SAfety of PARacetamol in OLDer adults

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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...

Ethische beoordeling	Niet van toepassing
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON20003

Bron
Nationaal Trial Register

Verkorte titel
SAPAROLD

Aandoening

Paracetamol toxicity

Ondersteuning

Primaire sponsor: UMCU
Overige ondersteuning: UMCU

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

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.

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

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.

Onderzoeksopzet

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).

Onderzoeksproduct en/of interventie

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

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

- 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

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

- 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.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Niet-gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	Actieve controle groep

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	01-08-2021
Aantal proefpersonen:	20
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nog niet bepaald

Ethische beoordeling

Niet van toepassing

Soort:	Niet van toepassing

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL9493
Ander register	METC UMCU : UMCU-77760

Resultaten