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RACP Foundation Research Awards

FINAL REPORT

Project / Program Title		The relationship between gut and glycaemia in type 2 diabetes: a longitudinal study of gastric emptying and the influence of the gut incretin axis on glycaemia
Name		Dr Liza Phillips
Award Received		2016 Diabetes Australia Research Establishment Fellowship
Report Date		1 April 2017
Chief Investigator / Supervisor		Dr Liza Phillips Supervisor: Michael Horowitz and Chris Rayner
Administering Institution		The University of Adelaide
Funding Period	Start Date:	1 January 2016
	Finish Date:	1 January 2017

PROJECT SUMMARY

It is becoming increasingly clear that the rate of gastric emptying (the speed at which food empties from the stomach) is an important determinant of blood glucose control. Indeed, therapies have been developed, which are widely used, which target the rate of gastric emptying for blood glucose lowering effects (e.g. short acting exenatide seems to exert much of its therapeutic potential through slowing of gastric emptying).

These projects were designed to document:

i) the relationship between the rate of gastric emptying and blood glucose control in patients with pre-diabetes or normal glucose tolerance, and

ii) the stability of the rate of gastric emptying in patients with type 1 and type 2 diabetes in both short and long term studies.

Project 1: Longitudinal follow up of gastric emptying in type 2 diabetes

This project evaluated the long-term stability of gastric emptying in patients with type 2 diabetes. Our findings in this study suggest that patients with long-term type 2 diabetes, gastric emptying of solids and liquids does not usually become more delayed over time, and abnormally slow gastric emptying of solids may improve.

Project 2: Gastric emptying in diabetic ketoacidosis

Patients with type 1 diabetes may present acutely unwell with diabetic ketoacidosis – they may experience prominent gastrointestinal symptoms such as abdominal pain, nausea and vomiting. This study aimed to determine whether the rate of stomach emptying (gastric emptying) is delayed in the acute phase of illness as this may inform recommendations for duration of fasting

in these patients. Initial findings have demonstrated that neither liquid nor solid emptying is reversibly changed.

Project 3: Does baseline gastric emptying predict glycaemic control over time?

In this study, patients with pre-diabetes or normal glucose tolerance, were asked to return for follow up ~ 5-8 years following baseline gastric emptying studies to determine whether baseline rates of gastric emptying could predict deterioration in glycaemic responses or indeed progression to type 2 diabetes. To date 30 subjects have been studied, however, this study is ongoing and expected to be completed by mid 2017.

PROJECT AIMS / OBJECTIVES

Project 1:

The rate of gastric emptying is a key determinant of postprandial glycaemia which can be manipulated for therapeutic gain in type 2 diabetes (T2DM). Measurements of gastric emptying using scintigraphy show good reproducibility within healthy individuals in the short term, although little is known about the natural history of gastric emptying in patients with T2DM. This study has been completed.

Project 2:

Aim: to quantify gastric emptying in patients with type 1 diabetes to determine: 1) whether gastric emptying is delayed in the acute recovery phase of DKA and 2) whether any abnormalities in gastric emptying during the acute phase are reversible. Thus far 5 subjects have been studied – anticipated completion mid 2017.

Project 3

The primary purpose of the proposed study is to evaluate, in a cohort of 'healthy' older subjects with normal or impaired glucose tolerance, the hypothesis that over a period of ~5 years deterioration in glucose tolerance (as assessed by blood glucose at 60 min during an OGTT) will be associated with relatively faster gastric emptying. This study is ongoing – completion anticipated mid 2017.

SIGNIFICANCE AND OUTCOMES

Project 1:

In this project, we identified that in patients with long-term type 2 diabetes, gastric emptying of solids and liquids does not usually become more delayed over time, and abnormally slow gastric emptying of solids may improve. This is pertinent when considering management of patients with gastroparesis and when evaluating the role of diabetic medications that target gastric emptying for therapeutic effect (e.g. short acting GLP-1 agonists such as exenatide bd).

Project 2

This study has demonstrated that in a small cohort of type 1 patients, gastric emptying of solids and liquids was not markedly delayed in the acute recovery phase of DKA, nor was there significant change in gastric emptying on follow-up when patients were clinically well. This helps inform practice in the acute management of DKA and suggests that prolonged fasting is not required.

Project 3

This study is ongoing – results of this study will provide preliminary evidence regarding the role of the rate of gastric emptying as a predictor of incident T2DM. If positive, further research in this

area would be conducted e.g. targeted intervention to slow gastric emptying as a preventative approach to T2DM.

PUBLICATIONS / PRESENTATIONS

Abstracts:

Longitudinal Evaluation of Gastric Emptying in Type 2 Diabetes

Liza K Phillips1, Linda E. Watson1, Tongzhi Wu1, Michelle J. Bound1, Helen Checklin1, Jacqueline Grivell1, Karen L. Jones1, Michael Horowitz1, Christopher K. Rayner1

Submitted to European Association for the Study of Diabetes

(EASD) 2018 Lisbon, Portugal

Manuscript in preparation

Preliminary observations of gastric emptying during diabetic

ketoacidosis

Liza K Phillips1,2, Chinmay Marathe1,2, Laurence Trahair1, Michelle J. Bound1, Seva Hatzinikolas1, Linda Mignone1,2, Adam Deane2, Chris Rayner1, Karen L. Jones1, Michael Horowitz1,2

Poster presentation at EASD 2017, Munich Germany

Study ongoing – hope to finish mid 2017

Contribution to other research:

Abstract:

A whey/guar “preload” improves postprandial glycaemia and HbA1c in type 2 diabetes: a 12-week, single-blind, randomised and placebo-controlled trial

Linda E. Watson1, Tongzhi Wu1, Liza Phillips1, Michelle J. Bound1, Helen Checklin1, Jacqueline Grivell1, Karen L. Jones1, Peter Clifton2 Michael Horowitz1, Christopher K. Rayner1

Submitted to European Association for the Study of Diabetes

(EASD) 2018 Lisbon, Portugal

Manuscript in preparation

Publications during fellowship year:

Original research:

1. Ali Abdelhamid Y, Plummer MP, Finnis ME, Biradar V, Bihari S, Kar P, Moodie S, Horowitz M, Shaw JE, Phillips LK, Deane AM. Long-term mortality of critically ill patients with diabetes who survive admission to Intensive Care. Critical Care and Resuscitation, submitted manuscript

2. Plummer MP, Finnis ME, Phillips LK, Kar P, Bihari S, Biradar V, Moodie, S. Horowitz, M. Shaw, J. E, Deane, A. M. Stress Induced Hyperglycemia and the Subsequent Risk of Type 2 Diabetes in Survivors of Critical Illness. PloS one. 2016;11(11):e0165923.

3. Ali Abdelhamid Y, Phillips L, Horowitz M, Deane A. Survivors of intensive care with type 2 diabetes and the effect of shared care follow-up clinics: study protocol for the SWEET-AS randomised controlled feasibility study. Pilot and Feasibility Studies (2016) 2:62

Reviews:

4. Nguyen TA, Ali Abdelhamid Y, Phillips LK, Chapple LS, Horowitz M, Jones KL, Deane AM, Nutrient stimulation of mesenteric blood flow – implications for older critically ill patients World J Crit Care Med 2017; 6(1): 28-36

5. Ali Abdelhamid Y, Kar P, Finnis ME, Phillips LK, Plummer MP, Shaw JE, Horowitz, Deane, A. M Stress hyperglycaemia in critically ill patients and the subsequent risk of diabetes: a systematic review and meta-analysis. Critical care. 2016 Sep 27;20(1):301.