Differences between method of blood propofol measurement in published studies involving pharmacokinetic analysis

Nick J Cowley¹,², Thomas H Clutton-Brock¹,²

¹ University Hospitals Birmingham NHS Foundation Trust, Edgbaston, Birmingham, United Kingdom, B15 2TT
² College of Medical and Dental Sciences, University of Birmingham Medical School, Birmingham, United Kingdom, B15 2TH

Contact: n.j.cowley@bham.ac.uk

Introduction

Significant risk of inconsistency exists, depending upon the chosen method of blood sample preparation for measurement of propofol concentrations for pharmacokinetic (pk) research. Propofol concentrations measured from immediately centrifuged plasma samples can be 30% higher than whole blood.[1] Venous samples will lead to falsely low propofol concentrations during the fast redistribution phase.[2]

Studies collecting specimens for development of propofol target controlled infusion (TCI) models are of particular importance, because the method of sample preparation may influence model performance.

Methods

Although not feasible to identify all published work involving the sampling of blood for propofol concentration, systematic search methodology was used to allow a picture of methods used and time related changes in practice. Ovid MEDLINE (1966 to June 2012) was searched for publications using the search term Propofol [Pharmacokinetics], and limited to humans. Visual screening of abstracts was performed to identify publications in which blood had been sampled. Following retrieval of the manuscript, detailed review was performed of sampling methodology. Subgroup analysis was performed on studies used to develop propofol TCI models.

Results

From an initial analysis of 328 publications, 66 studies were included. 12 were identified as being used for development of propofol TCI modelling. Year of publication ranged from 1985 to 2012. An increase from 21.4% prior to and 68.4% after year 2000 was detected in the proportion of samples separated into plasma before analysis (p<0.001), see figure 1. Time to centrifugation of plasma was documented as being performed immediately in only 15.6% studies. Whole blood specimens were stored at the recommended 5°C in 90% cases, but for longer than the recommended period of 8 weeks in 45.5% cases. 95.3% studies used high performance liquid chromatography (HPLC) for sample analysis. Figure 2 shows the change in practice from using venous in early studies to arterial blood in later studies. When analysing publications used to develop propofol TCI models, 58.3% were published prior to 1996, half of analyses used venous blood, and 58.3% used whole blood rather than plasma.

Discussion

Propofol sampling practice is changing over time. There should clearly be more consistency between study groups in order to avoid misinterpretation of results. Much of the pk work performed used to develop propofol TCI models has been performed in early studies, in which differing sampling methodology will lead to significant differences in measured propofol concentrations.

References