

Optimal glucose in critically ill children.

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1. In normoglycaemic critically ill children exogenous glucose administration diminishes endogenous glucose production; 2. Elevated blood glucose levels in critically ill children are caused by the sum of an increased endogenous glucose production...

Ethische beoordeling	Positief advies
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON26665

Bron

Nationaal Trial Register

Verkorte titel

Gluco1

Aandoening

Critically ill post-operative (surgical) children

Ondersteuning

Primaire sponsor: ErasmusMC-Sophia Childrens Hospital

Overige ondersteuning: Sophia Stichting Wetenschappelijk Onderzoek (SSWO)

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Glucose metabolism: Endogenous glucose production.

The study will be performed on the first day after surgery or admission to the PICU, once hemodynamically stable.

We will use stable isotope tracer infusions to measure glucose and protein

metabolism.

Toelichting onderzoek

Achtergrond van het onderzoek

Background: Glucose is an important energy source in humans. Glucose is utilised by all cells and serves as metabolic fuel for muscle, liver, heart, kidney and gut and as the obligate energy source for brain, medulla and erythrocytes. Hyperglycemia and insulin resistance are universal findings in critically ill adult patients. In the acute stress state this metabolic response can be regarded as an adaptive response. However more prolonged hyperglycemia has been associated with adverse outcome in adults. Adult studies show reduced mortality when blood glucose levels are strictly controlled by insulin (1). Intensive insulin therapy also will prevent complications such as nosocomial infections, acute renal failure, liver dysfunction, critical illness polyneuropathy, muscle weakness and anaemia and thus will reduce the length of stay on the intensive care (1).

In many children during critical illness blood glucose concentration rises due to the disruption of normal glucoregulation. Recent studies in critically ill children show that hyperglycaemia is associated with worsening of outcome and even an increase in mortality (2-6). The overall hypothesis is that critically ill children will benefit as well from strict glucose control via exogenous insulin. Recently, two studies in a small group of children with severe burns treated with insulin, reported beneficial effects on survival, infection rates and the inflammatory response (7, 8). The mechanism by which euglycemia reduces mortality is not yet understood. Probably, insulin acts by metabolic pathways (improved whole body protein balance and reduction of dyslipidemia) and non-metabolic pathways (reducing oxidative stress and endothelial dysfunction and control of inflammatory processes). It is also increasingly evident that lowering the blood glucose level and not the insulin infusion

itself, plays the critical role. The blood glucose concentration is controlled by regulatory factors governing both uptake from endogenous production and exogenous sources (enteral or parenteral nutrition). There are two components of endogenous glucose production: glycogenolysis and gluconeogenesis. The majority of studies to measure endogenous glucose production have been performed in neonates, using stable isotopic tracers and indirect calorimetry, while only very few studies are available for infants and children (9, 10). Recently, it was shown that in long stay ICU adult patients without glycemic control, the ICU and hospital mortality was independently related to the mean amount of infused glucose (11). Normal values for glucose intake in healthy children in the Netherlands are extrapolated from the study from Kalhan in 1999 (9). No data are available concerning the endogenous glucose production in critically ill children in relation with the amount of administered glucose. Additionally, it is also not known whether decreasing the exogenous

glucose administration would affect whole body protein balance in post-surgical children by decreasing the energy supply and thus increase protein oxidation as an energy source.

Aims: The present proposal is designed to define the optimal glucose intake in critically ill children.

Hypothesis:

1. In normoglycaemic critically ill children exogenous glucose administration diminishes endogenous glucose production;
2. Elevated blood glucose levels in critically ill children are caused by the sum of an increased endogenous glucose production rate and exogenous glucose administration;
3. Optimal glucose intake will vary with body weight;
4. The decrease in exogenous glucose administration will not affect whole body protein balance (synthesis $\text{ }^3\text{C}$ breakdown).

Study design and methods:

This is a prospective, randomized, crossover study, which will enrol 48 patients in the PICU divided in two study groups:

1. Critically ill pediatric patients after elective surgery (cardiac, craniofacial or scoliosis surgery);
2. Critically ill pediatric patients with various medical diseases and >1 organ failure.

The groups will be subdivided in subgroups as described below:

- 1a. After elective cardiac surgery, weight ≤ 30 kg (n=8) and >30 kg (n=8);
- 1b. After elective craniofacial or scoliosis surgery, weight ≤ 30 kg (n=8) and >30 kg (n=8);
2. With medical diseases and >1 organ failure, weight ≤ 30 kg (n=8) and >30 kg (n=8) .

Endogenous glucose kinetics will be qualified with stable isotope assays and the predominant fuel source will be determined by indirect calorimetry.

Data analysis: Differences between study groups will be assessed using student's t-test, Mann-Whitney test and ANOVA.

Relevance:

This study will lead to a better understanding of the causes of hyperglycemia in critically ill children and will help to develop new guidelines on parenteral and enteral glucose intake. Optimal glucose intake and treatment of hyperglycaemia with insulin will change metabolism of the critically ill child towards early reversal of catabolism. This is essential for reduction of morbidity of intensive care treatment and reduction of PICU and hospital stay. On the longer term this will also influence growth and development of the child.

Doel van het onderzoek

1. In normoglycaemic critically ill children exogenous glucose administration diminishes endogenous glucose production;
2. Elevated blood glucose levels in critically ill children are caused by the sum of an increased endogenous glucose production rate and exogenous glucose administration;
3. Optimal glucose intake will vary with body weight;
4. The decrease in exogenous glucose administration will not affect whole body protein balance (synthesis – breakdown).

Onderzoeksopzet

One day study, of which 8 hrs will be with a continuous tracer infusion.

Onderzoeksproduct en/of interventie

Two levels of glucose infusion in a randomized cross-over fashion on the first day post-surgery. During the study a 8 hr primed, continuous stable isotope tracer infusion will be administered.

Contactpersonen

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Infants and children older than 1 month of age admitted to the ICU;
2. After elective surgery (cardiac, craniofacial or scoliosis surgery);
3. With various medical diseases and > 1 organ failure;
4. Indwelling arterial line placed for clinical purposes;
5. Total parenteral glucose administration;
6. Hemodynamic stability.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Age <1 week after the term date;
2. Metabolic and endocrine disorders, liver failure, chromosomal disorders;
3. Pregnancy;

4. Patients on insulin therapy at the start of the study and patients with hyperglycemia > 11 mmol/L resulting in glucosuria needing insulin therapy during the study;
5. No arterial line or after removal of arterial line, no informed consent

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Cross-over
Toewijzing:	Gerandomiseerd
Blinding:	Enkelblind
Controle:	Actieve controle groep

Deelname

Nederland	
Status:	Werving nog niet gestart
(Verwachte) startdatum:	01-11-2009
Aantal proefpersonen:	60
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies	
Datum:	26-10-2009
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 35471
Bron: ToetsingOnline
Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL1962
NTR-old	NTR2079
CCMO	NL19433.078.08
ISRCTN	ISRCTN wordt niet meer aangevraagd.
OMON	NL-OMON35471

Resultaten

Samenvatting resultaten

N/A