A breakfast-centered meal plan for people with diabetes: A modest cohort study under free-living conditions

Elsamma Chacko*, Phyllis Awruch & Elina Schwartz

ABSTRACT

Aim: To test the efficacy of a new breakfast centered meal plan in improving weight, waist circumference, HbA1c and in preventing hypoglycaemia in people with diabetes and pre-diabetes under free-living conditions. Methods: Twenty-three adults with type 2 diabetes or pre-diabetes received half-day training in a personalized, low-carb meal plan which typically included one big breakfast and 4-5 small meals/snacks. Carb intake was individualized using ADA and AACE guidelines: ppg of <180 mg/dL (10.0 mmol/L) for the big meal (preferably breakfast) and <140 mg/dL (7.8 mmol/L) for the small meals. The subjects were also instructed not to eat during the three hours prior to bedtime. Reminders were through monthly meetings, and by phone or e-mail. Results: Of the 23 people trained, 11 (48%) adhered to the meal plan for 3 months. The subjects included 1 man and 10 women, age 47-69, BMI 27-39 Kg/m^2. Four had pre-diabetes and 7 had type 2 diabetes. Four took no diabetes medications, one type 2 patient was on insulin and the rest took oral agents for diabetes. Average weight reduction was 6 lbs (range +2 to -22). HbA1c came down by 0.5% (+0.2 to -1.66). Fasting glucose decreased by 44 mg/dL (+12 to -151). Waist circumference decreased by 0.47 inches, (+2" to -3.5") but was not a statistically significant. Glucose variability has been minimum for this meal plan by design. No hypoglycaemia or other adverse events intervened. All 11 subjects noted that eating close to bedtime raised fasting glucose. The consensus was that they were eating healthier than before and no instances of excessive hunger or hypoglycaemia occurred. Conclusion: A breakfast-centered (big breakfast and 5 small meals) offered improved satiety, weight, fasting glucose, glycemic variability and HbA1c under free-living conditions for people with diabetes and pre-diabetes – without precipitating hypoglycaemia.

Introduction

Importance of meal composition for glucose control is well documented [1-16]. They include meditaranean, Dash diet and plant-based meal plans [2-4]. Low carbohydrate meals balanced with extra protein, fiber and healthy fat are good for glucose control [6-16]. Strong evidence supporting the importance of meal timing also exists [17-23]: eating a healthy breakfast has many merits for people with insulin resistance. Mekary and colleagues showed risk for T2DM increasing in those who skipped breakfast [17]. Kahleova and group showed 2 large meals, breakfast and lunch, to be better than 6 small meals [20]. Another study showed big breakfast plus small supper was preferable to small breakfast plus big supper [21]. This would also benefit patients who have diurnal variation in glucose tolerance. A 1974 report found elderly patients have higher glucose levels in the evening mainly because of low insulin secretion [24]. Moreover, eating a breakfast itself moderates the glucose surge following lunch -- the so-called second meal phenomenon [22,23]. Another aspect of meal timing is eating every 2-4 hours

Connecticut Valley Hospital, 1000 Silver Street, Middletown, CT 06457, USA

**Author for correspondence: elsammac@msn.com*

KEYWORDS

- postprandial glucose
- glycemic variability
- American Diabetes Association
- American Association of Clinical Endocrinologists
- continuous glucose monitoring

to prevent hypoglycaemia [25-29]. Exercising post-breakfast moderates the glucose surges associated with breakfast, lunch and supper [30]. Taken together, it makes sense to have a big breakfast as the exercise meal and make all other meals small: the right exercise would lower postprandial glucose (PPG) of breakfast resulting in minimum glycemic variability (GV) [31]. The carb count can be adjusted as recommended by American Diabetes Association (ADA) and American Association of Clinical Endocrinologists (AACE) guidelines: PPG <180 mg/dL (ADA) for the big meal and PPG <140 mg/dL (AACE) for the small meals [32,33]. Such a meal plan was tried successfully by a type 2 diabetes patient (the corresponding author [34] to prevent hypoglycaemia in 2012. It also helped with managing weight, HbHbA1c and lipids for many years. Moderating glucose surges [35-42] without triggering hypoglycaemia [25-29] is a critical goal of diabetes management. This study had the objective of training the participants with diabetes and pre-diabetes to adopt this meal plan and evaluating its effects on HbA1c, weight, waist circumference, fasting glucose and hypoglycaemia incidence. Patients were free to keep daily carbohydrate intake in the range 30 - 75 gm to realize for the desired glucose levels and weight management goals [10-16]. (The second phase of the study would explore glucose response to exercise timing. A steady meal plan is necessary before studying the effect of exercise on glucose levels).

Methods

Upon IRB approval of the study protocol, employees of Connecticut Valley Hospital with diabetes and pre-diabetes were invited through the hospital's e-mail system to participate in the study. Inclusion criteria were the following: age 18 to 70, BMI >25 kg/m^2 and HbA1c ≥ 5.7% (38.8 mmol/mol). People with complicated medical conditions such as heart disease, stroke, connective tissue disease, cancer, BMI >45 and any condition that would make participation in exercise difficult were excluded from the study. This study was done in cooperation with the PCPs who ordered additional tests before the study as indicated as well as periodic blood tests. Medication adjustments were also done by the PCPs. Two subjects had their sulfonylureas replaced by DPP-4 inhibitors to minimize the risk for hypoglycaemia.

■ Training

One Saturday morning the subjects arrived with a 2-carb balanced breakfast for the half day training session. After the protocol was explained and consent signed, weight, waist circumference, blood pressure and fasting glucose were determined.

■ Meal plan

Subjects ate the breakfasts they had brought from home. It was a two-carb meal which could include two servings (30 grams) of such carbohydrates as grains, starchy vegetables (potato, sweet potato or corn), milk products or fruits. The breakfast also included one serving of protein, one egg, 3 pieces of bacon, 2 tablespoon nuts or ¼ cup cottage cheese. Using their glucometer 1-h, 2-h and 3-h glucose levels were checked. The participants also ate a 1-carb lunch, once the pre-lunch glucose came down to <126 mg/dl. Subsequently 1-h glucose was checked. They were told to lower carb intake if 1-h glucose was > 180 mg/dL (10 mmol/L) after breakfast. The remaining meals were low-carb (1 to 1½ carb) balanced by adding fiber, protein, vegetables and healthy fat, MyPlate style. Thus in a day or two, they were able to design their own personalized meal plan with 1-h glucose ~180 mg/dL after breakfast and <140 mg/dL after small meals. They were encouraged to eat every 3-4 hours during the day, with the caveat that no eating was permitted during the 3 h period before bedtime. Drinking 8-10 glasses of water was also encouraged.

■ Physical activity

During this phase of the study the subjects were told not to change their general activity level.

Weight was to be checked once a week. Daily checking of fasting glucose was encouraged. In general, we promoted frequent glucose checking as they wished. A data sheet was provided to keep track of the various readings. There were monthly meetings. Subsequent communications were through e-mails, phone calls or faxing. During this training session, there were talks by the research team, which included two diabetes educators and a physician, on various topics: macronutrients, micronutrients, carb counting, MyPlate and how glucose profile could be improved by meal plan alone.

■ Statistical analysis

Statistical comparisons were made for weight, waist circumference, fasting glucose and HbA1c by the student's paired t-testusing SPSS (**TABLES 1-3**). Values are expressed as mean ± SD. P-value <0.05 was deemed statistically significant.

Results

Of the 23 people trained, 11 (48%) adhered to the meal plan for at least 3 months and submitted their lab results, weight and waist circumference were measured by one of the researchers. The 52% who discontinued the program cited work- and family-related stress as the major impediment to participation. The 11 subjects who completed the study included 1 man and 10 women, age 47-69, BMI 27-39. Four of the adherent subjects had pre-diabetes and 7 had type 2 diabetes. Four took no diabetes medications, one type 2 patient was on insulin and the rest took oral agents for diabetes. Ten subjects found that two servings of carbohydrates were appropriate for breakfast. One person had three carbs in his breakfast. Most of them were eating 1 or 1½ -carb meals for the smaller meals. Average weight reduction was 6 lbs (range +2 to -22). HbA1c came down by 0.5% (+0.2 to -1.66). Fasting glucose decreased by 44 mg/dL (+12 to -151). Waist circumference decreased by 0.47 inches, (+2" to -3.5") but the improvement was found to be not statistically significant. No hypoglycaemia or other adverse events intervened. All 11 subjects noted that eating close to bedtime raised fasting glucose, they were eating healthier meals and were satisfied by the meal plan: they reported no excessive hunger. All 11 subjects held full time jobs and only two could designate breakfast as the exercise meal. Four subjects chose lunch and 5 had supper for the biggest meal of the day. The subjects felt that weight reduction

Table 1. Characteristics of the subjects before and after the intervention

Patient	sex	Age	BMI	Exercise meal	Diagnosis	weight (lbs)	WC (inches)	Fasting glucose (mg/dl)	HbA1c (%)
1	M	54	31.5	BF	T 2 DM	195 > 176	41.5 > 39.5	150 > 117	6.6 > 6.6
2	F	69	27	S	T 2 DM	167 > 161	44.5 > 44	238 >119	8.0 > 7.2
3	F	60	33	S	T 2 DM	186 > 1	41.5 >	114 >103	8.1 > 6.9
4	F	52	32	BF	Pre-DM	184 >186	41.2 > 41.5	100 > 92	6.0 > 6.2
5	F	52	30.5	L	T 2 DM	165.6 > 167	43 > 43.5	304 > 155	10.7 > 9.1
6	F	58	30.5	S	T 2 DM	184 >182	45 > 44.5	211 >129	7.7 > 7.5
7	F	59	36.5	L/S	Pre-DM	233 > 224	47 > 46	119 >100	6.3 >6.1
8	F	67	33	L	T 2 DM	203 >181	44 > 40.5	168 >108	6.9 > 6.2
9	F	47	33.5	S	Pre-DM	209 > 201	47 >47	119 >103	6.3 >6.2
10	F	47	31.5	S	T 2 DM	209 > 201	37 >39	80 > 92	6.8 > 6.0
11	F	51	39	L	Pre-DM	257 > 245	45 >45.5	101 >107	6.2 >6.1

BF – breakfast; L – Lunch, S – Supper; WC – waist Circumference

Table 2. Descriptive statistics

Variables	N	Minimum	Maximum	Mean	Std. Deviation
Age	11	47	69	56.00	7.362
BMI	11	27.0	39.0	32.545	3.1659
Weight 1	11	166	257	199.33	27.403
Weight 2	11	161	245	191.64	24.812
Waist Circumference 1	11	37.0	47.0	43.34	2.93
Waist Circumference 2	11	39.0	47.0	42. 96	2.72
Fasting glucose 1	11	80	304	154.91	69.469
Fasting glucose 2	11	92	155	111.36	18.32
HbA1c 1	11	6.0	10.7	7.236	1.364
HbA1c 2	11	6.0	9.1	6.736	0.93

Table 3. Paired samples test

	t	df	P
Pair 1 Weight 1- weight 2	3.30	10	.008
Pair 2 Waist circumference 1- Waist circumference 2	0.879	10	.400
Pair 3 Fasting glucose 1 – Fasting glucose 2	2.73	10	.021
Pair 4 HbA1c 1 – HbA1c 2	2.95	10	.015

was "proportional" to decreased carbohydrate consumption.

Discussion

■ "Breakfast glucose tolerance test" and glycemic variability

Continuous glucose monitoring (CGM) facilitates the determination of how much carb to eat and when to eat the next meal. The vast majority of diabetes patients worldwide do not currently have the CGM option. For them "breakfast glucose tolerance test" can be used as a valuable tool for adjusting carb count and meal frequency. Glycemic variability is getting recognized as a more important measure of diabetes management than HbA1c or mean glucose [6]. Minimum glycemic variability also means less hypoglycaemia, less time spend in hyperglycaemia and less complications. This meal plan is designed to have minimum GV: a well designed meal plan may be the simplest way the patient can control GV.

■ Outcome measures

The adherence rate of 48%, for these full time workers is encouraging. Diabetes patients are usually faced with hyperglycaemia, sometimes hypoglycaemia and excessive hunger. These subjects felt good with this meal plan, with predictable, moderate glucose excursions, which may have contributed to the relatively high adherence rate. Improvements in weight primarily reflect decreased carb intake. Weight management should be easier with the steady carb intake, minimal medication/insulin dose (and daily exercise). HbA1c improvement is independent of weight change [38]. Clearly, HbA1c depends on the amplitude of the daily glucose excursions. Several aspects of this meal plan are helpful to glycaemia. Lim and colleagues demonstrated that when calorie intake went down fat in liver and pancreas decreased and fasting glucose and HbA1c improved [10]. Glucose levels are sensitive to meal timing and meal composition [2-23]. This lifestyle calls for a big breakfast (exercise meal) and small lunch and supper and 2-3 snacks. Eating breakfast itself lowers glucose surge of lunch [22,23] because it lowers free fatty acid levels and offers favorable hormone levels: counterregulation is switched to the incretin-insulin system. Balancing the meal with protein, sources of fiber, vegetables and healthy fat improves satiety and lowers the amplitude of the glucose surges [2-16]. Since most meals are small, the overall glucose profile remains moderate. Although exercise is not done during this phase of the study one big meal (breakfast) being the exercise meal is expected to lower hyperglycaemia after breakfast lunch and supper [30]. Preventing hypoglycaemia is critical for people on sulfonylureas or insulin, especially if they have hypoglycaemia unawareness [29,31]. Exercise induced hypoglycaemia can occur after high-intensity exercise [26]. As a rule, eating every 3-4 hours during day time from a well-designed meal plan of one big meal and 4 or five small meals would go a long way toward guarding against hypoglycaemia and improving satiety. Most study subjects improved fasting glucose. As demonstrated by Lim and colleagues, lowering calorie intake improves fasting glucose [10]. On the contrary, eating extra carbs or eating too close to bedtime could increase fasting glucose presumably via increased fat deposition in liver and pancreas. Checking daily fasting glucose helped the subjects to stay on track by making quick changes in behavior. Improvements in weight, HbA1c and fasting glucose were statistically significant; improvement in waist circumference was not.

■ Strengths and weaknesses

Conducting this study under free-living conditions in cooperation with PCPs had its merits. It could be done with minimal funding. PCP keeping an eye on the patients could only help. Participants got to continue their own eating habits except for modest changes in meal selection, shopping and cooking in accordance with decreased carb intake. They did not have to buy pre-cooked frozen meal packages. Breakfast glucose tolerance test can be a valuable tool: patients may design their own meal plans, thereby improving their understanding of why carb counting is important. How often they eat (2-4 h) also depends on the contours of their personal glucose excursions. They may eat lunch when the pre-lunch glucose dips below 126 mg/dL. On the other hand, people who are prone to hypoglycaemia may eat 2 h after the exercise. Participants are entrusted with their own diabetes management. As for weaknesses, there is no control group: it was hard to find motivated people out of this hard working group for controls. For the same reason, sample size is small. The study suffers from all the usual liabilities of observational studies under free-living conditions: meals and physical activities are not supervised. We rely on self report except for

the objective outcome measures. Only 3 out of 11 had medication induced hypoglycaemia risk: one was on insulin who has been monitoring glucose levels closely and two people on sulfonylureas were switched to a DPP-4 inhibitors to prevent hypoglycaemia.

Conclusion

A low-carb, balanced, personalized meal plan with one big meal and 4-5 small meals daily improved satiety, weight, fasting glucose and HbA1c without precipitating hypoglycaemia. Randomized control studies with large sample size would be valuable toward accelerated translation.

Acknowledgement

Authors are thankful to Ruby Wright, RN and Wendy Daversa, Physical Therapist for their help with the training sessions. Also, the authors are indebted to Drs. Lori Hauser and James Poling for doing the statistical analysis. The authors deeply appreciate the dedication of our subjects all of whom are our colleagues.

Duality of Interest

The authors declare that there is no duality of interest associated with this manuscript.

Author's Contribution

The corresponding author is responsible for designing the study, and preparing the manuscript. The two diabetes educators Phyllis Awruch and Elina Schwartz, were actively involved with the training sessions.

References

1. Chacko E. A new meal plan for diabetes. Diabetes 66 (Suppl 1) A521 (Abstract, poster presentation at ADA 77th scientific session June 2017).
2. Esposito K, Maiorino, MI, Bellastella G *et al.* Mediterranean diet for type 2 diabetes: cardiometabolic benefits. *Endocrine.* 56(1), 27–32 (2017).
3. Sacks FM, Svetkey LP, Vollmer WM *et al.* Effects on blood pressure of reduced dietary sodium and the dietary approaches to stop hypertension (DASH) diet. *N. Eng. J. Med.* 344(1), 3–10 (2001).
4. Barnard ND, Katcher HI, Jenkins DJ *et al.* Vegetarian and Vegan diets in type 2 diabetes management. *Nutr Rev* 67(5), 255–263 (2009).
5. Miller V, Mente A, Dehghan M *et al.* Fruit, vegetable and legume intake, and cardiovascular disease and deaths in 18 countries (PURE): a prospective cohort study. *Lancet.* 6736(17), 32253–32255.
6. Bozzetto L, Costabile G, Luongo D *et al.* Reduction in liver fat by dietary MUFA in type 2 diabetes is helped by enhanced hepatic fat oxidation. Diabetologia 59(1), 2697–2701 (2016).
7. Gannon MC, Nuttall FQ. Control of blood glucose in type 2 diabetes without weight loss by modification of diet composition. *Nutr. Metab* 3, 16 (2006).
8. Reynolds LJ, Douglas SM, Kearney ML *et al.* A pilot study examining the effects of consuming a high-protein vs normal-protein breakfast on free-living glycemic control in overweight/obese 'breakfast skipping' adolescents. *Int. J. Obes. (Lond).* 39(9), 1421–1424 (2015).
9. Kuwata H, Iwasaki M, Shimizu S *et al.* Meal sequence and glucose excursion, gastric emptying and incretin secretion in type 2 diabetes: a randomized, controlled crossover, exploratory trial. *Diabetologia.* 59(3), 453–461 (2016).
10. Lim EL, Hollingsworth KG, Aribisala BS *et al.* Reversal of type 2 diabetes: normalisation of beta cell function in association with decreased pancreas and liver triacylglycerol. *Diabetologia.* 54(10), 2506–2514 (2011).
11. Tay J, Luscombie-Marsh ND, Thomson CH *et al.* Very low carbohydrate, low saturated fat diet for type 2 diabetes management: a randomized trial. *Diabetes. Care.* 37(11), 2909–2918 (2014).
12. Fenton CJ, Fenton TR. Dietary carbohydrate restriction: Compelling theory for further research. *Nutrition* 32(1), 153 (2016).
13. Snorgaard O, Poulson GM. Anderson HK *et al.* Systematic review and meta-analysis of dietary carbohydrate restriction in patients with type 2 diabetes. *BMJ. Open. Diabetes. Res. Care.* 5(1), e000354 (2016).
14. Neilsen JV, Gando C, Joensson E *et al.* Low carbohydrate diet in type 1 diabetes, long-term improvement and adherence: A clinical audit. *Diabetol Metab Syndr* 4(1), 23 (2012).
15. Dyson P. Low carbohydrate diets and type 2 diabetes: what is the latest evidence? Diabetes Therapy 6(4), 411–424 (2015).
16. Yancy WS, Foy M, Chalecki AM *et al.* A low-carbohydrate, ketogenic diet to treat type 2 diabetes. *Nutr Metab* 2, 34 (2005).
17. Mekary RA, Giovannucci E, Willett WC *et al.* Eating patterns and type diabetes risk in men: breakfast omission, eating frequency, and snacking. *Am. J. Clin. Nutr.* 5, 1182–1189 (2012).
18. Timlin MT, Perieira MA. Breakfast frequency and quality in the etiology of adult obesity and chronic diseases. *Nutr. Rev.* 65(6): 268–281 (2007).
19. Alwattar AY, Thyfault JP, Leidy HJ. The effect of breakfast type and frequency of consumption on glycemic response in overweight/obese late adolescent girls. *Eur. J. Clin. Nutr.* 69(8), 885–890 (2015).
20. Kahleova H, Belinova L, Malinska H *et al.* Eating two larger meals a day (breakfast and lunch) is more effective than six smaller meals in a reduced-energy regimen for patients with type 2 diabetes: a randomized crossover study. *Diabetologia* 57(8), 1552–1560. (2014).
21. Jakubowicz D, Wainstein J, Ahrēn B. High-energy breakfast with low-energy dinner decreases overall daily hyperglycaemia in type 2 diabetic patients: a randomized clinical trial. *Diabetologia*; 58(5), 912–919 (2015).
22. Jovanovic A, Gerrard J, Taylor R. The second-meal phenomenon in type 2 diabetes. *Diabetes. Care.* 32 (7), 1199–1201 (2009).
23. Lee SH, Tura A, Mari A *et al.* Potentiation of the early-phase insulin response by a prior meal contributes to the second-meal phenomenon in type 2 diabetes. *Am J Physiol Endocrinol Metab* 301(5), E984-E990 (2011).

24. Zimmet PZ, Wall JR, Rome R *et al*. Diurnal variation in glucose tolerance: associated changes in plasma insulin, growth hormone and non-esterified fatty acids. *Br. Med. J.* 1(5906), 485–488 (1974).

25. Cryer PE, Davis Snts. American College of Endocrinology Protocol for Standardized Production of Clinical Practice Guidelines, Algorithms, and Checklists - 2014 Update and the AACe G4G Program. *Endocr. Pract*. 20(7), 692-702 (2014).

26. Cryer PE, Davis SN, Shamoon H. Hypoglycaemia in diabetes. *Diabetes. Care.* 26(6), 1902–1912 (2003).

27. Zoungas S, Patel A, Chalmers J *et al.* Severe Hypoglycaemia and Risks of Vacular Events and Death. *N. Engl. J. Med*. 363(15), 1410–1418 (2010).

28. Reno CM, Litvin M, Clark AL *et al.* Defective counterregulation and hypoglycaemia unawareness in diabetes: Mechanisms and emerging treatments. *Endocrinol. Metab. Clin. North. Am.* 42(1), 15–38 (2013).

29. Maran A, Pavan P, Bonsembiante B *et al.* Continuous glucose monitoring reveals delayed nocturnal hypoglycaemia after intermittent high-intensity exercise in nontrained patients with type 1 diabetes. *Diabetes. Technol. Ther.* 12(10), 763–768 (2010).

30. Van Dijk JW, Venema M, Van Mechelen W *et al.* Effect of moderate-intensity exercise versus activities of daily living on 24-hourblood glucose homeostasis in Male patients with type 2 diabetes. *Diabetes. Care.* 36(11), 3448–3453 (2013).

31. Suh S, Kim JH. Glycemic Variability: How do we measure it and why is it important? *Diabetes. Metab. J.* 39(4), 273–282 (2015).

32. ADA 2014 Standards of Medical Care in Diabetes-2013. *Diabetes. Care.* Supplement 1, S11–S66 (2014).

33. Mechanick JI, Camacho PM, Garber AJ *et al*. Association of Clinical EndocrinologisCryer PE, Davis SNts and American College of Endocrinology Protocol for Standardized Production of Clinical Practice Guidelines, Algorithms, and Checklists - 2014 Update and the AACe G4G Program. *Endocr. Pract.* 20(7), 692–702 (2014).

34. Chacko E. Timing and intensity of exercise for glucose control. *Diabetologia.* 57(11), 2427 (2014).

35. Daenen S, Sola-Gazagnes A, M'Bemba J *et al.* Peak-time determination of post-meal glucose excursions in insulin-treated diabetic patients. *Diabetes. Metab.* 36(2), 165–169 (2010).

36. Ben-Haroush A, Yogev Y, Chen R *et al.* The postprandial glucose profile in the diabetic pregnancy. American *Am. J. Obstet. Gynecol.* 191(2), 576–581 (2004).

37. Zhou W, Gu Y, Luo M. Assessing 1-h plasma glucose and shape of the glucose curve during oral glucose tolerance test. *Eur. J. Endocrinol.* 155(1), 191–197 (2006).

38. Cavalot F, Petrelli A, Traversa M *et al.* Postprandial blood glucose is a stronger predictor of cardiovascular events than fasting blood glucose in type 2 diabetes Mellitus, particularly in woman: lessons from the San Luigi Gonzaga Diabetes Study. *Clin. Endo. Metab.* 91, 813–819 (2005).

39. Esposito K, Nappo F, Marfella R *et al.* Inflammatory cytokine concentrations are acutely increased by hyperglycaemia in humans. *Circulation.* 106(16), 2067–2072 (2002).

40. O'Keef JH, Bell DSH. Postprandial hyperglycaemia/hyperlipidemia (postprandial dysmetabolism) is a cardiovascular risk factor. *Am. J. Cardiol.* 100(5), 899–904 (2007).

41. Woerle HJ, Szoke E, Meyer C *et al.* Mechanisms for abnormal postprandial glucose metabolism in type 2 diabetes. *Am. J. Physiol. Endocrinol. Metab.* 290(1): E67–E77 (2006).

42. Rendell MS, Jovanovic L Targeting postprandial hyperglycaemia. *Metabolism* 55(9), 1263–1281 (2006).