Safety of paracetamol in older adults

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To assess the course of paracetamol and oxidative metabolite formation and their correlation with miR-122 in a therapeutic paracetamol regime of 1000mg every 6 hours for a period of at least 5 consecutive days.

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

Summary

ID

NL-OMON50956

Source
ToetsingOnline

Brief title
SAPAROLD

Condition

- Other condition

Synonym
acetaminophen use, safety

Health condition

bijwerking van medicatie

Research involving
Human

Sponsors and support

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

Intervention

Keyword: older patient, paracetamol, pharmacokinetics, safety

Outcome measures

Primary outcome

In the patient group treated with paracetamol: Difference in pharmacokinetic parameters of acetaminophen and six of its metabolites (APAP-Glc, APAP-Sul, APAP-OMe, APAP-GSH, APAP-Cys, and APAP-Cys-NAC) following the administration of paracetamol four times daily after 24 hours and 120 hours of treatment.

Secondary outcome

Secondary endpoints include the correlation between pharmacokinetic parameters of APAP and metabolites and levels of MiR-122. Furthermore, miR-122 levels of the patients treated with FICB and paracetamol will be compared with patients who received FICB only.

Study description

Background summary

Paracetamol (APAP) is one of the most widely used drugs. Theoretically (frail) older people are more susceptible for paracetamol hepatotoxicity due to age related pharmacokinetic changes such as reduced clearance and decreased volume of distribution, and lower capacity of glucuronidation and sulphation. However whether these changes are clinically relevant for the present guideline advice recommending 1,5 - 2,5 grams for chronic use remains unclear. Emerging techniques measuring oxidative APAP metabolites and microRNA-122 (miR-122) could make it possible to detect paracetamol induced liver injury earlier and more precisely than currently used paracetamol plasma concentrations and clinical chemical parameters such as alanine transaminase levels.

Study objective

To assess the course of paracetamol and oxidative metabolite formation and

their correlation with miR-122 in a therapeutic paracetamol regime of 1000mg every 6 hours for a period of at least 5 consecutive days.

Study design

Open-label proof of concept pharmacokinetic study

Study burden and risks

Treatment with FICB and paracetamol is conform local peri-operative pain regimen. The burden of this study solely consists of the additional venepunctures that will be done. The total number of punctures is variable. For the paracetamol group, this will be 15 vials (46.5ml) in 8 individual venepunctures, depending on the route of paracetamol administration (orally of intravenously). For the control group, this will be 4-8 vials (12-24ml) in 3-6 individual venepunctures, depending on when paracetamol is started (see table 1). It is estimated that patients will have standard of care venepunctures twice in the 5 five post-operative days, thus the maximum number of additional single punctures is 6 within one patient. However, the amount of additional blood drawn is low, with a maximum total volume of 46,5ml. This amount is not expected to have any negative consequences for the individual.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Elderly (65 years and older)

Inclusion criteria

- (Intended) admission to the geriatric trauma unit (OLVG West) (post-operative acute hip fracture patients)
- Age >=70 years
- Received a Fascia Iliaca Compartiment Block (FICB) on admission on the ER (hospital standard of care protocol acute hip fracture) or other adequate pain medication
- Written informed consent by patient or witness when the patient is analphabetic and oral consent is given or legal representative

Exclusion criteria

- Use of paracetamol in 72 hours prior to admission
- Known allergy or contra indication for use of paracetamol (i.e. severe liver cirrhosis, G6PD deficiency)
- Abnormalities in AST / ALT / Bilirubin / gGT / ALP (> 2.5 x upper limit of normal)
- Alcoholism (>= 2 units of alcohol per day)
- Difficulty in donating blood or limited accessibility of a vein
- Use of tobacco products (causing induction CYP1A2) in 7 days prior to admission [27].
- Use of other CYP inducers/inhibitors which may have impact on acetaminophen metabolism.
- Inability to understand and give informed consent due to (temporally) incapacitation

Study design

Design

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:	Pending
Start date (anticipated):	01-09-2022
Enrollment:	20
Type:	Anticipated

Ethics review

Approved WMO

Date:	20-10-2021
Application type:	First submission
Review commission:	METC NedMec

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
Other	Netherlands Trial Register onder nummer: NL9493
CCMO	NL77760.041.21