Canterbury Medical Research Foundation

Final report for Grant in Aid GIA2020-5

Grant recipient

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Grant details

GRANT TYPE	Grant in Aid	FUNDING ROUND	2020 Grant In Aid
GRANT REFERENCE	GIA2020-5	GRANT AMOUNT	$5,000

Final report

1. Scientific Assessing Committee report

Introduction: Metformin is the first line medication for the treatment of type 2 diabetes. Lactic acidosis is a rare but life-threatening complication that can occur due to metformin accumulation during treatment. Metformin is eliminated from the body by the kidneys. Diabetes is the most common cause of chronic kidney disease (CKD). As CKD progresses, impaired renal function can lead to the accumulation of metformin and increased risk of lactic acidosis. Recent studies have shown metformin can still be used effectively in patients with CKD, but to enable the safe use of metformin in patients with CKD, it is recommended that metformin concentrations are checked to ensure they remain below 5 mg/L. We received a Canterbury Medical Research Foundation Grant in Aid and have used this grant to develop a LC-MS/MS (liquid chromatography/tandem mass spectrometry) method for monitoring metformin concentrations in plasma, which can be used in clinical services to enable the safe use of metformin in patients with CKD.

Outcome of the grant: We have used the LC-MS/MS system in Toxicology, Canterbury Heath Laboratories (CHL), to develop and validate the method for the determination of metformin concentrations in plasma. The metformin standard curve was linear over the concentration range 0.005 to 10 mg/L ($r > 0.999$), and the lower limit of quantification (LLOQ) of metformin was 0.005 mg/L in plasma. The accuracy and precision were assessed at LLOQ, low, medium and high metformin concentration levels (0.005, 0.1, 2.0 and 10 mg/L). There was no constant direction to the bias (i.e. + or -) at each concentration level, and the mean values were within ±10% of the spiked values. Error was very small, as indicated by both intra- and inter-day coefficients of variation of <5.0% at each concentration level, which is well below the 15% limit stipulated by the US FDA guidelines for bioanalytical method validation.

We analysed 38 plasma samples from patients on metformin using this validated LC-MS/MS method for metformin monitoring. The concentrations of metformin measured in patient samples were well covered by the concentration range of the metformin plasma standard curve. All patient samples were analysed in duplicate, and the variations between duplicates were <5.0%. The method has therefore proven to be simple, rapid, robust and reliable.

There is no publication arising from the grant so far, but the analytical method paper for publication is in preparation.

Professional value resulting from the outcome: The LC-MS/MS method for metformin monitoring is now available for use in the therapeutic drug monitoring (TDM) services within Toxicology, CHL, to enhance the safe and effective use of metformin for patients with type 2 diabetes and CKD.

This LC-MS/MS method will both help patient care and provide income to CHL. Further, this assay will contribute to Toxicology, Canterbury Health Laboratories, being a centre of excellence as the sole laboratory providing this service in New Zealand. Finally, it will provide opportunities for the researchers to conduct metformin pharmacokinetic-pharmacodynamic studies to better define the relationship between metformin concentrations and clinical response.

2. Photographs

View an attachment by double clicking the icon to the left of the file name. Icons are not displayed and attachments are not accessible when this PDF is viewed in a web browser; you must open it in PDF reader software.

Photographs of Metformin Project Final Report.20210120.docx
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4. Feedback

Publication

Date