A HIGHLY SENSITIVE METHOD FOR THE SIMULTANEOUS UHPLC-MS/MS ANALYSIS OF SEDATIVE DRUGS AND THEIR METABOLITES IN BLOOD PLASMA USING HFIP AS THE ELUENT ADDITIVE

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Sedation is commonly used in intensive care units (ICU) [1]. Sedative and analgesic requirements of children admitted to neonatal or pediatric ICU are under-studied, meaning optimal dosing is unclear.

The aim of this work was to develop and validate a rapid ultra-high performance liquid chromatographic-tandem mass spectrometric method for the analysis of three common sedative and analgesic agents: morphine, clonidine and midazolam, and their metabolites (morphine-3-glucuronide, morphine-6-glucuronide and 1'-hydroxymidazolam) in blood plasma at trace level concentrations. The simultaneous quantitation of sedatives and analgesics and their active metabolites will allow complex evaluation of the pharmacokinetic/pharmacodynamic relationships and defining optimal dosing for sedation at the same time limiting sample volumes and resource needs.

Low concentrations and low sampling volumes may be expected in pediatric patients; we report the lowest limit of quantification for all analytes as 0.05 ng/mL using only 100 µL of blood plasma. The analytes were separated chromatographically using the C18 column with the weak ion-pairing additive 1,1,1,3,3,3-hexafluoro-2-propanol and methanol. The method was fully validated and a matrix matched calibration range of 0.05 – 250 ng/mL was attained for all analytes In addition, between-day accuracy for all analytes remained within 93 – 108 %, and precision remained within 1.5 – 9.6 % for all analytes at all concentration levels over the calibration range.

References

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