

Abstract

Development of an HPLC based method for GFR measurement using Iohexol clearance

Introduction

The glomerular filtration rate (GFR) is currently accepted as the best indicator of renal function in clinical medicine. Accurate measurement of the glomerular filtration rate (mGFR) is currently performed at our institution by measurement of plasma clearance of parenterally administered technetium-99mTc-diethylenetriaminepentaacetic acid (^{99m}Tc-DTPA).

Due to various reasons, alternate methods such as those utilizing the clearance of radio-opaque tracers such as Iohexol and Iothalamate are increasingly being implemented for determination of mGFR.

Aims

To develop and validate a quantitative method for serum Iohexol on High Performance Liquid Chromatography with Ultraviolet detection (HPLC-UV) or High Performance Liquid Chromatography with Time-of-flight mass spectrometry (HPLC-TOF-MS).

To demonstrate that the method, as described above and evidenced by the literature, can be used successfully to measure GFR in five healthy volunteers by means of comparing the measured GFR with creatinine clearance.

Method

Initial method development will be done using pure Iohexol standard with spiking experiments in various solvents. Determination of the analytical performance characteristics or validation tests will be performed, based on guidelines from the Clinical Laboratory Improvement Amendments (CLIA) document EP15 and the FDA bioanalytical validation guidelines. Precision, accuracy (intra- and inter run; within-batch and between-batch), sensitivity (detection limit; quantitation limits), matrix effects, recovery, effect of dilution (linearity and range), carryover and stability of the analytes and stock solutions will be determined.

As proof of principle, mGFR will be performed in five healthy volunteers, comparing results to creatinine clearance.

Conclusion

This study aims to develop a viable new means for clinicians to effectively and accurately measure serum Iohexol concentration to determine Iohexol clearance as a proxy of glomerular filtration rate in kidney donors or patients with kidney failure.

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Commented [DVDW2R1]: Done

Commented [MOU3]: I would not compare it to creatinine clearance but to a DTPA GFR. We know creatinine clearance is not optimal. The radiation dose of 10 MBq DTPA is quite low. However you may have issues with the ethics committee

Commented [JH4R3]: I tend to agree with Anita. Are you sure the creatinine clearance is going to be reliable enough? What if you get large discrepancies? It will be difficult to know for sure whether the problem lies with the Iohexol measurement or the inherent error associated with creatinine clearance.