Anaesthesia. 2018 Jan;73(1):40-48.

Evidence of hysteresis in propofol pharmacodynamics.

Pablo Sepúlveda, E. Carrasco, Luis Tapia, Mario Ramos, F. Cruz, Paulette Conget, Q. Olivares y I. Cortínez.

Abstract

It is commonly assumed that loss of responsiveness and recovery of responsiveness occur at similar concentrations of propofol. However, the 'conscious' and 'anaesthetised' conditions produced by general anaesthetics may behave as two bistable states. We hypothesised that loss of responsiveness and recovery of responsiveness occur at different propofol concentrations. Propofol was administered to 19 healthy volunteers by effect-site target-controlled infusion using increasing and decreasing stable concentration steps of 7 min. Propofol serum concentrations were measured from venous blood samples at the end of each 7-min step. A long step of 14 min was performed at loss of responsiveness. At this step, propofol concentrations were measured at 7 and 14 min. Propofol concentrations measured at loss of responsiveness and recovery of responsiveness were 2.6 (1.2-4.7) $\mu g.ml^{-1}$ and 1.6 (0.6-3.3) $\mu g.ml^{-1}$, respectively ($p < 0.001$). Propofol plasma concentration and the corresponding bispectral index values measured at minute 7 and minute 14 of the long step performed at loss of responsiveness were 2.6 (1.2-4.7) vs. 2.6 (1.3-4.3) at recovery of responsiveness, ($p = 0.96$) and 61.2 (49.0-77.0) vs. 58.4 (45.0-74.0), ($p = 0.058$), respectively. Loss of responsiveness and recovery of responsiveness appear to occur at different propofol concentrations. However, it is possible that, if equilibration was not achieved between plasma and effect-sites at the end of each 7-min step, the higher concentrations found at loss of responsiveness compared with those observed during recovery of responsiveness could be explained by a possible bias in estimations of the effect-site concentrations of propofol by the Schnider model, rather than neural inertia.