** is to evaluate the relationship between genetic variants and ICU LOS, time on MV, possible ADRs and death.

METHODS

- This is a prospective, observational study in three UMMC ICUs. Patients will be approached for informed consent based on criteria at time of ICU admission.
- 10 ml blood will be obtained for DNA extraction and genotyped on a comprehensive genetic panel.
- Sedative choice, dosing and duration will be at the discretion of the ICU care team.
- RASS scores will be measured every 2 or 4 hours per usual clinical practice and clinical outcomes collected from the Electronic Health Record (EHR).
- Participants will be offered the opportunity to receive their clinically actionable pharmacogenomics (PGx) results at the end of the study with medication interpretation by a pharmacist trained in PGx.

ACKNOWLEDGEMENTS

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RESULTS

From May through August 2018, **21** mechanically ventilated patients were enrolled at three UMMC ICU sites: Surgical ICU (4A), Medical ICU (4C) and Cardiovascular ICU (4E).

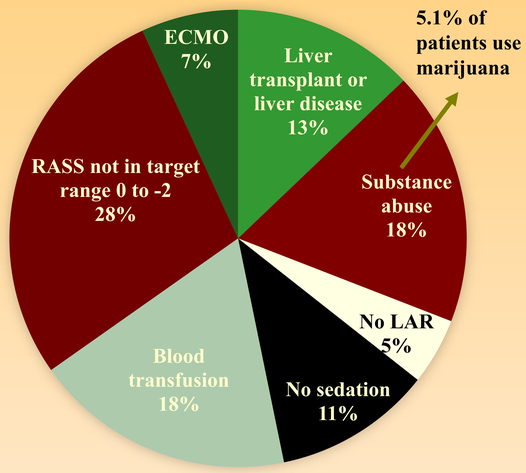
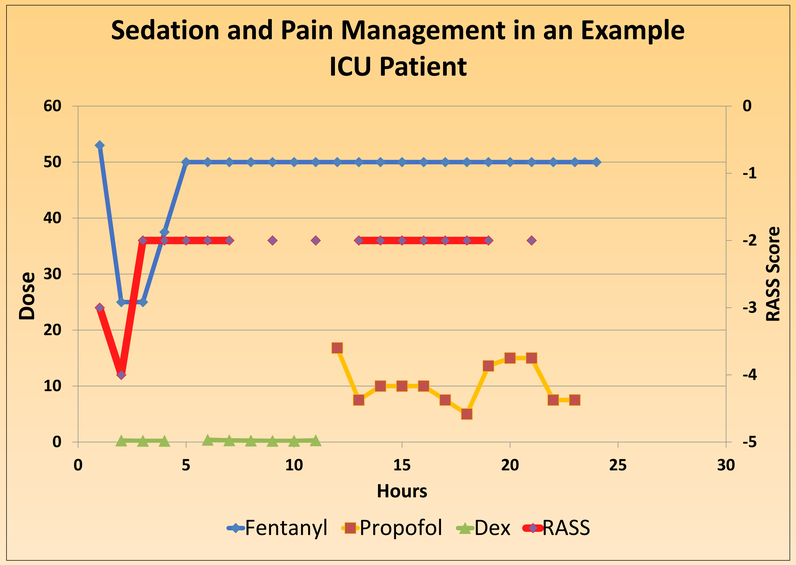


Figure 1: Percentage of the most common exclusion criteria

	Percentage (%) (N=20)
Patients require alternative sedative drugs	37.5
Patients require more than 2 sedative drugs	37.5
% of patients on propofol	62.5
% of patients on dexmedetomidine	37.5
% of patients on midazolam	37.5
% of patients on fentanyl	91.6
% of patients who require additional doses of sedatives	50

Table 1: Descriptive data of participants



INCLUSION/EXCLUSION CRITERIA

INCLUSION

- Male or female at least 18-year-old admitted to MICU, SICU or CV-ICU
- Receiving acute MV via an endotracheal tube and opioids and/or sedative medications with a target RASS of 0 to -2
- Expected to be ventilated for at least 48 hours
- Expected length of ICU stay is at least 48 hours
- Participant or legally authorized representative (LAR) provides informed consent

EXCLUSION

- Admission for head trauma or other neurologic event that may reduce cognition
- History of or current liver disease or substance abuse
- Acute hepatitis or liver failure
- History of liver transplant
- Receiving neuromuscular blockade
- Blood transfusion within 48 hours
- Moribund state with planned withdrawal of support

DISCUSSION

- Current sedative practice in critical care has evolved over the past few years favoring a lighter depth of sedation. Lighter sedation intensity with the RASS goal between +1 to -2 has been associated with positive outcomes.[1,2] Clinicians in the ICU are adapting and applying the updated guidelines into routine practice choosing a sedative target of 0 to -1 for most critically ill patients requiring sedation while on MV. In addition, some patients on MV can be managed without sedation. Clinicians aggressively seek to liberate patients from MV as quickly as possible, often less than 48 hours.
- In the first 48 hours in the ICU, sedative drugs and doses are often changed depending on patient's individual response to treatments (Table 1). The PGx results of this study will provide additional information as to which sedative drugs may require higher or lower than usual doses or which drugs may not be effective or cause untoward adverse drug effects based on metabolic status. This PGx information will assist clinicians in quickly prescribing correct doses and sedatives to optimize sedation for comfort and safety of ICU patients.

TRANSLATIONAL PERSPECTIVES

- Deep sedation is associated with delirium and poor cognitive outcomes. Lighter sedation with the target RASS between +1 to -2 is recommended to achieve optimal outcomes.
- Our results help clarify the best choice of sedative and doses to obtain optimal sedation management faster with minimal titration for ICU patients receiving MV.
- Our study serves as an educational opportunity to reinforce the importance of daily sedation reassessment and targeting a light level of sedation for ICU patients.
- Clinically important PGx results will be implemented into clinical practice by ICU pharmacists, nurses, and physicians providing a 21st century ICU practice.

REFERENCES

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