Central Manchester University Hospitals NHS
NHS Foundation Trust

norchi
northern congenital hyperinsulinism service

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

A Pilot Trial with MaxEPA

Louise Caine
Specialist Practitioner in Congenital Hyperinsulinism
Royal Manchester Children's Hospital
Manchester, England

Current CHI Medications

- 1st Line
  - Diazoxide
- 2nd 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 neuroglcopaenia
  - Low BG on home monitoring <once a week
- CHI Mutations not considered
- Gastrostomy Feeding

Parental Responsibilities

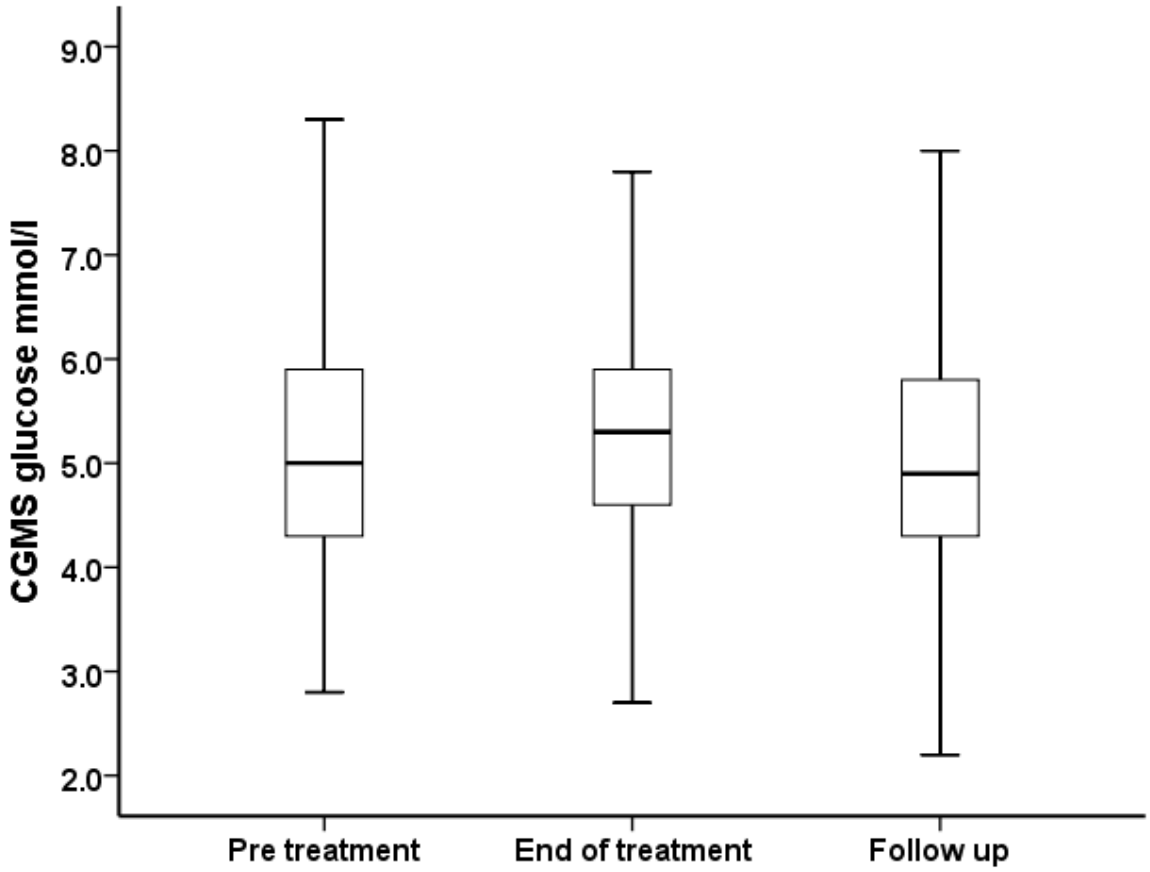
- Consent
- 5 visits to RMCH over 44 days
- Daily food diary
- Activity logbook
- Medication compliance diary
- Twice daily BG measurements
  - GlucomenLxPlus (Menarini Diagnostics UK), OneTouchUltra2 (LifescanUK), Accu-Check Aviva (Roche UK)

Blood Glucose Monitoring

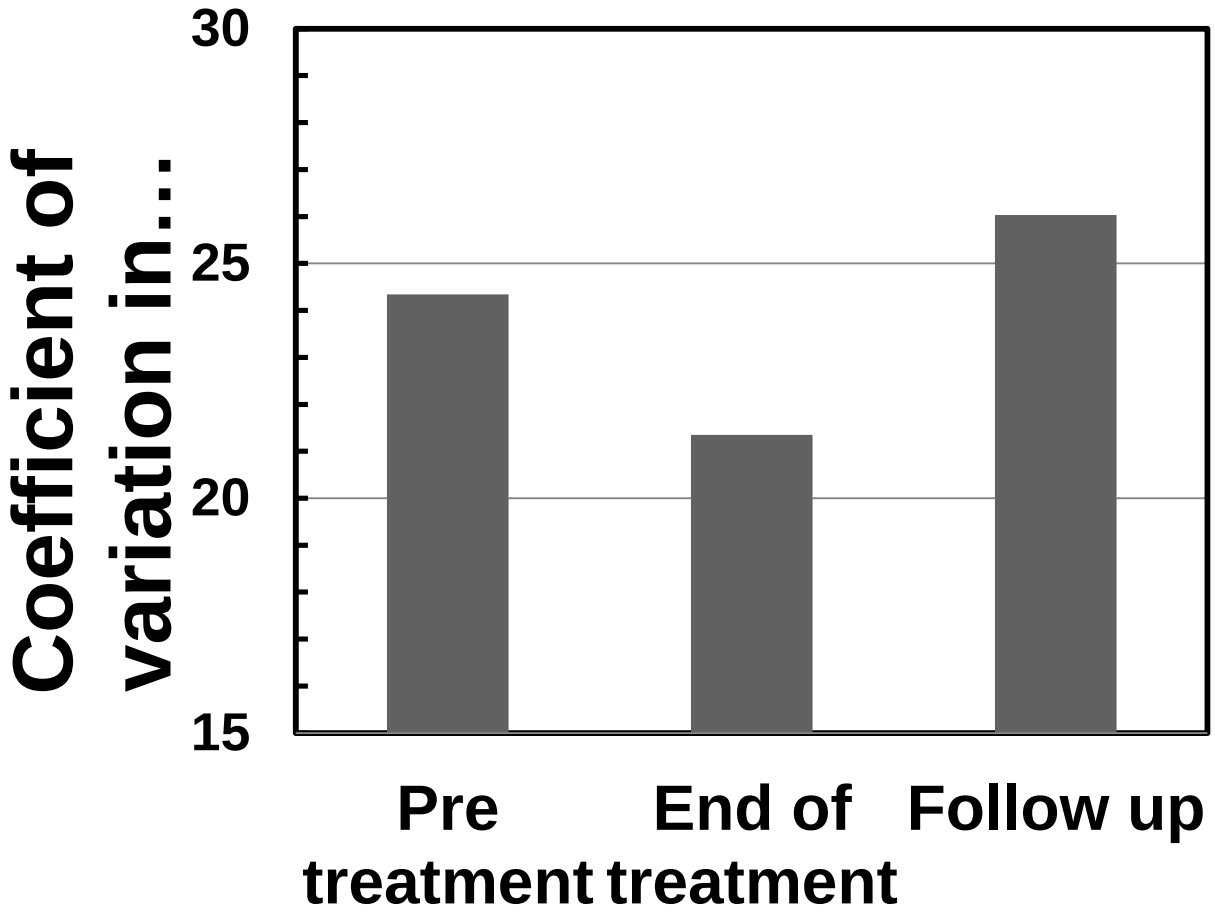
- Continuous Glucose monitoring Systems (CGMS)
  - IPRO2 (medtronic)
  - Subcutaneous device
  - Specified time periods
  - Glycaemic trends over time
- Home BG monitoring
- Lab Glucose/POCT
  - Practical and logistic difficulties
    - Hospital admission, repeated venepunture

Day	Period	Procedures
1	Pre-Treatment	Consent form; Baseline observations (heart rate and BP); **48 hour subcutaneous continuous glucose monitoring**; Baseline **blood investigations** (fasting blood glucose, insulin, lipids, liver function tests); education of parents regarding administration of fish oil.
3	On Treatment	Start 3 week trial of fish oil treatment **Remove subcutaneous continuous glucose monitoring**
10	On Treatment	Baseline observations **Blood investigations** Monitoring of logbook activity
23	End of Treatment	Baseline observations **Repeat 48 hour subcutaneous glucose monitoring** **Blood investigations** Monitoring of log book activity
44	Follow Up	Baseline observations (heart rate and BP); **repeat 48 hour continuous glucose monitoring**; **blood investigations** (fasting blood glucose, insulin, lipids, liver function tests); advice to continue pre trial doses of diazoxide; monitoring of log book activity

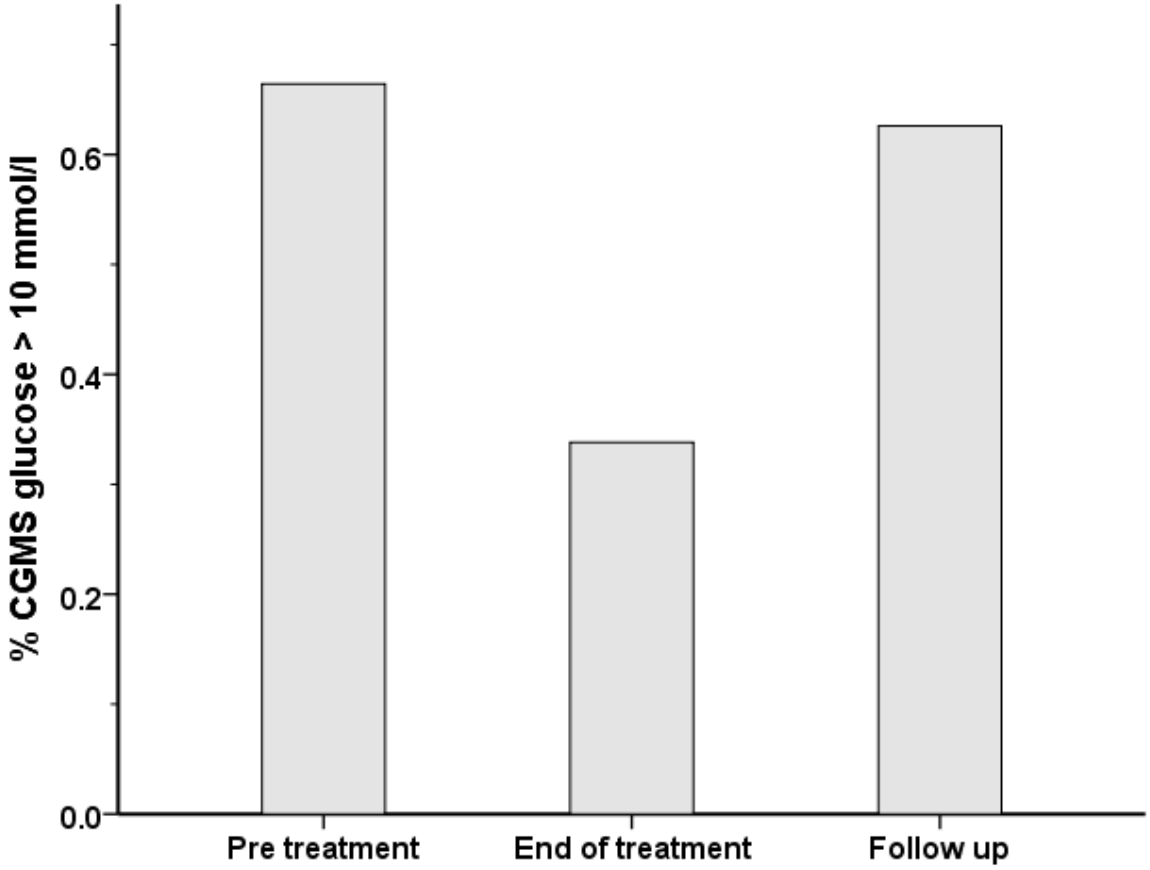
Results


CGMS glucose mmol/l
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
Pre treatment
End of treatment
Follow up

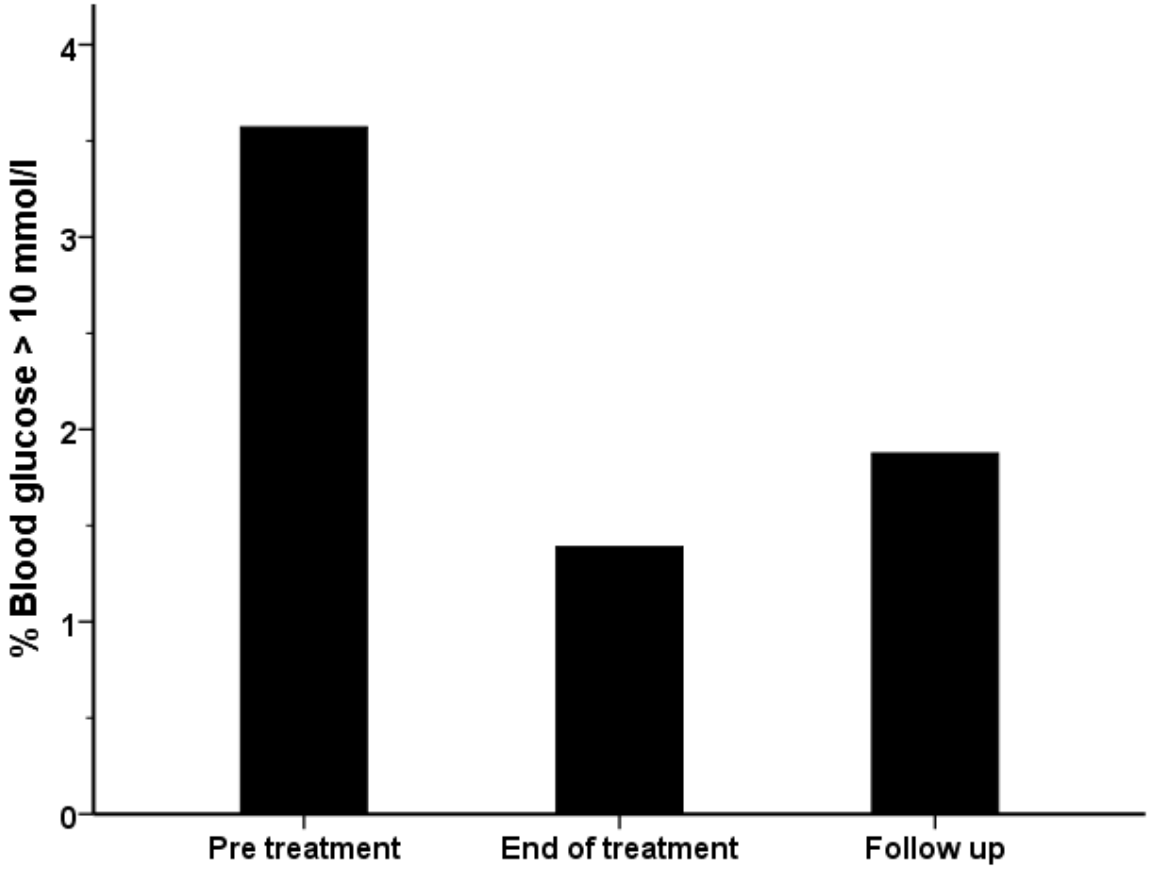
Results


Coefficient of variation in…
30
25
20
15
Pre treatment
End of treatment
Follow up

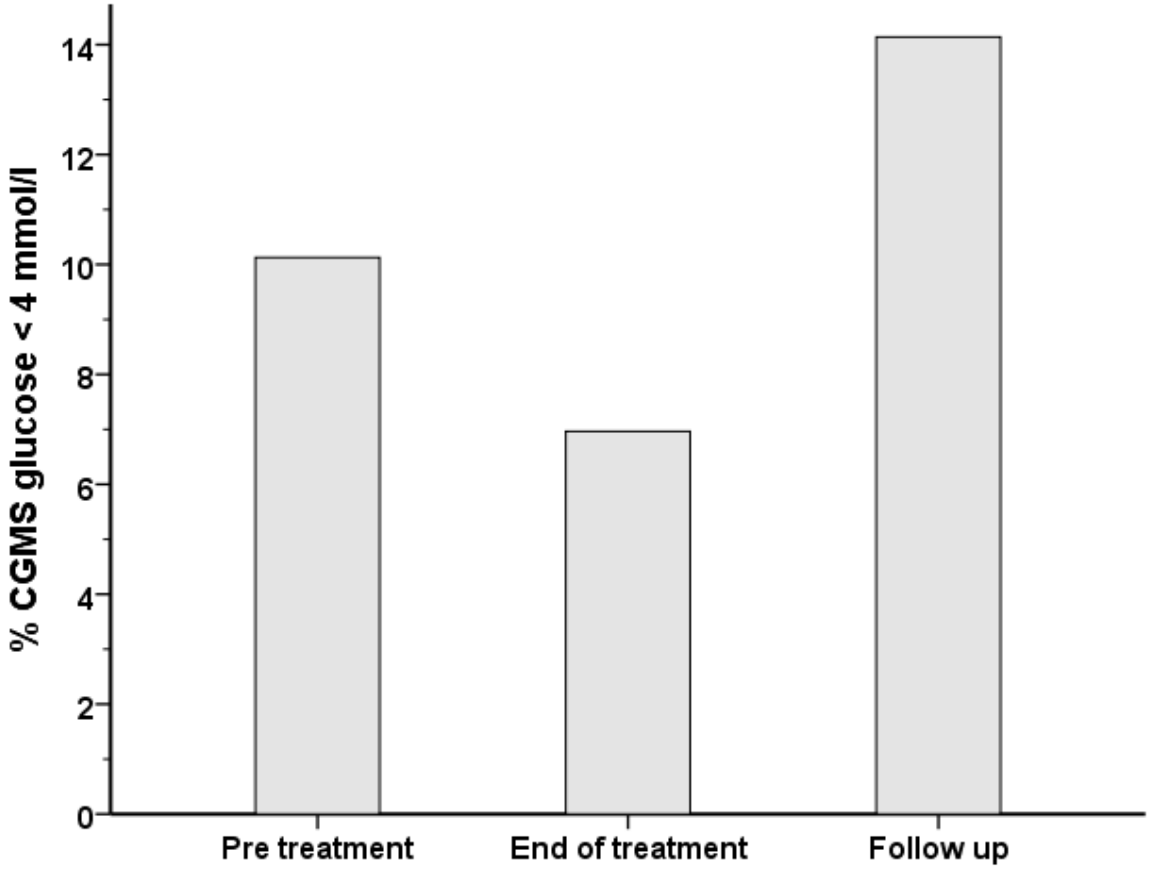
Results


% CGMS glucose > 10 mmol/l
0.0
0.2
0.4
0.6
Pre treatment
End of treatment
Follow up

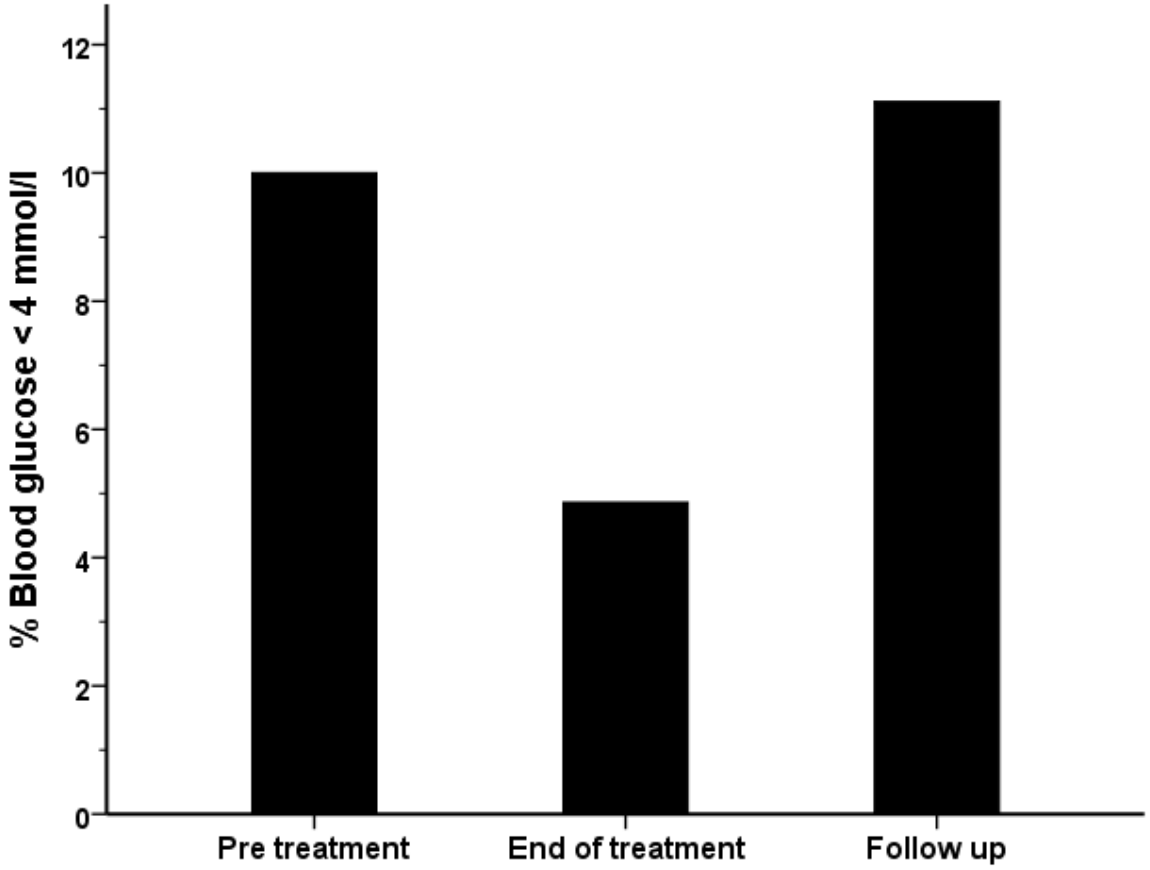
Results


% Blood glucose > 10 mmol/l
4
3
2
1
0
Pre treatment
End of treatment
Follow up

Results


% CGMS glucose < 4 mmol/l
0
2
4
6
8
10
12
14
Pre treatment
End of treatment
Follow up

Results


% Blood glucose < 4 mmol/l
12
10
8
6
4
2
0
Pre treatment
End of treatment
Follow up

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 subcutaenous 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