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FINAL REPORT

Project / Program Title		Gastric emptying in non-diabetic Afro-Caribbeans (AfC) - implications for the pathogenesis of type 2 diabetes
Name		Dr Chinmay Marathe
Award Received		2017 Diabetes Australia Research Establishment Fellowship
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Chief Investigator / Supervisor		Dr Chinmay Marathe Supervisor: Prof Michael Horowitz
Administering Institution		King's College London
Funding Period	Start Date:	1 January 2017
	Finish Date:	1 January 2018

PROJECT SUMMARY

It is well recognised that there are major differences amongst specific ethnic groups in the risk of type 2 diabetes (T2D), but the underlying pathophysiology remains poorly defined. Within the UK, diabetes and its complications disproportionately affect ethnic minority groups, particularly Afro-Caribbeans (AfC), the second largest minority ethnic group making up approximately 25% of the non-White population. In South-east London, ≈ 40% of people with new-onset T2D are black Africans. The rate of gastric emptying is a major determinant of postprandial glycaemic excursions and insulinaemia in Caucasians in both health and type 2 diabetes. It is not widely appreciated that gastric emptying exhibits substantial inter-individual, but relatively low intra-individual, variation, usually being in the range 1-4 kcal/min in he9lth. In Caucasians, the initial rises in postprandial glucose and insulin are proportional to the rate of gastric emptying (from ≈ t=O to ≈ t=60 min) following an oral glucose challenge. There is now suggestive evidence that gastric emptying is influenced by ethnicity; for example, rapid gastric emptying has been reported to be relatively more rapid in Mexican Americans when compared with non-Hispanic whites and it has been suggested that this may predispose to the development of type 2 diabetes, particularly in individuals with impairments in insulin secretion or increased insulin resistance. Gastric emptying has not been evaluated in the Afro-Caribbean community.

PROJECT AIMS / OBJECTIVES

The aim of this study is to compare gastric emptying in non-diabetic Afro-Caribbeans and Caucasians and to determine the relationships of glycaemia, with the rate of gastric emptying in these ethnic groups. Accordingly, eligible participants of either ethnicity are being recruited from

the community (primarily from the boroughs of South London which has a high Afro-Caribbean population). This study is currently ongoing – completion anticipated late 2018.

Our hypothesis is that gastric emptying will be relatively more rapid in Afro-Caribbean group resulting in higher initial postprandial glycaemic excursions.

SIGNIFICANCE AND OUTCOMES

It is now appreciated that the development of type 2 diabetes (T20) is characterized by a failure of the beta cells to compensate for the worsening insulin sensitivity, rather than a defect in insulin sensitivity per se. Prevention of T20 should, accordingly, focus on 'resting' the beta cell by reducing postprandial glycaemia. This is the first study to compare gastric emptying between non-diabetic Afro-Caribbean and Caucasian participants, as well as its relationship with glycaemia. If our hypothesis is correct i.e. gastric emptying is relatively more rapid in Afro-Caribbeans, an ethnic group with high incidence of type 2 diabetes, a more targeted approach in the prevention and management of type 2 diabetes in Afro-Caribbeans is likely to be appropriate. Thus, there may be a greater role for dietary and pharmacological strategies that reduce postprandial glycaemia by slowing gastric emptying, such as nutrient 'preloads' and short-acting GLP-1 agonists like exenatide. This initial study also has the potential to develop into a longitudinal study of incidence and progression to impaired glucose tolerance and type 2 diabetes in Afro-Caribbeans. We recognize that ultimately, the hypothesis that relatively more rapid gastric emptying represents a risk factor for impaired glucose tolerance and T20 must be evaluated in a prospective study.

PUBLICATIONS / PRESENTATIONS

We anticipate that an abstract resulting from this project will be presented at Diabetes UK annual conference in 2019.

Other abstracts during fellowship year

1. The impact of variable duodenal glucose load on insulin clearance in health. Marathe CS, Rayner CK, Jones KL, Horowitz M Australian Diabetes Society Annual Conference, Perth 2017 (Oral presentation)

2. Comparative effects of low-carbohydrate-, full-strength- and low-alcohol beer on gastric emptying, alcohol absorption and glycaemia in healthy young subjects. Stevens JE, Trahair LG , Marathe CS, Sardana R, Horowitz M , Jones KL.

3. Insulin secretion in Black West African and White European men with type 2 diabetes: comparison of indices derived from glucose clamps and mixed meal tests. Marathe CS, Mohandas C, Bello 0, Amiel SA, Goff LM. Diabetes UK Annual Conference, Manchester 2017

4. Insulin sensitivity indices in Black Africans and White Europeans with type 2 diabetes: a comparison of fasting, meal tolerance test and hyperinsulinaemic-euglycaemic clamp indices. ·Bello 0, Marathe CS, Mohandas C, Amie! SA, Goff LM. Diabetes UK Annual Conference, Manchester 2017

Publications during fellowship year

1. A Glucagon receptor signalling - backwards and forwards. Wu T, Rayner CK, Marathe CS, Jones KL, Horowitz M. Expert Opin lnvestig Drugs. 2018 Feb;27(2):135-138. doi: 10.1080/13543784.2018.1428306.

2. Impact of variations in duodenal glucose load on insulin clearance in health and type 2 diabetes. Marathe CS, Rayner CK, Jones KL, Horowitz M. Acta Diabetol. 2018 Feb;55(2):205-207. doi: 10.1007/s00592-017- 1073-z. Epub 2017 Nov 13.

3. Gastrointestinal motility in people with type 1 diabetes and peripheral neuropathy. Marathe CS, Rayner CK, Jones KL, Horowitz M. Diabetologia. 2017 Nov;60(11):2312-2313. doi: 10.1007/s00125-017- 4391-3.

Relationships of the early insulin secretory response and oral disposition index with gastric emptying in subjects with normal glucose tolerance. Marathe CS, Rayner CK, Lange K, Bound M, Wishart J, Jones KL, Kahn SE, Horowitz M. Physiol Rep. 2017 Feb;5(4). pii: e13122. doi: 10.14814/phy2.13122.

4. Acute effects of the glucagon-like peptide-1 receptor agonist, exenatide, on blood pressure and heart rate responses to intraduodenal glucose infusion in type 2 diabetes. Thazhath SS, Marathe CS, Wu T, Chang J, Khoo J, Kuo P, Checklin HL, Bound MJ, Rigda RS, Horowitz M, Jones KL, Rayner CK. Diab Vase Dis Res. 2017 Jan;14(1):59-63.

5. Effects of small intestinal glucose on glycaemia, insulinaemia and incretin hormone release are load-dependent in obese subjects. Trahair LG, Marathe CS, Standfield S, Rayner CK, Feinle-Bisset C, Horowitz M, Jones KL. Int J Obes (Lond). 2017 Feb;41(2):225-232. doi: 10. 1038/ijo.2016.202.

6. Reactive hypoglycaemia with seizure fo llowing intraduodenal glucose infusion in a pati~nt with type 2 diabetes. Marathe CS, Rayner CK, Jones KL, Horowitz M. Acta Diabetol. 2017 Feb;54(2):215-218. doi: 10.1007 /s00592-016-0888-3. ·