Propofol Dose Response Analysis for Procedural Sedation: A Mathematical Modeling Study

by

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Background

Propofol is the most commonly used agent for procedural sedation in this emergency department (65%).
Deep versus Moderate Sedation

- Close to half of the patients receiving propofol receive deep sedation which is defined by the Ramsay score of 5 or 6.
Research Design

- Retrospective convenient sample design including all patients receiving propofol for the purpose of procedural sedation.
- This study included all patients regardless of age or gender.
- This study excluded any Kaiser Permanente patients.
Methods

- All patients who receive procedural sedation in the emergency department are audited by the PSVMC Emergency Department Quality Improvement Committee.
- Those patients who received any propofol for the purpose of procedural sedation during their emergency department visit were included in the study.
- Patient, weight, gender, clinical procedure requiring procedural sedation, age, ASA (Anesthesia Society of America) score, level of sedation (Ramsay score), and any complications were recorded into the database.
Propofol Dosing

- The propofol dose is determined by the ED physician. Most of the patients received 1 mg/Kg.

<table>
<thead>
<tr>
<th>Mean</th>
<th>Mode</th>
<th>Median</th>
<th>Min</th>
<th>Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.4</td>
<td>1</td>
<td>1</td>
<td>0.4</td>
<td>8.7</td>
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</tbody>
</table>
The Need for Targeted Propofol Dosing

Example of Potential Oversedation with Propofol
### ASA Score Breakdown

<table>
<thead>
<tr>
<th>ASA Score</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Patients</td>
<td>286</td>
<td>141</td>
<td>12</td>
<td>2</td>
<td>1</td>
</tr>
</tbody>
</table>

### Age Breakdown

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Mode</th>
<th>Median</th>
<th>Min</th>
<th>Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>50.2</td>
<td>54</td>
<td>54</td>
<td>1</td>
<td>95</td>
</tr>
</tbody>
</table>
ASA and Age as Independent Factors for Propofol Dose Response

ASA Breakdown versus Propofol Dose Response

ASA Score

Ramsay Score/Propofol Dose (mg/Kg)

Age (years)

Ramsay Score/Propofol Dose (mg/Kg)
Statistical Analysis

Multiple regression was employed to determine the statistical significance of the age and the ASA score as independent variables and their individual as well as combined effect on propofol dose response.

<table>
<thead>
<tr>
<th>ANOVA</th>
<th>df</th>
<th>SS</th>
<th>MS</th>
<th>F</th>
<th>Significance F</th>
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<tbody>
<tr>
<td>Regression</td>
<td>2</td>
<td>268.6739182</td>
<td>134.3369591</td>
<td>56.88878069</td>
<td>1.07436E-22</td>
</tr>
<tr>
<td>Residual</td>
<td>439</td>
<td>1036.652998</td>
<td>2.36139635</td>
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<td></td>
</tr>
<tr>
<td>Total</td>
<td>441</td>
<td>1305.326916</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Coefficients</th>
<th>Standard Error</th>
<th>t Stat</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>1.85800946</td>
<td>9.150937262</td>
<td>2.14006E-18</td>
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<tr>
<td>Age</td>
<td>0.025527704</td>
<td>7.80476276</td>
<td>4.40658E-14</td>
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<tr>
<td>ASA</td>
<td>0.404932401</td>
<td>2.906871399</td>
<td>0.003835503</td>
</tr>
</tbody>
</table>

Therefore, an equation including the independent variables and their effect on the dependent variable (propofol dose response) can be determined with the reassurance of statistical significance as:

\[
\text{mg of propofol} = \frac{\text{Ramsay score} \times \text{weight (Kg)}}{1.86 + 0.03(\text{Age}) + 0.4(\text{ASA score})}
\]
Examples:

70 Kg patient who is 62 years old with an ASA score of 2 requires procedural sedation with a physician goal of a Ramsay score of 4.

\[ mg \text{ of propofol} = \frac{\text{Ramsay score} \times \text{weight (Kg)}}{1.86 + 0.03(\text{Age}) + 0.4(\text{ASA score})} \]

\[ mg \text{ of propofol} = \frac{(4)\times 70 \text{ Kg}}{1.86 + 0.03(62) + 0.4(2)} \]

\[ mg \text{ of propofol} = \frac{280}{1.86 + 1.86 + 0.8} \]

\[ mg \text{ of propofol} = \frac{280}{4.52} \]

mg of propofol = 62
One More Example:

70 Kg patient who is 32 years old with an ASA score of 4 requires procedural sedation with a physician goal of a Ramsay score of 4.

\[
\text{mg of propofol} = \frac{\text{Ramsay score} \times \text{weight (Kg)}}{1.86 + 0.03(\text{Age}) + 0.4(\text{ASA score})}
\]

\[
\text{mg of propofol} = \frac{(4) \times 70 \text{ Kg}}{1.86 + 0.03(32) + 0.4(4)}
\]

\[
\text{mg of propofol} = \frac{280}{1.86 + 0.96 + 1.6}
\]

\[
\text{mg of propofol} = \frac{280}{4.42}
\]

\[
\text{mg of propofol} = 63
\]
Clinical Implications

- This mathematical model can allow for suggestion of propofol targeted dosing based on the desired level of sedation (based on the Ramsay score), the patient’s age, and their ASA score.
- This math model is clinically important for those patients with elevated ASA scores and/or advanced age.
- Whenever the calculation of the dose is greater than the manufacturer’s recommendation of 1 mg/Kg (as in the healthy pediatric patient population), the clinician usually will give the 1 mg/Kg as the initial dose of propofol.
Study Limitations

- This retrospective study looked at the total dose of propofol and not the individual subsequent doses. Typically, the physician will order the standard 1 mg/Kg with subsequent doses of 0.5 mg/Kg until the clinically desired level of sedation is reached.

- This study did not take into account any of the opiate medications that were given immediately before or during the procedural sedation.
Future Research in Propofol Dose Response

- Another retrospective review will use a retrospective repeated measures design taking into account serial doses of propofol as well as any opiates given prior to or during procedural sedation.

- Prospective study repeated measures design which include more demographic data than the previous retrospective studies.
Questions?