Paracetamol intravenously in neonates with a gestational age of less than 32 weeks

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Primary objective: to study the pharmacokinetics and pharmacodynamics of paracetamol intravenously in preterm infants with a gestational age of less than 32 weeks:Secondary objective(s): to study the safety and dose-effect relationship of...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON37018

Source
ToetsingOnline

Brief title
PIN32

Condition

- Other condition
- Neonatal and perinatal conditions

Synonym
Discomfort, Pain

Health condition

nociceptie

Research involving
Human

Sponsors and support

Primary sponsor: Maxima Medisch Centrum
Source(s) of monetary or material Support: Wetenschapsfonds Máxima Medisch Centrum

Intervention

Keyword: Neonate, Pain, Paracetamol, Premature

Outcome measures

Primary outcome

• Time - paracetamol serum concentration profile

• Covariate effects on pharmacokinetics.

• Determine estimates of clearance

• Volume of distribution

Secondary outcome

• Glutathion, unconjugated bilirubin, LD, AST and ALT levels

• Paracetamol glucuronid and paracetamol sulphate

• Painscores

Study description

Background summary

In neonatology therapeutic options to treat pain are sparse. Opiates are known to have side effects like hypotension, decrease of intestinal function, respiratory depression, habituation and withdrawal symptoms. For systemic treatment of neonatal pain the only non-opioid alternative is paracetamol. Pharmacokinetic data shows that absorption of this drug when administered rectally is highly unpredictable. The source of neonatal pain frequently is manipulation, and one has to manipulate the neonate when a drug is administered rectally.
There is no evidence for the minimum amount of oral feeding a neonate has to receive to safely administer drugs orally. In every day practice the neonate

receives medication orally only if feeding by mouth has reached 60 ml/kg/day. In a preterm infant of less than 32 weeks that amount will be reached on the 4th day of life (day of birth being day 0). In a preterm of less than 28 days 60 ml/kg/day oral feeding will be reached no earlier than on the 7th day of life. This means that currently the only therapeutic option to treat neonatal pain in preterm infants of less than 32 weeks in the first 5 days of life are opioids or paracetamol rectally.

The intravenous (i.v.) form of paracetamol (Perfalgan®) has recently become available in the Netherlands. Until now, studies on i.v. paracetamol in neonatology have mainly been performed with the pro-drug propacetamol or with paracetamol in preterm infants > 32 weeks of gestation. Propacetamol is a pro-drug of paracetamol and is hydrolyzed by plasma esterases after i.v. administration such that 1 g of propacetamol is hydrolyzed to 0.5 g of paracetamol. Limited data is available concerning the pharmacokinetics of propacetamol and paracetamol. There is no data on the efficacy of parecetamol intravenously.

Study objective

Primary objective: to study the pharmacokinetics and pharmacodynamics of paracetamol intravenously in preterm infants with a gestational age of less than 32 weeks:

Secondary objective(s): to study the safety and dose-effect relationship of paracetamol intravenously.

Study design

The study is a prospective, observational, longitudinal study.

Study burden and risks

As the cohort is, due to the gestational age, subject to frequent blood sampling through an arterial indwelling catheter, the only burden consists of little amounts of extra blood being sampled (5 times 0,25ml) for measurement of paracetamol serum levels. Levels of unconjugated bilirubin, AST,ALT and glutathion require a total of 2 x0,15 ml of blood. The risk of liver failure due to high paracetamol serum levels is expected to be low.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

• Gestational age less than 32 weeks
• Analgesia indicated as per pain protocol
• Indwelling arterial catheter available
• Informed consent

Exclusion criteria

• Co-medication: analgesia, sedatives, muscle relaxants, phenobarbital
• Asphyxiated patients
• Signs of liver failure prior to inclusion

Study design

Design

Study phase:	3
Study type:	Observational invasive
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	21-10-2011
Enrollment:	15
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Perfalgan
Generic name:	Acetaminophen
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	01-07-2011
Application type:	First submission
Review commission:	METC Maxima Medisch Centrum (Veldhoven)
Approved WMO Date:	29-07-2011
Application type:	First submission
Review commission:	METC Maxima Medisch Centrum (Veldhoven)

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	EUCTR2010-019678-34-NL
CCMO	NL27531.015.11