Towards more tolerable therapy for CHI

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Treatment options in CHI

- Diazoxide, octreotide, lanreotide
- Sirolimus

- Therapies in trial

- ? Supplementary therapy
Fish Oil - PolyUnsaturated Fatty Acids (PUFA)

- GISSI myocardial infarction trial – PUFA reduces abnormal heart rhythms after heart attack *GISSI* investigators, *Lancet* 1999
- GISSI Heart Failure – PUFA restores autonomic variability *La Rovere et al, Heart Rhythm* 2013
- GISSI Heart Failure – PUFA reduces life threatening ventricular arrhythmias *Finzi AA, Am Heart J* 2011
- Reduction in all-cause mortality after heart attack *Green SJ et al, Am J Cardiology* 2016
Trial of PolyUnsaturated Fatty Acids (PUFA) in children treated with Diazoxide

MaxEPA (liquid) 3 mL/day [EPA 459 mg, DHA 310 mg] (n=13)

Modest effect in improving Sugar profiles (subcutaneous glucose)
Significant response in some children, e.g. in a child with a metabolic cause for Hyperinsulinism (HADH mutation)
Reduced risk of low blood sugars with PUFA treatment

Glucose 4 mmol/L = 72 mg/dL
Mechanism of better sugar levels?

• Calcium channels that cause insulin secretion in beta cells may become more resistant – may explain less hypoglycaemia

• Better beta cell membrane stability?

• Other effects?
PUFA effects in glucose metabolism

- PUFA reduces GLP-1 secretion after meals
  Bozzetto et al, *Diabetologia* 2015

GLP-1 plays a role in CHI

GLP-1 block lowers insulin


EPA 260 mg in 5 ml

EPA 460 mg in 5 ml

Progressive dose reduction in diazoxide: 12 mg/kg/d to 1 mg/kg/d
Post trial PUFA use

- 9 patients – with and without genetic mutations
- 4 children stopped medication
  - 2 children with no CHI mutations
  - 1 child with PHOX2B mutation
  - 1 child with homozygous ABCC8 mutation previously treated with lanreotide
- Others – reducing diazoxide dosage
Reducing diazoxide dose to reduce excess body hair

Need to treat hypoglycaemia, while recognising Transient forms of CHI
Understanding the basis of complications in CHI

No biomarkers that predict adverse neurodevelopment at the time of hypoglycaemia

Hypoglycaemia and Adverse Neonatal NeuroDevelopment (HANND)

Neuroglycopenia:
54 mg/dl = 3.0 mmol/l
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