Descriptive Toxicogenomics of paracetamol in humans

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The primary objective of this study is to assess whether *omics technologies are sensitive and specific enough to be used as a chemical risk assessment tool for humans. More specifically the study will demonstrate if there are different and / or...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Hepatobiliary therapeutic procedures
Study type	Interventional

Summary

ID

NL-OMON35449

Source
ToetsingOnline

Brief title
Toxicogenomics of paracetamol

Condition

- Hepatobiliary therapeutic procedures

Synonym
liver resection, partial chirugical removal of the liver

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Maastricht
Source(s) of monetary or material Support: ASAT (Assuring Safety without Animal Testing: http://www.asat-initiative.eu/index.htm)

Intervention

Keyword: drug safety, liver resection, paracetamol, Toxicogenomics

Outcome measures

Primary outcome

The main study parameters are changes in gene expression profile and

metabolomic profile measured after and caused by APAP exposure.

Secondary outcome

n.a.

Study description

Background summary

Chemical compounds have to be toxicologically evaluated before the are allowed on the market. Studying *omics effects of low to high paracetamol (APAP) dose exposure in humans enables the validation of *omics technologies as a chemical risk assessment tool for humans. Validation of these techniques might in future enable us to reduce or maybe even replace the need of animal testing in chemical risk assessment.

Study objective

The primary objective of this study is to assess whether *omics technologies are sensitive and specific enough to be used as a chemical risk assessment tool for humans.
More specifically the study will demonstrate if there are different and / or similar toxicological effects caused by a low, normal or high dose of APAP, and whether these effects can be seen in human peripheral lymphocytes and / or urine.

Study design

This study includes 5 study groups: patients with liver resection, patients with pancreas resection and 3 groups of healthy volunteers. Liver and pancreas resection patients receive a daily dose of 4*1 gram APAP over 24 hours, which is a commonly used analgesic therapy and should therefore not be regarded as an intervention. Group 3-5, consisting of healthy volunteers receive once a dose

of 0.5, or 2 or 4 grams APAP (4 portions over 24 hours). Blood samples will be collected before the intake of APAP, and 1 hour after the first, second and fourth administration of APAP. Urine samples will be collected before and after the intake of APAP.

Intervention

An intervention is only applicable to study group 3-5, healthy volunteers, receiving a low dose of 2 gram APAP (4*0.5 gram APAP over 24 hours).
In study group 1 and 2, the administration of 4 grams APAP is not considered an intervention since it is part of the normal analgesic treatment after resection surgery.

Study burden and risks

The risks and burden associated with participation include:
- blood sampling (15 samples for the patients, 4 samples for the volunteers)
- urine collection (1 spot urine before, 24 h during APAP use)
- intake of APAP for the volunteers (not being part of a personal therapy)

Contacts

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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

For liver / pancreas resection patients:
•All patients undergoing a non laparoscopic liver or pancreas resection.
•Age above 18 years
For healthy volunteers:
•Age match to liver / colon resection group

Exclusion criteria

•Alcohol abuse up to 6 months before participation in this research.
•Aberrations or insufficiency of kidney, liver, gut, heart or longs apart from the disease to be treated.
•Presence of persistent inflammation in the gut or liver.
•Use of drug known to affect the liver metabolism.
•Endocrine or metabolic aberrations.
•Anaemia or infection.
•HIV infection or hepatitis.

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	22-06-2009

Enrollment:	30
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	N-(4-hydroxyphenyl)acetamid
Generic name:	acetaminophen
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	24-02-2009
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	03-06-2009
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	06-08-2010
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	06-10-2010
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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	EUCTR2009-010279-25-NL
CCMO	NL26884.068.09
Other	trialregister.nl