What happens to propofol during prolonged sedation in ICU?

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Introduction

There is little published data on the pharmacokinetics of propofol infusion for prolonged periods in critical care.1-4 Propofol is frequently infused for days or weeks in critically ill patients with organ dysfunction. We aimed to determine propofol concentrations required to achieve adequate sedation in critically ill patients using the Richmond agitation score (RAS). Additionally we aimed to determine whether propofol levels are predictable in critically ill patients during constant rate infusion, and whether significant organ failure might lead to accumulation when compared to conventional pharmacokinetic models.

Methods

Following local ethics committee consent, we compared blood propofol levels with total dose and duration of propofol infusion in 53 samples from 43 patients on a mixed acute critical care unit undergoing prolonged sedation. Inclusion criteria were intubated patients with arterial access receiving propofol sedation. Estimated propofol concentration was calculated using the Marsh algorithm. The Richmond agitation scale at the point of propofol measurement was recorded, and the sequential organ failure assessment (SOFA) score was recorded for assessment of the impact of organ dysfunction on propofol levels. Concurrent sedative or opioid analgesic use was recorded. Propofol levels were measured from fresh discard whole blood within 8 hours of sampling using solid phase extraction and fluorescence spectroscopy using an analyser loaned from Sphere Medical Ltd, UK.

Results

• Propofol was infused for a mean of 33 hrs (IQR 14-44hrs).

• Average rate of propofol infusion was 2.18mg/kg/hr.

• Mean measured propofol concentration was 1.37µg/ml (range 0.29 to 2.60). There was fairly good correlation between estimated propofol concentrations (based on Marsh model) and measured levels with a R² value of 0.500, shown in figure 1.

• Level of organ failure did not impact significantly on accuracy of predicted propofol levels.

• Blood propofol levels were correlated with level of sedation, shown in figure 2. This correlation was maintained in patients receiving no concurrent sedation (44 patients).

• Average blood propofol level of patients on muscle relaxants was 1.2µg/ml, although these patients received other sedatives concurrently.

Conclusions

We were able to demonstrate a correlation between predicted propofol levels and those measured in blood. Predicted propofol levels were on average lower than measured levels, suggesting a reduced capacity to metabolise propofol in critical illness, although this effect was not marked. We were unable to demonstrate an association between severity of organ failure and deviation of measured from predicted propofol levels. There was a correlation between depth of sedation and measured propofol level, although blood propofol levels were lower than levels expected for similar levels of sedation in well patients.5 Propofol levels in patients receiving muscle relaxation were not regarded high enough to cause awareness.

References


Figure 1 – Plot of blood propofol level measured using analyser against blood propofol level estimated from Marsh algorithm. Samples split into those with and without significant organ failure (SOFA = sequential organ failure assessment)

Figure 2 – Histogram showing average measured propofol levels for each given score on the Richmond Agitation Scale (p= patient receiving muscle relaxation)