Treatment of CHI with long acting Octreotide

Dr Pratik Shah
Clinical Research Fellow

Dr Khalid Hussain
Reader and Consultant in Paediatric Endocrinology
Great Ormond Street Hospital and Institute of Child Health
London
Diffuse CHI

- Autosomal recessive (or dominant) - mutations in genes encoding $K_{ATP}$ channels ($ABCC8$, $KCNJ11$)

- May be amenable to medical therapy

- Severe cases require near-total pancreatectomy

- Post op complications – diabetes mellitus, exocrine pancreatic insufficiency
Management

• Medical management:
  - Diazoxide
  - Glucagon/Octreotide

• Surgery

• New medical treatment
  Long acting Octreotide
Long acting Octreotide

- Octreotide, an octapeptide, is a long-acting analog of somatostatin, has inhibitory effects on the release of insulin from pancreatic β-cells.

- Lanreotide has high binding affinity for human somatostatin receptors (SSTR) 2 and 5, and a reduced binding affinity for human SSTR 1, 3 and 4.

- The half-life of long acting octreotide is much higher and is usually given every 4 weekly
Successful treatment of congenital hyperinsulinism with long-acting release octreotide

• **Objective:** This study aims at replacing three daily s.c. octreotide injections by a single and monthly i.m. injection of long-acting release (LAR) octreotide in HI patients.

• **Subjects and method:** LAR octreotide was injected every 4 weeks during 6 months and s.c. octreotide injections were stopped after 3rd injection. Average follow-up of 17 months. Ten HI pediatric patients (age 1.3 - 8.5 yrs) unresponsive to diazoxide and currently treated with s.c. octreotide were included in the trial.
Successful treatment of congenital hyperinsulinism with long-acting release octreotide

• Results: For all ten patients, glycemias were maintained in the usual range, HbAlc and IGF1 were unchanged. Patients gained height significantly (mean 2.7 cm; 95% CI: 1.9–3.4) and no side effect was noted during the study and the later follow-up. Parents’ questionnaires of general satisfaction were highly positive whereas children’s QoL evaluation remained unchanged.

• Conclusion: In these diazoxide-unresponsive HI patients, LAR octreotide was efficient, well tolerated and contributed to a clear simplification of the medical care.
Treatment of Congenital Hyperinsulinism with Lanreotide Acetate (Somatuline Autogel)

Dalit Modan-Moses et al.

Objective: two children treated with a once-monthly injection of a long-acting somatostatin analog.

Patients and Methods: Both patients presented immediately after birth and were diagnosed with CHI. Patients were initially treated with diazoxide, hydrochlorothiazide, frequent feedings, and octreotide. With this therapy, they were normoglycemic with a good growth rate, normal weight gain, and excellent neurodevelopment. Treatment with the long-acting somatostatin analog lanreotide acetate (Somatuline Autogel), administered by deep sc injection of 30 mg once a month, was started at the ages of 41/2 and 4 yr, respectively.
Treatement of Congenital Hyperinsulinism with Lanreotide Acetate (Somatuline Autogel)

Dalit Modan-Moses et al.

- Octreotide infusion was gradually weaned over 1 month. The first patient has now been treated with the lanreotide acetate for over 5 yr, and the second for 3 yr. Treatment is well-tolerated, and both the patients and their parents are satisfied with the transition from pump therapy to once-a-month injection and prefer it to pump therapy.

- **Conclusion**: Lanreotide acetate may be a safe and effective alternative to octreotide pump therapy in patients with CH, offering an improved quality of life. Longer follow-up of a larger patient group is needed.
Licensed indications

- Lanreotide and Octreotide are both analogues of the hypothalamic release-inhibiting hormone somatostatin. They are indicated for the relief of symptoms associated with neuroendocrine (particularly carcinoid) tumours and acromegaly. Lanreotide is licensed for the treatment of thyroid tumours.
Adverse effects

• Rarely allergic type reactions - local reactions

• Gastrointestinal side effects include anorexia, nausea, abdominal pain, bloating, flatulence, loose stools and diarrhoea.

• Octreotide causes suppression of growth and thyroid hormones.

• Octreotide can decrease gallbladder contractility and bile secretion leading to steatorrhoea, cholestasis, hepatic dysfunction and cholelithiasis.
Treatment at GOSH

- Insertion of CGMS pre Lanreotide
- Baseline bloods
- USS gall bladder
Treatment at GOSH

• 1st dose of Lanreotide – ametop/paracetamol/Ibuprufen
• Monitoring BM
• Insertion of CGMS
• Gradual wean of daily Octreotide/Diazoxide
Treatment at GOSH

• Monitor BM at home
• Gradual reduction of daily Octreotide/Diazoxide
• Lanreotide injection every 28 days – to give injections on Kingfisher ward for first 6 months
• F/up in clinic
Treatment at GOSH

• Patients treated so far: 8
• Children on Octreotide: 6
• Children on Diazoxide: 2
• Age range: 3.5 yrs to 16 yrs
## Summary

<table>
<thead>
<tr>
<th></th>
<th>Child 1</th>
<th>Child 2</th>
<th>Child 3</th>
<th>Child 4</th>
<th>Child 5</th>
<th>Child 6</th>
<th>Child 7</th>
<th>Child 8</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td>14</td>
<td>7</td>
<td>6</td>
<td>3.9</td>
<td>3.7</td>
<td>5</td>
<td>6</td>
<td>5</td>
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<tr>
<td><strong>Treatment</strong></td>
<td>Diazoxide 7mg/kg/day</td>
<td>Octreotide 10mcg/kg/day</td>
<td>Octreotide 11mcg/kg/day</td>
<td>Octreotide 11mcg/kg/day</td>
<td>Diazoxide 15mg/kg/day</td>
<td>Octreotide 23mcg/kg/day</td>
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<td>Octreotide 30mcg/kg/day</td>
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<td><strong>Off treatment</strong></td>
<td>8 weeks</td>
<td>4 weeks</td>
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<td>12 weeks</td>
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<td>4 week</td>
<td>4 week</td>
<td>Current weaning</td>
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<td><strong>Side effects</strong></td>
<td>Loose stools on day 2 – 24 hrs</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
</tbody>
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Child 1

- 14 yr old on Diazoxide
- Issues: Excessive hair growth, coarse features, psychological and compliance issues
- Started on Lanreotide 30mg every 4 weekly
- Had diarrhoea on day 2 after giving 1\textsuperscript{st} injection – improved after 24 hours
- Gradually weaned Diazoxide and stopped before 3\textsuperscript{rd} dose of Lanreotide
Child 1

• Currently – “Child’s self esteem and confidence vastly improved”, more sociable
• Improvement in appetite and well being
• Reduced hair growth
• No hypoglycaemia