Pharmacokinetics of nutritional conditioning

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To assess the effect of short term starvation and short term high fat feeding on drug metabolism of different drugs, metabolized by different metabolic pathways in healthy subjects using a cocktail approach.

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

Summary

ID

NL-OMON39061

Source
ToetsingOnline

Brief title
PK of nutritional conditioning

Condition

- Other condition

Synonym
not applicable (zie C21)

Health condition

farmacokinetiek van geneesmiddelen en galzouten, niet specifiek tbv een/meerdere aandoeningen

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: bile acids, first pass metabolism, nutrition, pharmacokinetics

Outcome measures

Primary outcome

Primary study endpoint is the difference in area under the plasma concentration versus time curve (AUC) for each drug following the administration of the drug cocktail after 36 hours of starvation (A2,A5) and after 3 days of a high fat meal (A3,A6) in comparison with the control situation of an overnight fast (A1,A4).

Secondary outcome

Secondary endpoints include the difference in the PK parameters clearance, volume of distribution, absorption rate, mean residence time and elimination half-life.

Furthermore, to study the effect of nutritional conditioning on first pass metabolism, the difference in area under the plasma concentration versus time curve (AUC) of the intravenous (A4,A5,A6) and oral (A1,A2,A3) drug cocktail will be studied.

Also, the effect of short term starvation and short term high fat diet on metabolic parameters, such as postprandial glucose, insulin, GLP-1, FGF 19 and bile acid levels will be assessed.

Study description

Background summary

The activity of many enzyme systems in the liver is modulated by nutritional factors. Although hardly studied in humans, there are indications that nutritional conditioning, i.e. the composition of the previous nutrition, influences drug metabolism and bile acid metabolism. Therefore, nutritional conditioning may contribute to both inter- and intra-individual variations in drug metabolism.

Study objective

To assess the effect of short term starvation and short term high fat feeding on drug metabolism of different drugs, metabolized by different metabolic pathways in healthy subjects using a cocktail approach.

Study design

Open-label, single-dose crossover intervention study

Intervention

This study consists of six treatment arms (N=9 per arm). Subjects will be randomized for the sequence in which they receive a single oral (A1,A2,A3) or intravenous (A4,A5,A6) administration of a drug cocktail and a standardized meal (Nutridrink) (A1, A4) after an overnight fast (controls) , (A2, A5) after 36h of starvation, (A3, A6) after 3 days of a high fat meal. The oral drug cocktail consists of: 100mg caffeine, 5mg warfarin, 20mg omeprazole, 100mg metoprolol and 0.03mgkg-1midazolam. The intravenous drug cocktail consists of: 50mg caffeine, 5mg warfarin, 20mg omeprazole, 20mg metoprolol and 0.015mgkg-1 midazolam.

Study burden and risks

The burden of this study includes a screening visit, six 1-day 12-hour hospital admissions, two overnight fasts, two periods of 36h of starvation, two times three days of a high fat meal, six administrations of the drug cocktail (3x oral and 3x intravenous), six standardized meals (Nutridrink). Bloodsamples (n=13 samples of 4,5ml, n=12 samples of 2,0ml and 6x an intravenous catheter) will be drawn for PK analysis and monitoring of laboratory parameters. A total volume of about 499ml blood will be obtained in a period of eight months. For the healthy volunteers the risks are low. This study will generate information regarding the drug metabolizing activity during nutritional conditioning and may therefore be of future benefit for patients with differences in nutritional

status using medication.

Contacts

Public
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105AZ
NL
Scientific
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105AZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Healthy (determined by an experienced physician) male of 18 years or older at the time of signing the informed consent.
- Normal renal and liver function
- Capable of giving written informed consent and to comply with the requirements and restrictions listed in the informed consent form

Exclusion criteria

- Major illness in the past 3 months
- Gastrointestinal disease which may influence drug absorption,
- Abnormalities in ASAT / ALAT / Bilirubin / gammaGT / AF laboratory data
- Drug abuse or alcoholism (>3 units of alcohol per day)
- Participation in another clinical trial in the past 12 months,
- Difficulty in donating blood or limited accessibility of a vein
- Use of tobacco products (induction liver enzymes)
- (chronisch) gebruik van medicatie

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	18-12-2012
Enrollment:	9
Type:	Actual

Ethics review

Approved WMO

Date:	05-11-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	03-01-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-05-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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
CCMO	NL40834.018.12