Protein and Energy Interactions in Critically Ill Children

Published: 01-09-2009
Last updated: 04-05-2024

Objective of the study: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 HyperinsulinemicEuglycemic Clamp, while...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Glucose metabolism disorders (incl diabetes mellitus)
Study type	Interventional

Summary

ID

NL-OMON33362

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, Insuline 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

Whole body protein balance at baseline and during a HEC with standard and high

protein intake

in critically ill children.

Secondary outcome

- 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.

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

Objective of the study:
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

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

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.

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

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Diagnosis of SIRS, sepsis or septic shock
Indwelling central venous access placed for clinical purpose.

total parenteral nutritional support for at least 2 days.

Exclusion criteria

Patients with metabolic diseases i.e.: urea cycle disorders, cystinuria and insulin dependent diabetes mellitus
Patients with hepatic or renal failure
Enteral feeds providing more than 20% of total daily protein and energy intake based on age and weight.
Insulin therapy prior to the start of the study

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-11-2009
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO

Date:	01-09-2009
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den

	Haag)
Approved WMO Date:	07-07-2010
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	EUCTR2009-010999-19-NL
CCMO	NL28671.000.09