SAfety of PARacetamol in OLDer adults

No registrations found.

Ethical review	Not applicable
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON20003

Source
Nationaal Trial Register

Brief title
SAPAROLD

Health condition

Paracetamol toxicity

Sponsors and support

Primary sponsor: UMCU
Source(s) of monetary or material Support: UMCU

Intervention

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

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

Rationale: 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.
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 population: Twenty patients aged 70 years or older, admitted to the geriatric trauma ward of olvg hospital because of a femoral fracture with indication for surgery. Conform peri-operative standard of care, patients receive a fascia iliaca compartiment block (FICB) as local pain blockade followed by paracetamol 1000mg every 6 hours for a period of at least 5 consecutive days. Two groups will be formed based on duration of FICB effectiveness, one (control) group receiving no paracetamol during 24 hours post-operative (having adequate pain control due to FICB). The other (paracetamol) group will receive paracetamol within 24 hours after surgery.
Intervention: Ten patients will be included in the paracetamol group, and ten patients in the control group. Blood samples will be drawn in the first 5 days after surgery in order to measure miR-122 and plasma concentrations of paracetamol and its metabolites.

Study objective

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 design

Primary and outcomes: venipunctures before surgery and then at time =0, 24, 72, 96 and 120 hours. (PCM group; serum APAP and metabolites at 0, 24, 72, 96, 120 hours; serum

miR-122 before surgery and t = 0, 24, 72, 96 and 120 hours. Control group: miR-122 before surgery and t = 0 and 24 hours. If in unexpected cases no PCM is needed after this, also t = 72,96 and 120 hours will be measured).

Intervention

Venipunctures for APAP metabolite and MiR-122 assays (otherwise standard of care post-operative paracetamol pain treatment).

Contacts

Public
UMCU
Hiltsje Heemskerk

0642412837
Scientific
UMCU
Hiltsje Heemskerk

0642412837

Eligibility criteria

Inclusion criteria

- Admitted 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)
- Written informed consent by patient or legal representative

Exclusion criteria

- Use of paracetamol in 72 hours prior to admission
- Exclusion criteria for FICB: complicated fractures, femoral nerve damage, bupivacaine/ levobupivacaine allergy, infections in pelvic area, anti-coagulation therapy, INR > 4,5, history of femoral bypass surgery, planned operation < 60 minutes of ER admission, peripheral neuropathy with sensory loss.

- 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.
- Use of other CYP inducers/inhibitors which may have impact on acetaminophen metabolism.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-08-2021
Enrollment:	20
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Not applicable

Application type:	Not applicable

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	NL9493
Other	METC UMCU : UMCU-77760

Study results