Performance evaluation of improvements in a rapid propofol concentration analyser

The authors evaluated a new referencing approach implemented in the Pelorus 1000, a research analyserthat uses solid phase extraction and colorimetry to rapidly quantify the concentration of the intravenous anesthetic propofol in whole blood samples. Previous characterization of the instrument demonstrated a small systematic bias in operation, resulting in a Limit of Quantification of 0.75 ug/ml [1]. The colorimetric analysis approach has been refined to normalize absorbance before and after development of the characteristic indophenol complex [2]. The performance of the modified analyzer was characterized with respect to linearity, precision in control solutions and whole blood and limit of quantification and compared to the HPLC based reference method. The Pelorus 1000 was also evaluated for cross interference by substances that could be expected to potentially interfere with the solid phase extraction step or the analyte detection principles of the system.

Methods

All testing was carried out using the Pelorus 1000 device (Sphere Medical Ltd, Cambridge, UK, http://www.spheremedical.com) in a laboratory setting according to the manufacturer's operating instructions. The reference method used was a high performance liquid chromatography (HPLC) assay based on the method described by Cussonneau [3]. It uses a Luna C18(2) HPLC column (3µm 150 x 4.6mm) from Phenomenex. The results were analysed using Excel and an Excel add-in Analyse-It program. Whole blood testing was carried out using freshly drawn human blood from healthy volunteers. Propofol spiked samples were used to obtain the concentration range for the linearity, precision and the limit of quantification. Written informed consent was obtained from donors who were all enrolled in Sphere Medical's blood donation program, a waived program for the performance evaluation of instrumentation that has been reviewed and approved by the company's independent directors.

Results

The assay was found to be linear with a R^2 of 0.994 in the range of 0-20 µg propofol /ml. The Limit of Quantification (LOQ) was calculated as the lowest concentration at which the bias or imprecision is no more than 20% of the target value. The LOQ of the assay is 0.25 µg /ml. Total imprecision reported in SD (CV%) in control solutions containing propofol in solvent using three different instruments was 0.28 (5.39%) at 5.27 µg /ml and 0.47 (4.34%) at 10.82 µg /ml. Within run imprecision in whole blood from healthy blood donors was 0.06 (8.00%) at 0.75 µg /ml, 0.03 (0.99%) at 3.03 µg /ml, 0.09 (1.44%) at 6.21 µg propofol/ml and 0.29 (2.00%) at 14.46 µg /ml. The only cross interference found was for the bilirubin conjugated where the system was over reading 1.14 µg propofol /ml for the concentration of bilirubin tested of 342 µM with respect to the HPLC reference (A dose response study suggests that a total error of +/-0.5µg/ml is met at a concentration of 137µM). Also a 50% hematocrit level was found to cause a small bias of 0.06 µg propofol/ml over reading with respect to the HPLC reference. In comparison to the reference method, the overall bias of the Pelorus 1500 system over the range of 0-12 µg propofol/ml is estimated to be 0.048 µg/ml (95% confidence interval -0.57 to 0.66 µg/ml). This comparison was performed using three different instruments.

Discussion

The modified Pelorus 1000 analyser has been demonstrated to have an analytical performance for the measurement of propofol concentrations in whole blood samples comparable to that previously reported [2]. The modified Pelorus 1000 analyser fulfils the requirements for measurement of propofol levels in whole blood samples with precision and accuracy suitable for investigating propofol pharmacokinetics. A significant improvement is the reduction on the limit of quantification to 0.25 ug/ml, which in principle allows quantitative measurement of drug concentrations in light sedation during research.

References

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