A pilot study to evaluate the effects of a dietary supplement with slow digesting-low GI (SD-LGI) carbohydrates in obese pregnant women using continuous glucose monitoring

A collaboration between Abbott Nutrition and King’s College London

Maitland R.A.\textsuperscript{1}, Patel N.\textsuperscript{1}, Sherry C.\textsuperscript{2}, Marriage B.\textsuperscript{2}, Barr S.\textsuperscript{1}, Lopez J.M.\textsuperscript{3}, Murphy H.\textsuperscript{4}, Thomas S.\textsuperscript{5}, Fernández L.G.\textsuperscript{6}, Rueda R.\textsuperscript{3}, Poston L.\textsuperscript{1}

\textsuperscript{1}King’s College London, Women’s Health Academic Centre, London, UK, \textsuperscript{2}Abbott Nutrition, Paediatric Research & Development, Columbus, United States, \textsuperscript{3}Abbott Nutrition, Discovery: Research and Development, Granada, Spain, \textsuperscript{4}University of Cambridge, Department of Clinical Biochemistry, Cambridge, United Kingdom, \textsuperscript{5}Guy’s and St. Thomas’ NHS Foundation Trust, Diabetes and Endocrinology, London, United Kingdom, \textsuperscript{6}Seplin Statistical Solutions, Granada, Spain
Maternal obesity is associated with abnormal glucose homeostasis

1. Greater glucose exposure in early/late gestation (CGMS & AUC) ¹
2. Greater post-prandial glucose response¹

A  EARLY  B  LATE

3. Insulin resistance and dysregulation of lipid metabolism²
4. Macrosomia¹ & fetal adiposity¹,³

Could a low GI diet improve glucose homeostasis in pregnant women?

The Camden study (2004)\(^4\)

- Glycemic index positively & significantly related to maternal HbA1c and plasma glucose concentration
- Women with LGI diet had < birth weight but increased risk of SGA

RCTs of high risk pregnant women

1. **ROLO\(^5\): n=800**
2. **LIMIT\(^6\): n=2152**
3. **PREGGIO\(^7\): n=691**

Aims

• To determine the glycaemic response following consumption of a slow-digesting low glycaemic index (SD-LGI) supplement in obese pregnant women

• To inform the design of a nutritional intervention RCT of dietary advice plus SD-LGI supplement in obese pregnant women at high risk of gestational diabetes:

Nutritional Intervention during Gestation and Offspring Health Health study (NIGO)
# Composition

<table>
<thead>
<tr>
<th>Serving size 8oz</th>
<th>Test (12539RF)</th>
<th>Control (12551RF)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calories (Kcal)</td>
<td>303</td>
<td>303</td>
</tr>
<tr>
<td>Total fat (g)</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>% calories from</td>
<td>20.8</td>
<td>20.8</td>
</tr>
<tr>
<td>Protein (g)</td>
<td>14</td>
<td>14</td>
</tr>
<tr>
<td>% calories from protein</td>
<td>18.5</td>
<td>18.5</td>
</tr>
<tr>
<td>Carbohydrate (CHO) (g)</td>
<td>46</td>
<td>46</td>
</tr>
<tr>
<td>% calories from CHO</td>
<td>60.7</td>
<td>60.7</td>
</tr>
<tr>
<td>• Rapid digesting (%)</td>
<td>8.4</td>
<td>100</td>
</tr>
<tr>
<td>• Slow digesting (%)</td>
<td>71.6</td>
<td>0</td>
</tr>
<tr>
<td>• Resistant starch (%)</td>
<td>16.3</td>
<td>0</td>
</tr>
<tr>
<td>• Indigestible fibre (%)</td>
<td>3.7</td>
<td>0</td>
</tr>
</tbody>
</table>
Participant flow chart

Day 1: test day
Thursday
- Attend research facility:
  1. Provide supplement with breakfast meal: control or test
  2. Venous biochemistry sampling
  3. Fit & calibrate CGMS.
  4. Dietary intake: standardised diet provided plus mid afternoon supplement

Day 2: test day
Friday
- Do not attend research facility

Day 3-4: washout period
Saturday & Sunday
- Do not attend research facility
  1. Standardised diet with supplement (control or test) at breakfast meal & mid-afternoon.
  2. Complete food & activity diary.
  3. Wear CGMS

Day 5: test day
Monday
- Attend research facility:
  1. Habitual dietary intake & lifestyle
  2. Provide supplement with breakfast meal: control or test
  3. Venous biochemistry sampling
  4. Fit & calibrate CGMS sensor.
  5. Dietary intake: standardised diet provided plus mid afternoon supplement

Day 6: test day
Tuesday
- Do not attend research facility:

Day 7: end of study
Wednesday
- Research facility:
  1. CGMS removed collect or return
  2. Reimburse with expenses
  3. Answer any queries
Continuous Glucose Monitoring Sensors
Abbott FreeStyle® Navigator One

- Subcutaneous electrochemical enzymatic sensor inserted under the skin (depth ~5mm)
- Connects via blue-tooth technology to receiver
- Measures glucose concentration of interstitial fluid
- Lag time: physiological delay 10-15 min between change in blood & interstitial glucose
- Calibration with CBG measurements at 5 time points: 1, 2, 10, 24 & 72-hrs
- In-built glucometer
- Worn up to 5 days
Data analysis

Criteria for “cleaning” CGMS data agreed between senior diabetes clinicians with experience of CGMS and expedited by 2 clinicians in parallel.

Data points were treated as repeated measures and **mixed linear model** regression analysis was performed to generate predicted mean estimates for the test and control products.
Results: Total Study Duration

Estimates of 24-hour means for treatment vs control

<table>
<thead>
<tr>
<th>Day</th>
<th>Treatment</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thursday</td>
<td>4,556</td>
<td>4,679</td>
</tr>
<tr>
<td>Friday</td>
<td>4,753</td>
<td>4,841</td>
</tr>
<tr>
<td>Weekend-Habitual</td>
<td>4,750</td>
<td>4,750</td>
</tr>
<tr>
<td>Monday</td>
<td>4,470</td>
<td>4,725</td>
</tr>
<tr>
<td>Tuesday</td>
<td>4,742</td>
<td>4,777</td>
</tr>
</tbody>
</table>

Predicted mean and 95% CI by treatment
Post prandial glucose - Breakfast (180min)

![Graph showing glucose concentration over time for control and treatment groups.]

<table>
<thead>
<tr>
<th></th>
<th>Estimate</th>
<th>SE</th>
<th>P value</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control v Treatment</td>
<td>0.09</td>
<td>0.04</td>
<td>0.03</td>
<td>0.01-0.18</td>
</tr>
<tr>
<td>Interaction hospital v home</td>
<td>0.18</td>
<td>0.07</td>
<td>0.007</td>
<td>0.05-0.31</td>
</tr>
</tbody>
</table>
Post prandial glucose - Lunch (180min)

a) Model-based estimations

b) Model-based estimations by day

<table>
<thead>
<tr>
<th>Estimates of Fixed Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parameter</td>
</tr>
<tr>
<td>Control v Treatment</td>
</tr>
<tr>
<td>Hospital v Home</td>
</tr>
</tbody>
</table>
Post prandial glucose - Dinner (180min)

a) Model-based estimations

b) Model-based estimations by day

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Estimate</th>
<th>SE</th>
<th>P value</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control v Treatment</td>
<td>-0.021</td>
<td>0.055</td>
<td>0.71</td>
<td>-0.13 - 0.09</td>
</tr>
<tr>
<td>Hospital v Home</td>
<td>-0.045</td>
<td>0.057</td>
<td>0.43</td>
<td>-0.16 - 0.07</td>
</tr>
</tbody>
</table>
Blood glucose measured by CGMS for daytime observations

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Estimate</th>
<th>SE</th>
<th>P value</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Habitual v Treatment</td>
<td>0.25</td>
<td>0.03</td>
<td>&lt;0.001</td>
<td>0.19-0.31</td>
</tr>
<tr>
<td>Control v Treatment</td>
<td>0.26</td>
<td>0.04</td>
<td>&lt;0.001</td>
<td>0.18-0.34</td>
</tr>
<tr>
<td>Hospital v Home</td>
<td>-0.02</td>
<td>0.03</td>
<td>0.54</td>
<td>-0.08-0.04</td>
</tr>
</tbody>
</table>
Night observations measured by CGMS (p29)

### Estimates of Fixed Effects

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Estimate</th>
<th>SE</th>
<th>P value</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Habitual v Treatment</td>
<td>0.355</td>
<td>0.034</td>
<td>&lt;0.001</td>
<td>0.29-0.42</td>
</tr>
<tr>
<td>Control v Treatment</td>
<td>0.050</td>
<td>0.030</td>
<td>0.09</td>
<td>-0.01-0.11</td>
</tr>
</tbody>
</table>

The graph illustrates the predicted mean glucose concentration (mmol/l) over time (hour) for different conditions: Habitual, Control, and Treatment.
Study limitations

1. CGMS technical issues

3. High number of black Afro-Caribbean women

3. One woman likely to have overt T2DM therefore skewed results

4. Small sample size: to be validated in a larger pilot study

5. Duration
Summary of Results

In obese pregnant women, consumption of a SD-LGI carbohydrate drink:

1. Significant reduction in post prandial glycaemia at breakfast
2. Significant reduction in overall daytime glucose vs. control and habitual diet
3. Significant reduction in nocturnal glucose vs. habitual diet
The future: NIGO randomised controlled trial

- RCT of a structured dietary intervention with a SD-LGI nutritional supplement against a control of habitual diet
- Obese pregnant women (BMI ≥30kg/m²) at risk of GDM
- Primary outcome: 5% reduction in glucose AUC for intervention versus control
- Secondary outcome: neonatal adiposity
Research team:

• **King’s College London**: Rahat Maitland, Suzanne Barr, Eirini Platsa,
• **Abbott Granada**: Ricardo Rueda and Jose M Lopez
• **Abbott Ohio**: Barbara Marriage and Christina Sherry
• **Statistical Support**: Llenalia Garcia (Seplin Solutions)
• **Diabetologist**: Helen Murphy (University of Cambridge)

Laboratory Support

• Carolyn Gill, Jo Gill (KCL)

Supervisors

• Professor Lucilla Poston and Dr Ricardo Rueda
Questions?

Dr Nashita Patel
Clinical Research Fellow
KCL Division of Women’s Health
Women's Health Academic Centre KHP
10th floor North Wing, St.Thomas' Hospital
London SE1 7EH

nashita.r.patel@kcl.ac.uk