Glycaemic Control in Diazoxide-Treated Children with CHI using Supplementary Omega-3-Polyunsaturated Fatty Acids: A Pilot Trial with MaxEPA

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Current CHI Medications

• 1\textsuperscript{st} Line
  – Diazoxide

• 2\textsuperscript{nd} Line
  – Somatostatin Agonists

• Need for further treatment options
Polyunsaturated Fatty Acids (PUFA): MaxEPA

• PUFA
  – Cardiac use, suppress electrical activity
  – Insulin-Secreting Cells
  – Safe for adults & children
  – Food supplement

• MaxEPA
  – Dose 3ml per day for 21 days
  – Equivalent to adult dose in trials
  – Pilot study not dose finding study
Recruitment of Patients

- Children aged 6 months to 11 years
  - 14 children, I withdrew assent – excluded
- Confirmed persistent CHI
- Diazoxide
  - Dose 5-12mg/kg/day
  - Satisfactory glycaemic stability
  - No reported hypo’s requiring treatment in previous month
  - No episodes of symptomatic neuroglycopaenia
  - Low BG on home monitoring <once a week
- CHI Mutations not considered
- Gastrostomy Feeding
Parental Responsibilities

- Consent
- 5 visits to RMCH over 44 days
- Daily food diary
- Activity logbook
- Medication compliance diary
- Twice daily BG measurements
  - GlucomenLxPlus (Menarini Diagnostics UK), OneTouchUltra2 (LifescanUK), Accu-Check Aviva (Roche UK)
Blood Glucose Monitoring

• Continuous Glucose monitoring Systems (CGMS)
  – IPRO2 (medtronic)
  – Subcutaneous device
  – Specified time periods
  – Glycaemic trends over time

• Home BG monitoring

• Lab Glucose/POCT
  – Practical and logistic difficulties
    • Hospital admission, repeated venepuncture
<table>
<thead>
<tr>
<th>Day</th>
<th>Period</th>
<th>Procedures</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pre-Treatment</td>
<td>Consent form; Baseline observations (heart rate and BP); <strong>48 hour subcutaneous continuous glucose monitoring</strong>; Baseline <strong>blood investigations</strong> (fasting blood glucose, insulin, lipids, liver function tests); education of parents regarding administration of fish oil.</td>
</tr>
<tr>
<td>3</td>
<td>On Treatment</td>
<td>Start 3 week trial of fish oil treatment <strong>Remove subcutaneous continuous glucose monitoring</strong></td>
</tr>
<tr>
<td>10</td>
<td>On Treatment</td>
<td>Baseline observations <strong>Blood investigations</strong> Monitoring of logbook activity</td>
</tr>
<tr>
<td>23</td>
<td>End of Treatment</td>
<td>Baseline observations <strong>Repeat 48 hour subcutaneous glucose monitoring</strong> <strong>Blood investigations</strong> Monitoring of logbook activity</td>
</tr>
<tr>
<td>44</td>
<td>Follow Up</td>
<td>Baseline observations (heart rate and BP); <strong>repeat 48 hour continuous glucose monitoring</strong> <strong>blood investigations</strong> (fasting blood glucose, insulin, lipids, liver function tests); advice to continue pre trial doses of diazoxide; monitoring of log book activity</td>
</tr>
</tbody>
</table>
Results

![Box plot showing CGMS glucose levels over time](image)
Results

Coefficient of variation in...

<table>
<thead>
<tr>
<th></th>
<th>Pre treatment</th>
<th>End of treatment</th>
<th>Follow up</th>
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</thead>
<tbody>
<tr>
<td>Coefficient of variation</td>
<td>24</td>
<td>22</td>
<td>28</td>
</tr>
</tbody>
</table>
Results

% CGMS glucose > 10 mmol/l

Pre treatment  | End of treatment | Follow up
---|---|---

0.6 | 0.2 | 0.6
Results

% Blood glucose > 10 mmol/l

- Pre treatment
- End of treatment
- Follow up
Results

% CGMS glucose < 4 mmol/l

- Pre treatment
- End of treatment
- Follow up
Results

![Bar chart showing % Blood glucose < 4 mmol/l at different time points: Pre treatment, End of treatment, Follow up.](chart.png)
Points to Consider

• Increased LDL Cholesterol
  – 1 patient, familial history hypercholesterolaemia

• Protocol Deviation
  – +/- duration of treatment, home BG levels not measured, monitoring stopped due to infection, CGMS <48 hours

• Blood Glucose Monitoring
  – Home BG meters
  – Study design – not to use CGMS during treatment
  – Frequent multiple insertion of subcutaneous needle devices = intrusive & impractical

• Small number of children
  – Pilot study – basis for comprehensive clinical trial
Conclusions

- Pilot Trial
- PUFA – safe
- Reduced risk of hypoglycaemia & hyperglycaemia
- Adjunct treatment option to Diazoxide
- Involvement of other centres
Thank You