Long-term treatment with Lanreotide in CHI

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Treatment of CHI

**Diazoxide**
- K-ATP-channel opener
- Re-constitution of channel structure and function
- Acting on sulfinylurea (SU) binding site
- Effective in ca. 20-30%
- 70% resistance in neonatal form
- Very effective in metabolopathies (GK- od GLUD1-defects)

**Carbohydrate feeding**
- i.v. or oral continuous
- Hypercaloric situation inappropriate weight gain

**Glucagone**
- Release glucose from liver glycogen
- "glucose recycling"
- Reduces glucose requirement
- Counter-hormone to insulin
- Drug of first choice in short-term in-house management

**Calcium antagonists** (Nifedipine)
- Inhibits Ca-channel function
- May reduce insulin secretion
- Effective at all? (single publ.)

**Octreotid**
- Reduces gene expression of hormones
- Inhibits Chromogranin A
- Reduces secretory vesicles
- Insuline gene expression ↓

**Somatostatin** Ca++ antagonists
**Action of somatostatine**

- Specific somatostatine receptors on beta-cell-surface
- Down-regulation of Chromogranin A (building of secretory vesicles)
- Supressed mRNA expression of insulin-gene

**Indications:**
- neuroendocrine tumors
- acromegaly
- CHI

**Pharmacologic preparations:**
- somatostatine (very-short-acting)
- octreodtide (long-acting, 6-8 hours)
- lanreotide (very-long-acting (4-6 weeks))
Lanreotide

- deep subcutaneous injection
- 60 mg, 90 mg, 120 mg available
- Injection every 28d recommended

Reported use in children:
Constitutional overgrowth
(Carel et. al. 2007)

Reported use in CHI:
1. Kuehnen, P; *Horm. Res* 2009 (*abstr.*).
BZ unter kontinuierlicher Octreotid-Gabe s.c.

BZ mit monatlicher Lanreotide-Gabe.
Berlin treatment study

- **6 Patients** with CHI (diffuse form) with treatment failure of established medical therapy (daizoxide, nifedipine, octreotide) – 1 patient with partial pancreatectomy (50%).

- **Age** of patients: 7 Monate up to $4^{7/12}$ yr. (mean $2^{11/12}$ yr.)

- **Dose adjustment**: Start with 60 mg (independent from age and weight)
  - if frequent hypoglyxcaemias $\rightarrow$ increase dosage (90, 120 mg)
  - if frequent hyperglycaemia $\rightarrow$ reduce dose down until 60 mg

- **Study period**: 60d before and 31 d after lanreotide dose adjustment period
  4-time daily bood-sugar measurements, documentation of hypoglycaemia

**Duration of therapy**: mean 4 years (3 – 5 yr.)
Results: mean blood-sugar values

- Patient 1: Before Lanreotide (p=0.963), After Lanreotide
- Patient 2: Before Lanreotide, After Lanreotide
- Patient 3: Before Lanreotide, After Lanreotide
- Patient 4: Before Lanreotide (p<0.001***), After Lanreotide
- Patient 5: Before Lanreotide, After Lanreotide
- Patient 6: Before Lanreotide (p<0.001***), After Lanreotide

Blood-sugar in mg/dl

Before Lanreotide

After Lanreotide
Results: Frequency of hypoglycaemia

- Reduced risk for hypoglycaemia with Lanreotide (odds ratio 0.38)
Safety, adverse events, side effects

• Side effects:
  – Induration at injection site (maybe when injected i.m.) – slowly resolving.
  – Gallbladder concrements (sludge, stones) developed under octreotide-therapy remained unchanged, no clinical symptoms.
  – No "new" gall concrements

• Safety:
  – No serious adverse events
  – No alteration of longitudinal growth, no effect on other hormonal axis
Lanreotide: Pros and Cons

**Pros**

- Injection performed by medical person (nurse)
  - Easing the burden of parents
- Blood-sugar values improved compared to former treatment
- Single injection every 4 – 6 weeks

**Cons**

- Lanreotide effect is stronger in some patients and minimal in other pt.
- Injection with a large needle for 2 – 5 min.
- Side effects (gallbladder concrements)
Biggest advantage: Independence…!

- Reduces problem with day care, kindergarten, school
- No need to give medication between injections
- If responsive only measurement of blood sugar and meals has to be organized
  - Staying with family or friends over night
  - Travels with groups or school
It's not sooo bad…
Conclusion

- Long-term treatment of (diffuse) CHI is feasible
- Reduced hypoglycaemia frequency
- Trend to higher blood-sugar levels observed
so much left to do…

Your questions… ????