



RACP Foundation Research Awards

FINAL REPORT

Project Title	Closed Loop Insulin Delivery and Islet Cell Transplantation in Adults with Type 1 Diabetes Mellitus and Severe Hypoglycaemia: An Evaluation of Glycaemia, Counter-Regulatory Hormones, Hypoglycaemia Awareness, and Psychosocial and Physical Well-Being.	
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Award Received	2017 Shields Research Entry Scholarship	
Report Date	31 December 2018	
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Administering Institution	The University of Melbourne	
Funding Period	Start Date:	6 March 2017
	Finish Date:	5 March 2018

PROJECT SUMMARY

Type 1 diabetes (T1 D) affects over 120,000 people in Australia. Fear of hypoglycaemia remains the greatest barrier to maintaining glucose levels within target range. Severe hypoglycaemia is experienced by 1 in 5 Australian adults, and is associated with increased morbidity and mortality. Approximately 20% of adults with T1 D of long-duration subsequently develop impaired awareness of hypoglycaemia. Repeated episodes of severe hypoglycaemia and impaired awareness of hypoglycaemia can have consequences on a person's physical and psychological well-being, impacting overall quality of life.

Therapeutic strategies to reduce hypoglycaemia and restore hypoglycaemia awareness have been widely explored. Current clinical practice recommendations for this high-risk group with T1 D, severe hypoglycaemia and impaired awareness of hypoglycaemia incorporate educational, technological and transplantation interventions.

Recent advances in modern diabetes technology are rapidly changing the landscape of T1 D management. An 'artificial pancreas' or hybrid closed-loop insulin pump system is an investigational device that combines glucose sensors and insulin delivery systems. This pump automatically delivers basal insulin doses to maintain blood glucose levels in a healthy range. It may provide a better match than current insulin delivery, resulting in improved glucose control with less hypoglycaemia. However, this technology is yet to be evaluated in a group at high-risk of hypoglycaemia.

Currently, islet transplantation is the benchmark therapeutic option for those with repeated severe hypoglycaemia and life-threatening impaired awareness of hypoglycaemia. However, transplantation is limited by the need for life-long immunosuppression and limited availability of donor cells.

Evaluation of these two therapies - the 'artificial pancreas' and islet transplantation - is warranted in this high-risk group with repeated episodes of hypoglycaemia. This research project aims to assess

the clinical utility of the 'artificial pancreas' and islet transplantation, compared with usual insulin therapy, in improving overall glucose control, reducing hypoglycaemia and its effects on other health aspects over a 6- month period. This project has potential to expand therapies used in current clinical practice.

PROJECT AIMS / OBJECTIVES

To evaluate the efficacy of islet transplantation, compared to hybrid closed-loop insulin delivery systems, compared to usual diabetes therapy for adults with T1 D and impaired awareness of hypoglycaemia and recurrent severe hypoglycaemia to determine effects pertaining to:

1. Restoration of counter-regulatory hormonal responses
2. Glucose control: time-in-target range, hypoglycaemia and related glycaemic parameters
3. Restoration of hypoglycaemia awareness.
4. Non-glycaemic clinical measures: sleep quality, cardiac rhythm, cognitive function
5. Psychological outcomes: fear of hypoglycaemia, diabetes distress, treatment satisfaction

SIGNIFICANCE AND OUTCOMES

This study offers novel and unique information regarding whether closed-loop insulin delivery systems are beneficial for those with severely compromised glucose counter-regulation and impaired awareness of hypoglycaemia, without the need to transplant islet cells.

Other novel aspects include evaluation of non-glycaemic measures of sleep quality, cardiac rhythm, cognitive function and psychological outcomes in this high-risk group. These findings have potential to mitigate the burden of hypoglycaemia, and quantify the relative benefits of each therapy for use in this cohort of individuals with impaired awareness of hypoglycaemia and recurrent severe hypoglycaemia.

If the results of this study are promising, we plan to follow-up with larger-scaled randomised controlled studies to further evaluate these therapeutic modalities within this group of individuals with type 1 diabetes.

PUBLICATIONS / PRESENTATIONS

Lee MH, Ward GM, Macisaac RJ , et al. Mortality in People with Type 1 Diabetes, Severe Hypoglycemia, and Impaired Awareness of Hypoglycemia Referred for Islet Transplantation. *Transplantation Direct*. 2018;4(11):e401 .

Lee MH, Paldus B, O'Neal ON. Type 1 Diabetes and the Artificial Pancreas. *Diabetes Management Journal*. 2017 September.

McAuley SA, de Bock MI, Sundararajan V, Lee MH, et al. Effect of 6 months of hybrid closed-loop insulin delivery in adults with type 1 diabetes: a randomised controlled trial protocol. *BMJ Open*. 2018;8:e02027 4. doi: 10.1136/bmjopen-2017-02027 4

Lee MH, et al. Mortality amongst people with severe unstable type 1 diabetes referred for islet cell transplantation. Accepted for Oral Presentation, Australian Diabetes Society Annual Conference, Perth August 2017