Elimination kinetics of propofol in those receiving long term propofol infusions

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INTRODUCTION

Propofol is a commonly used sedative on the Critical Care Unit. It is easy to titrate, metabolised by the liver into inactive metabolites and is highly lipophilic. Following termination of a prolonged infusion, the lipid rich, poorly perfused tissues in the critically ill may act as a reservoir to maintain plasma levels. Altered protein binding and hepatic blood flow may also impact on the kinetics of propofol during critical illness.
OBJECTIVE

To determine the elimination profile of propofol following the termination of a long term infusion, in critically ill adult patients
METHODS

- An observational prospective cohort study.
- Adult patients who had received >72 hours of continuous propofol infusion.
- Blood sampling:
  - During the infusion: 1-2 samples every 12-24h
  - Following termination of the infusion:
    - 10, 30, 60, 90, 120 min and every 12-24h
  - Plasma propofol concentration measured using the Pelorus 1500 (Sphere Medical, UK).
Propofol Measurement

Rapid Measurement
- Small vol. ≤1ml
- Easy operation

Small Footprint
- Bench top device
- Single use cartridge

Precision & Accuracy
- Daily calibration
- 3 points QC
RESULTS

- Total of 12 patients were included in data analysis.
- The duration of the infusion: median 93h & IQR 72-143h.
- The concentrations decreased by 50% within the 1st 10min (42% of patients), much slower steady decline thereafter.
- No correlation between the concentration and RASS sedation score (*rho* -2.98%, *p*=0.778).
# RESULTS

**Table 1: Summarized pharmacokinetic parameters (mean ±SEM, this study and data from the literature)**

<table>
<thead>
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<tbody>
<tr>
<td>Population</td>
<td>ICU Sedation</td>
<td>Anaesthesia</td>
<td>ICU Sedation</td>
</tr>
<tr>
<td>Duration (h)</td>
<td>93</td>
<td>2</td>
<td>72</td>
</tr>
<tr>
<td>No of Patients</td>
<td>12</td>
<td>18</td>
<td>9</td>
</tr>
<tr>
<td>$V_{dss}$ (L)</td>
<td>1247 ±181</td>
<td>287 ±212</td>
<td>1666 ±756</td>
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<tr>
<td>CL (mL)</td>
<td>794 ±288</td>
<td>1770 ±322</td>
<td>1570 ±560</td>
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<tr>
<td>$t_{1/2}$ β (min)</td>
<td>479 ±181</td>
<td>355 ±227</td>
<td>1878 ±672</td>
</tr>
</tbody>
</table>
RESULTS

Figure 1: Proportional decline of plasma concentration following termination of the infusions

\[ y = -0.107 \ln(x) + 1.0991 \]

\[ R^2 = 0.8246 \]
CONCLUSIONS

The study data is preliminary but reveals a long projected elimination time for propofol from the plasma of critically ill patients and a marked variation in half-life. Very low concentrations in the elimination phase represents the slow return of propofol from the poorly perfused tissue compartment. Although patients were rapidly awoken following termination of infusions, it remains unclear the neurological impact of low concentrations may have on higher functions, warranting for further investigation.
REFERENCES


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