Creating A 21st Century Precision Medicine Intensive Care Unit

Tam Nguyen1, Debra J. Skaar1, Pamala Jacobson1
1University of Minnesota College of Pharmacy, Minneapolis, MN

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 genotyping 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

This research was supported by the National Institutes of Health’s National Center for Advancing Translational Sciences, grant UL1TR002494. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health’s National Center for Advancing Translational Sciences.

This research is supported by the Enhance Pharmacist Services to Improve Patient Health Clinical Research Award Comprehensive by the College of Pharmacy.

This research is supported by the Melendy/Peter’s Summer Research Scholarship 2018 by the College of Pharmacy.

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).

<table>
<thead>
<tr>
<th>Percentage (%)</th>
<th>(N=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients require alternative sedation</td>
<td>37.5</td>
</tr>
<tr>
<td>Patients require more than 2 sedative drugs</td>
<td>37.5</td>
</tr>
<tr>
<td>% of patients on propofol</td>
<td>62.5</td>
</tr>
<tr>
<td>% of patients on dexmedetomidine</td>
<td>37.5</td>
</tr>
<tr>
<td>% of patients on midazolam</td>
<td>37.5</td>
</tr>
<tr>
<td>% of patients on fentanyl</td>
<td>91.6</td>
</tr>
<tr>
<td>% of patients who require additional doses of sedatives</td>
<td>50</td>
</tr>
</tbody>
</table>

Figure 1: Percentage of the most common exclusion criteria

Table 1: Descriptive data of participants

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. 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
