Pediatric Microdosing midazolam: elucidating age-related changes in oral drug absorption

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON26131

Source
NTR

Brief title
PedMic

Health condition

Midazolam, ontogeny, children, absoprtion, metabolism.

Sponsors and support

Primary sponsor: Erasmus Medical Center
Source(s) of monetary or material Support: ZON-MW, The Netherlands Organization for Health Research and Development

Intervention

Outcome measures

Primary outcome

Plasma midazolam to midazolam and metabolite clearance, as surrogate marker of CYP3A activity in vivo

Secondary outcome

The following parameters will be estimated for both formulations: midazolam and metabolite plasma and urinary clearance, volume of distribution, AUC, Cmax, Tmax. In feces: midazolam and metabolite appearance. Oral bioavailability of midazolam. Description of the feasibility of a microdosing study in a pediatric population.

Study description

Background summary

De meeste orale geneesmiddelen voor volwassenen zijn niet geschikt voor kinderen. Het is noodzakelijk om geneesmiddelen specifiek voor kinderen te ontwikkelen en te registreren voor het gebruik bij kinderen. Ondanks onze groeiende kennis over leeftijdsafhankelijke veranderingen in geneesmiddel dispositie, blijven er hiaten over het effect van leeftijd op het hepatische en intestinale metabolisme. Veel medicijnen die aan kinderen worden gegeven worden oraal gegeven. De orale absorptie van geneesmiddelen is bij kinderen weinig onderzocht. Het doel van het onderzoek is meer informatie krijgen over de opname van medicijnen in de darmen, die oraal worden toegediend. De reden voor de keuze van midazolam is omdat het een veelgebruikte medicijn is op de IC. En omdat ze als voorbeeldmedicijnen gebruikt kan worden voor vele medicijnen, vanwege dezelfde verwerking (CYP3A) in de darm en lever.
Gezien praktische en ethische beperkingen van farmacokinetische studies in kinderen, is microdosing waarbij simultaan de IV midazolam dosering en de orale microdosis onderzocht kan worden, een interessante techniek.

Study objective

We hypothesize that age-related changes in hepatic and intestinal drug metabolism affect the pharmacokinetics of midazolam.

Study design

Duriation of maximum 24 hours

Intervention

If the probe drug (midazolam) is given IV for clinical therapy at a therapeutic dose, a 14C-labeled-midazolam microdose will be given simultaneously orally.

Contacts

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Eligibility criteria

Inclusion criteria

Age 0 to 6 years inclusive - At least 36 weeks of post conceptual age or bodyweight >2,5kg - Intravenous or intra-arterial access for blood sampling in place - Receiving midazolam IV - Parental informed consent

Exclusion criteria

Anticipated death in 48 hours - No informed consent - ECMO treatment - Circulatory failure: receiving more than 1 vasopressor or increase of vasopressor drug dose in the last 6 hours. - Chronic liver cirrhosis or chronic renal failure - Renal disorders: Estimated risk for kidney injury or failure at least ‘risk for renal dysfunction’ according to pRIFLE criteria - Hepatic failure: >2SD in age appropriate liver enzyme measurement (ASAT and ALAT) - Gastrointestinal disorderse - Use of co-medication known to affect midazolam metabolism (according to the Farmacotherapeutische Kompas, www.fk.cvz.nl, and Micromedex)

Study design

Design

Study type: Interventional

Intervention model:	Factorial
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	09-11-2015
Enrollment:	60
Type:	Actual

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Positive opinion

Date:	04-05-2016
Application type:	First submission

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
NTR-new	NL5698

Register	ID
NTR-old	NTR5850
Other	NL50470.000.14 : METC 2015-257

Study results