Protein and energy interactions in critically ill children

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1) To assess insulin sensitivity and response in critically ill septic neonates and children. 2) To determine protein balance in septic, critically ill children at baseline and during a Hyperinsulinemic Euglycemic Clamp, while receiving standard or...

Ethical review	Not approved
Status	Will not start
Health condition type	Glucose metabolism disorders (incl diabetes mellitus)
Study type	Interventional

Summary

ID

NL-OMON32972

Source
ToetsingOnline

Brief title
Insulin in critically ill children

Condition

- Glucose metabolism disorders (incl diabetes mellitus)
- Protein and amino acid metabolism disorders NEC

Synonym
Diabetes type 2, Insulin resistance

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Sophia Stichting voor Wetenschappelijk Onderzoek

Intervention

Keyword: Catabolism, Glucose, Insulin, Protein

Outcome measures

Primary outcome

Children: Whole body protein balance at baseline and during a HEC with standard and high protein intake in critically ill children.

Neonates: Whole body protein balance at baseline and during a HEC with standard protein intake in critically ill term and preterm neonates.

Secondary outcome

Children:

- Insulin resistance with standard and high protein intake in critically ill children
- Glucose metabolism at baseline and during a HEC with standard and high protein intake in critically ill children.
- Lipid metabolism at baseline and during a HEC with standard and high protein intake in critically ill children.
- To determine the fractional (FSR) and absolute (ASR) synthesis rate of albumin and C-reactive protein at baseline and during HEC with standard and high protein intake in critically ill septic children.

Neonates:

- Insulin resistance in critically ill term and preterm neonates.
- Glucose metabolism at baseline and during a HEC in critically ill term and

preterm neonates.

- Gluconeogenesis and glycogenesis at baseline and during a HEC in critically

ill term and preterm neonates.

- Compare plasma glucose values with continuous subcutaneous glucometer values

at baseline and during a HEC in critically ill term and preterm neonates.

Study description

Background summary

It has been reported that tight glucose control with insulin in adult critically ill surgical patients has reduced mortality rates. However, there is no evidence that this approach may be beneficial in critically ill children. In theory, insulin has several potential beneficial effects. It has metabolic effects (glycemic control, improve protein balance and dyslipidemia) and non-metabolic effects (protect against oxidative stress, endothelial dysfunction and regulation of inflammation). Under physiological conditions, there is a close interrelationship between protein and energy (glucose and fat) metabolism. An increase in the energy supply will not promote nitrogen retention unless the amino acid supply is adequate, and conversely an increased amino acid supply will be useless if energy is limiting. Furthermore, protein requirements in critically ill children reach beyond the traditional areas of nitrogen balance and protein metabolism. Individual amino acids exert a functional impact during critical illness on which insulin might have a significant effect. Endothelial health and protection against oxidative stress are some of these *non-protein* functions exerted by amino acids. The effect of tight glucose control with insulin on protein requirements, and on the regulation of substrate metabolism in critically ill septic children of all ages needs further study.

Study objective

1) To assess insulin sensitivity and response in critically ill septic neonates and children.
2) To determine protein balance in septic, critically ill children at baseline and during a Hyperinsulinemic Euglycemic Clamp, while receiving standard or high protein intake based on age group.
3) To assess the relationship between protein turnover and glucose and fat metabolism in critically ill septic children.
4) To compare the continuous subcutaneous glucometer with standard plasma

glucose monitoring during a Hyperinsulinemic Euglycemic Clamp in septic neonates.
5) To determine the fractional (FSR) and absolute (ASR) of albumin and C-reactive protein at baseline and during HEC with standard and high protein intake in critically ill septic children.

Study design

Neonates: The study consists of one day, where they will receive an intravenous bolus of 2H2O and a primed 7-hour continuous intravenous study with [6,6 2H2]Glucose, [1-13C]Leucine, [ring-2H5]Phenylalanine and [3,3 2H2]Tyrosine of which the last three hours will be with insulin (HEC; Hyperinsulinemic Euglycemic Clamp). Glycemic control will be achieved by using a continuous subcutaneous glucometer in comparison with the standard plasma glucose.

Children: The study consists of a 2 day, 7-hour primed continuous intravenous tracer infusion studies of which the last three hours will be with a HEC. The protocol will consist of a tracer study ([1-13C]Leucine, [ring-2H5]Phenylalanine and [3,3 2H2]Tyrosine, [6,6 2H2]Glucose and [1,1,2,3,3 2H5]Glycerol) on two days in which they will receive parenteral nutrition with two different amounts of protein intake (according to age) in a cross over fashion.

Intervention

Children:
The subjects will be studied in two occasions, 24 h apart while receiving TPN at two different amounts of protein intake (standard vs. higher protein intake) with a Hyperinsulinemic Euglycemic Clamp.

Neonates:
The subjects will be studied on one occasion, with a Hyperinsulinemic Euglycemic Clamp.

Study burden and risks

The risk of insulin infusion is hypoglycemia and hypokalemia.

During the insulin infusion, small blood samples will be obtained from the indwelling I.V. catheter every 5 minutes to monitor whole blood glucose concentration, at the bedside with the aid of a Y.S.I. stat plus analyzer.
Blood glucose concentration will be maintained between 90 to 110 mg/dl (the amount of blood drawn during the 3 hour HEC for blood glucose determination will be approximately 2 ml total). If the plasma glucose concentration reaches 6.1mM (110mg/dl), the glucose infusion will be decreased to maintain the plasma glucose concentration between 5.0 - 6.1 mM (90-110 mg/dl).

Whole blood potassium will be checked at 30, 60 and 120 minutes after the beginning of the insulin infusion; if the potassium concentration is below 3 mmol/L, a potassium chloride infusion will be administered intravenously at a dose of 0.5 mEq/kg of body weight , no more than 15 mEq over 1 h, followed by further potassium concentration monitoring. If the potassium concentration is again below 3 mmol/L, then a second dose of potassium chloride will be administered at the same dose and it will be monitored again 1 hour later.

There will be no direct benefit to the subject. The goal for the future is a general advice on nutrition and specifically protein intake based on agegroups in critically ill children who receive insulin in the neonatal and pediatric critical care.

Contacts

Public
Erasmus MC, Universitair Medisch Centrum Rotterdam

Dr Molewaterplein 60
3015 GJ
NL
Scientific
Erasmus MC, Universitair Medisch Centrum Rotterdam

Dr Molewaterplein 60
3015 GJ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

Hyperglycemic critically ill

Exclusion criteria

metabolic disease (eg Diabetes Mellitus)

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Start date (anticipated):	01-04-2009
Enrollment:	46
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Actrapid
Generic name:	Insulin
Registration:	Yes - NL intended use

Ethics review

Not approved

Date:	24-04-2009
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2009-01-0999-1-NL
CCMO	NL26604.000.09