Treatment of CHI with long acting Octreotide

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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
European Journal of Endocrinology (2012) 166 333–339

- 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.

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- 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)

J Clin Endocrin Metab. First published ahead of print June 22, 2011 as doi:10.1210/jc.2011-0605

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.

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- 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
- Montoring 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

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

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 1st injection – improved after 24 hours
- Gradually weaned Diazoxide and stopped before 3rd 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