Pharmacokinetics of Paracetamol before and after Roux-en-Y gastric bypass

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To assess the effect of a Roux-en-Y gastric bypass on the pharmacokinetics of a single oral dose of 1000 mg paracetamol

Ethical review	Not approved
Status	Will not start
Health condition type	Gastrointestinal therapeutic procedures
Study type	Observational invasive

Summary

ID

NL-OMON48508

Source
ToetsingOnline

Brief title
PAPAYA

Condition

- Gastrointestinal therapeutic procedures

Synonym
Roux-en-Y gastric bypass; gastric bypass

Research involving
Human

Sponsors and support

Primary sponsor: Albert Schweitzer Ziekenhuis
Source(s) of monetary or material Support: Stipendium Wetenschapsfonds ASz is aangevraagd

Intervention

Keyword: paracetamol, pharmacokinetics, Roux-en-Y gastric bypass

Outcome measures

Primary outcome

The primary end point is the pharmacokinetics (absorption constant, clearance, distribution volume, peak concentration, time at which peak concentration was observed, area under the curve) of paracetamol and its metabolites (paracetamol glucuronide, paracetmol sulfate, paracetamol mercatopurate and paracetamol cysteine) after a single oral dose of 1000 mg paracetamol before and after RYGB.

Secondary outcome

Secundary end points are ASAT, ALAT, *-GT and bilirubin values at T=0 min and T=6 h.

Study description

Background summary

The number of bariatric procedures performed in the Netherlands is increasing, especially the Roux-en-Y gastric bypass (RYGB). Little is known about the effect of RYGB on the pharmacokinetics of drugs. First of all, the absorption of drugs could be altered in a reversible or irreversible way. Secondly, the body composition will change after surgery which could further influence the pharmacokinetics. In the period after RYGB, the effect on the pharmacokinetics of a drug may gradually change.

In morbidly obese people, pharmacokinetics of paracetamol (PCM) is different compared to healthy non-obese volunteers. The peak concentration (Cmax) of and total exposure (AUC, area under the plasma concentration versus time curve) to PCM are lower in morbidly obese people. The metabolism of PCM was shown to be increased with higher activity of glucuronidation, sulfatation and CYP2E1-mediated metabolism, resulting in higher concentrations of paracetamol

glucuronide (PCM-GLU), paracetamol sulfate (PCM-SUL), paracetamol mercapturate (PCM-MER) and paracetamol cysteine (PCM-CYS). This effect was demonstrated after administration of a single dose of 2 g PCM.

A pharmacokinetic study in RYGB patients showed that the absorption of PCM was faster and that Cmax and AUC increased to values that are comparable to non-obese patients. An important limitation of this study is that the dose used was a single dose of 500 mg PCM, whereas the usual dose of PCM in the Netherlands is 1000 mg per dose.

Study objective

To assess the effect of a Roux-en-Y gastric bypass on the pharmacokinetics of a single oral dose of 1000 mg paracetamol

Study design

This study is an open-label, longitudinal pharmacokinetic study. 20 morbidly obese patients will be included, who are planned to undergo a Roux-en-Y gastric bypass surgery. Pharmacokinetics of a single oral dose of 1000 mg paracetamol (PCM) will be assessed at 3 time points: up to 2 months before RYGB, and at 2-6 weeks and 5-7 months after surgery.

The moments for pharmacokinetic sampling will be combined with regular visits of the patients to the hospital to avoid unnecessary burden for the patients. Furthermore, eight healthy non-obese volunteers will be included to assess the pharmacokinetics of a single oral dose of 1000 mg PCM.

All participants will be screened and asked for informed consent.

Study burden and risks

In this prospective study, pharmacokinetics of a single oral dose of 1000 mg paracetamol (PCM) will be assessed at three time points: once before and twice after RYGB. Pharmacokinetics of a single oral dose of 1000 mg PCM will be assessed once in healthy volunteers.

For this study, patients will be asked to extend their stay in the hospital on visit days to at least 6 hours. At 8 time points, blood samples will be drawn. To minimize burden for patients, they will receive a venflon allowing multiple blood sampling via the same venepuncture. Moreover, visits of patients will be combined with regular visits of participants, so that they do not need to come to the hospital for an extra time. Blood sampling will be done by trained personnel. Thus, risks during withdrawal of blood are minimized as much as possible.

The outcomes of this study are important to assess to what extent pharmacokinetics of PCM will change after RYGB. This could have consequences for the advised PCM dosing for patients after RYGB, especially since paracetamol is a freely available over the counter drug. Moreover, paracetamol is a first choice drug to treat pain and fever. If the exposure to PCM after RYGB is lower, higher dosages could be justified in case of inadequate pain control. However, this must not lead to higher exposure to toxic metabolites of PCM.

Participants need to stay at least 6 hours in the hospital. There are 8 time points to withdraw blood of the participants. In this study, burden for participants is minimalized. Participants receive a venflon. As a result of this, multiple blood sampling can take place via the same venapunction.

Contacts

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Eligibility criteria

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

Inclusion criteria

- * 18 years old
- on the waiting list of getting a Roux-en-Y gastric bypass
- mentally competent
- provided informed consent

Exclusion criteria

- patient undergoing different types of bariatric surgery, such as gastric band, gastric sleeve, mini gastric bypass or revision RYGB
- patient who previously underwent a gastric surgery, such as gastric band, RYGB or gastric sleeve
- taken paracetamol < 24 h before blood sampling at t=0
- allergy or intolerance for paracetamol
- not being able to take paracetamol orally
- to vomit after intake of paracetamol
- to be pregnant

Study design

Design

Study phase:	4
Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	28
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Panadol
Generic name:	Paracetamol / acetaminophen
Registration:	Yes - NL intended use

Ethics review

Not approved

Date:	15-05-2019
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	2018-005006-62
CCMO	NL68663.078.18