Reducing the postprandial glycaemic impact of dietary protein in type 1 diabetes mellitus

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Statement of Originality

I hereby certify that the work embodied in the thesis is my own work, conducted under normal supervision.

The thesis contains no material which has been accepted, or is being examined, for the award of any other degree or diploma in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text. I give consent to the final version of my thesis being made available worldwide when deposited in the University's Digital Repository, subject to the provisions of the Copyright Act 1968 and any approved embargo.

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Thesis by Publication

I hereby certify that the work embodied in this thesis is in the form of a series of papers. I have included as part of the thesis a written declaration from each co-author, endorsed in writing by the Faculty Assistant Dean (Research Training), attesting to my contribution to any jointly authored papers.

Megan Paterson

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List of Publications

List of publications included as part of this thesis

Paterson MA, Smart CE, Lopez PE, McElduff P, Attia J, Morbey C, King BR. Influence of dietary protein on postprandial blood glucose levels in individuals with Type 1 diabetes mellitus using intensive insulin therapy. Diabetic Medicine 2016; 33(5): 592–98

Paterson MA, Smart CEM, Lopez PE, Howley P, McElduff P, Attia J, Morbey C, King BR. Increasing the protein quantity in a meal results in dose-dependent effects on postprandial glucose levels in individuals with Type 1 diabetes mellitus. Diabetic Medicine 2017; 34(6): 851–4

Paterson MA, King BR, Smart CE, Smith T, Rafferty J, Lopez, P. Impact of dietary protein on postprandial glycaemic control and insulin requirements in type 1 diabetes: A systematic review. Diabetic Medicine 2019; DOI: 10. 1111/dme.14119.

Paterson MA, Smart CEM, Howley P, Foskett D, Price D, King BR. High protein meals require 30% additional insulin to prevent delayed hyperglycemia. (Manuscript in preparation)

List of additional publications relevant to the thesis

Lopez P, Smart C, Morbey C, McElduff P, Paterson MA, King, BR. Extended insulin boluses cannot control postprandial glycemia as well as a standard bolus in children and adults using insulin pump therapy. BMJ Open Diabetes Research and Care 2014; 2:e000050

Paterson MA, Bell K, O'Connell S, Smart C, Shafat A, King B. The role of dietary protein and fat in Glycaemic Control in type 1 diabetes: Implications for Intensive Diabetes Management. Current Diabetes Reports 2015; 15: 61. DOI 10.1007/5/1892-015-0630-5.

Lopez P, Smart CE, McElduff P, Foskett D, Price DA, Paterson MA, King BR. Optimising the combination insulin bolus split for children and young people with type 1 diabetes mellitus using insulin pump therapy for a high fat, high protein meal. Diabetic Medicine 2017; 34(10): 1380–84

Paterson M. The glycaemic impact of dietary protein in Type 1 diabetes: Implications for glycaemic control and insulin requirements. The Australian Diabetes Educator 2016; 19(3).

Paterson M, Smith T, Smart CM. Managing the ups and downs of dietary protein and fat: The John Hunter Children's Hospital Approach in type 1 diabetes care. The Australian Diabetes Educator 2019; 22(3).

List of conference presentations of relevance to the thesis

Paterson MA, Smart C, Lopez P, Morbey C, McElduff P, King B. The effect of pure protein on post-prandial blood glucose levels in individuals with type 1 diabetes. American Diabetes Association 74th Annual Scientific Sessions, San Francisco, CA USA, June 2014.

Paterson MA, Smart C, Lopez P, Morbey C, McElduff P, King B. The effect of pure protein on post-prandial blood glucose levels in individuals with type 1 diabetes. APPES and Australian Paediatric Endocrine Group (APEG) meeting, Darwin Australia, November 2014.

Paterson MA, Smart C, Lopez P, McElduff P, Morbey C, King B. The effect of protein plus carbohydrate with no fat on postprandial glycaemia in individuals with type 1 diabetes. APEG + ISPAD (International Society of Paediatric and Adolescent Diabetes), Brisbane, Australia, 2015.

Paterson MA, Smart C, Lopez P, Morbey C, McElduff P, Goodwin G, King B. The impact of the quantity of protein in a meal on postprandial blood glucose levels in individuals with type 1 diabetes mellitus using intensive insulin therapy. Advanced Technologies and Treatments for Diabetes, Milan, Italy, February 3–6 2016.

Paterson MA, Smart C, Foskett D, Price D, Howley P, Maher A, Fenton B, Rafferty J, King B. A 30% increased insulin dose is necessary to control postprandial hyperglycaemia for high protein meals in individuals with type 1 diabetes using insulin pump therapy. American Diabetes Association 79th Annual Scientific Sessions, San Francisco, CA USA, June 2019.

Paterson MA. The glycaemic impact of dietary protein in type 1 diabetes. Australian Diabetes Educator Association NSW Branch conference (invited speaker), May 2015.

Statements of Contribution by Others

STATEMENT OF CONTRIBUTION: PAPER 1

I attest that Research Higher Degree candidate Megan Paterson contributed substantially in terms of study concept and design, data collection and analysis, and preparation of the manuscript entitled:

'Impact of dietary protein on postprandial glycaemic control and insulin requirements in type 1 diabetes: A systematic review'.

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AUC	area under the curve
BG	blood glucose
BGL	blood glucose level
BMI	body mass index
CHO	carbohydrate
CI	confidence interval
CVD	cardiovascular disease
CMIT	carotid intima-media thickness
CGM	continuous glucose monitoring
CSII	continuous subcutaneous insulin infusion
DKA	diabetic ketoacidosis
FPU	fat protein unit
FGM	flash glucose monitoring
FII	food insulin index
FFAs	free fatty acids
GAD	glutamic acid decarboxylase
GIP	gastric inhibitor polypeptide
GLP-1	glucagon-like peptide-1
GI	glycaemic index
GL	glycaemic load
HbA1c	glycated haemoglobin
HCL	hybrid closed loop
HDL	high-density lipids
HLA	human leukocyte antigen

HP/HF	high-protein/high-fat
HP/LF	high-protein/low-fat
IA-2	insulinoma-associated 2 molecule
IAA	insulin autoantibodies
ICR	insulin to carbohydrate ratio
IGF-1	insulin-like growth factor
IIT	intensive insulin therapy
IPT	insulin pump therapy
IV	intravenous
LDL	low-density lipids
LF/LP	low-fat/low-protein
MDI	multiple daily injections
NICE	National Institute for Health and Care Excellence
OR	odds ratio
SMBG	self blood glucose monitoring
SD	standard deviation
TIR	time in range
TAGs	triacylglycerols
T1DM	type 1 diabetes mellitus
T2DM	type 2 diabetes mellitus
ZnT8	zinc transporter 8

Abstract

Type 1 diabetes is a serious, life-long, autoimmune condition that occurs predominantly during childhood and adolescence. It is well recognised that intensive insulin therapy is the optimal method of managing type 1 diabetes. This approach has been demonstrated to reduce the risk of long-term complications of diabetes by reducing glycaemic variability and HbA1c. Despite the increased use of intensive insulin therapy, postprandial glycaemic excursions remain a significant challenge for many people living with type 1 diabetes. This is important as postprandial hyperglycaemia has been identified as an independent risk factor for the development of long-term complications of type 1 diabetes, often despite careful pre-meal insulin dosing and in-target HbA1c.

A key component of intensive insulin therapy is matching meal-time insulin doses to the carbohydrate content of a meal, together with the pre-prandial blood glucose level. This is based on the assumption that carbohydrates are the main macronutrient to influence postprandial glycaemia. However, there is increasing evidence that other macronutrients – protein and fat – can also have a significant impact on postprandial glycaemia. The primary purpose of this thesis is to investigate the postprandial glycaemic effects and subsequent insulin requirements of dietary protein.

A systematic review of the literature revealed that dietary protein can cause significant delayed and sustained postprandial hyperglycaemia and increased insulin requirements in individuals with type 1 diabetes. This review has highlighted that gaps in the literature exist regarding how dietary protein impacts postprandial glycaemia in type 1 diabetes and that strategies to reduce glycaemic excursions following high-protein meals are needed.

Overall, the sequence of studies presented in this thesis have sought to gain an improved understanding of the glycaemic effects of dietary protein, in order to improve the effectiveness of meal-time insulin dosing strategies and reduce the risk of postprandial hyperglycaemia. The clinical implications of the findings of the studies conducted are presented, with practical recommendations described for the management of high-protein meals with the aim of improving long-term outcomes for people living with type 1 diabetes.