The effect of intranasal insulin on development and behaviour of children with Phelan-McDermid syndrome

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The aim of this project is to validate the hypothesis that intranasal insulin improves development and behaviour in children with Phelan-McDermid syndrome.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Chromosomal abnormalities, gene alterations and gene variants
Study type	Interventional

Summary

ID

NL-OMON37136

Source
ToetsingOnline

Brief title
Intranasal insulin in PMS

Condition

- Chromosomal abnormalities, gene alterations and gene variants

Synonym
22q13.3 deletion syndrome, Phelan-McDermid syndrome

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: ZonMW

Intervention

Keyword: behaviour, development, insulin, Phelan-McDermid syndrome

Outcome measures

Primary outcome

The primary end point is developmental pace. Development is assessed by the Bayley-III-NL (Dutch version of the Bayley-III, Bayley, 2006) or WPPSI-III-NL (Dutch version of the WPPSI-III, Wechsler, 2009) dependent on the developmental age of the children. Both the Bayley-III and the WPPSI are individually administered tests that provide subtests and composite scores that represent general functioning. Developmental pace is calculated as the difference in developmental age equivalent between two assessments divided by the difference in calendar age in months at the time of these assessments (typically 6 months), resulting in a value for developmental age increase / month.

Secondary outcome

The secondary end point is behaviour. Behaviour is assessed by the following questionnaires: Vineland screener, ESSEON, CBCL1,5-5, and Brief-P. To evaluate behaviour in several domains, raw scores are determined. Improvement of behaviour is represented by the increase in test scores in a certain period (typically 6 months).

Other study parameters are genotypic characteristics, phenotypic characteristics and motor behaviour.

Study description

Background summary

Children with Phelan-McDermid syndrome have a severe general developmental delay and behavioural problems. The syndrome is caused by a deletion of 22q13.3 and the neurological problems are thought to result from haploinsufficiency of SHANK3. The SHANK3 protein is located in the postsynaptic density of neurons in conjunction with the insulin receptor. Insulin exerts effects on signal transduction and protein interactions in the postsynaptic density. It induces rapid delivery of glutamate receptors to the cell surface and stimulates expression of dendritic scaffolding protein PSD-95.
Previous studies with intranasally administered insulin show a beneficial effect on cognitive function, declarative memory and behaviour. Moreover, a pilot study with six children demonstrated that intranasal insulin improves development and behaviour in children with the Phelan-McDermid syndrome. It is hypothesized that a decreased availability of SHANK3 can be compensated by insulin-mediated activation of PSD-95, explaining this supposed positive effect.

Study objective

The aim of this project is to validate the hypothesis that intranasal insulin improves development and behaviour in children with Phelan-McDermid syndrome.

Study design

Randomized double-blind placebo controlled stepped wedge design

Intervention

At the start of the clinical trial phase each patient is given a nose apray which contains either insulin or placebo treatment. Groups with placebo will change from placebo to intranasal insulin at different time points. From then all patients remain under intranasal insulin until the end of the study. Administration of the intranasal solution will occur 1 or 2 times per day, 1 puff in 1 or both nostrills, depending on body weight.

Study burden and risks

The burden and risks associated with participation are limited. For this study, development of children will be assessed four times. Each assessment takes maximal two hours. If children do not have sufficient attention span or if they do not co-operate, testing will be ceased. Risks of severe adverse effects have not been reported by previous studies. Adverse effects that have been reported are mild and virtually always temporarily. Potential issues of concern are transitory nasal irritation, rhinitis, spontaneous nosebleeds and headache. Intranasal administration of insulin has been demonstrated to be safe and it

does not have systemic effects on blood glucose levels.

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

• Age between 12 months and 18 years 0 months old at 1-1-2013
• Proven SHANK3 deletion by array-comparative genomic hybridization (array-CGH)
• Parents need to speak and understand Dutch

Exclusion criteria

• A contra-indication for the use of intranasal application (e.g. anatomical obstruction)
• Severe perinatal brain damage (e.g. asphyxia, haemorrhage, infection)
• A metabolic or muscle disease responsible for neurological symptoms, independent of the 22q13 deletion

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Double blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	12-02-2013
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Humuline Regular
Generic name:	Normal human insulin
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	01-11-2012
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Approved WMO

Date:	25-01-2013
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	EUCTR2012-002873-77-NL
CCMO	NL41213.042.12