An explorative study determining the oral antibiotic drug absorption in patients with short bowel syndrome.

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Our hypothesis is that the enteral absorption of orally administration of clindamycin, ciprofloxacin, flucloxacillin and fluconazole are sufficient in patients with short bowel syndrome.

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

Samenvatting

ID

NL-OMON27546

Bron
Nationaal Trial Register

Verkorte titel
ABSORB_2

Aandoening

Short Bowel Syndrome

Ondersteuning

Primaire sponsor: Radboudumc
Overige ondersteuning: Institutional

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

The primary endpoint of the study is the enteral absorption of orally administered ciprofloxacin, clindamycin, flucloxacillin and fluconazole, defined as the blood plasma concentration (µg/ml). The total concentration will be measured.

Toelichting onderzoek

Achtergrond van het onderzoek

Rationale: In patients with short bowel syndrome administering oral antibiotics can be problematic since the changes in anatomy of the gastrointestinal tract with a diminished absorptive capacity result in alterations in drug disposition, and the bioavailability of oral drugs is primarily affected by reduced bowel length. For this reason, the American Gastroenterological Association (AGA, 2003) advises prolonged intravenous therapy in patients with SBS. Other concomitant factors influence drug absorption and metabolism in the case of short bowel as well, such as mucosal integrity, intestinal motility, site of drug absorption, type of formulation, presence of co-morbidities, pH and parenteral nutrition-associated metabolic changes (Ward et al. 2010). However, successful treatment with orally administered antimicrobial agents has been reported in selected, mostly pediatric, cases with SBS (Dressman et al. 1993, Iacono et al. 1993, Joe et al. 1994, Parsons et al. 1977, Thielman et al. 1998). Unfortunately, more recent, let alone well-designed interventional studies researching biologic availability and other pharmacokinetic parameters of antimicrobial agents in HPN patients with SBS are completely lacking

Objective: The primary objective is to determine the absorption of orally administered antibiotics in patients with SBS, to guide in clinical decision making when faced with catheter related infections.

Study design: Explorative single-centre study (research with a medicinal product)

Study population: Adults (>18 years) with SBS

Intervention : A single dose of two registered antibiotics will be administered. At four timepoints blood will be drawn. Group CC (n=8) will receive an oral dose of Clindamycin 600mg and Ciprofloxacin 750mg together with the infusion of a low concentration of the same antibiotics. Group FF (n=8) will receive an oral dose of Flucloxacillin 1000mg and Fluconazol 400mg together with the infusion of a low concentration of the same antibiotics.

Main study parameters/endpoints:

The primary endpoint of the study is the enteral absorption of flucloxacillin, clindamycin, ciprofloxacin and fluconazol, defined as the concentration (µg/ml) in blood plasma concentration.

Secondary study parameters are:
• Comparison with results of the ‘normal population’

• Plasma concentration curve, consisting of 4 measurements in blood plasma.
• Blood biochemical analysis
• Demographic information, medical history, concomitant medication
• Complications or adverse events

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: Possible risks associated with participation are adverse reactions to the administration of antibiotics, however as all antibiotics are given as a single dose, and patients will be questioned about allergic reactions to antibiotics, we deem this risk to be low. Since we draw blood from the patient's own central venous access, no possible side effects or adverse events related to vena punctures are expected to occur. Blood will be obtained at four time intervals, mostly during a routine scheduled daytime hospital admission (for HPN training) and additional withdrawal of blood (approximately 22.5 ml). There are no extra site visits necessary.

HPN patients, and likely other patient groups with reduced bowel length, will benefit from an evidence-based individualized antibiotic treatment guideline in case of an infection. Ultimately, this will lead to a reduced hospitalization rate with reduced length of stay and subsequently, a reduction in health care related costs. Also this study will provide guidance for further policy development and implementation of antibiotic drug administration protocols specific for patients with reduced bowel length.

Doel van het onderzoek

Our hypothesis is that the enteral absorption of orally administration of clindamycin, ciprofloxacin, flucloxacillin and fluconazole are sufficient in patients with short bowel syndrome.

Onderzoeksopzet

T0, T1, T2, T4

Onderzoeksproduct en/of interventie

We designed a single-centre explorative in vivo study of enteral antibiotic absorption in patients with short bowel syndrome.
1. We will include a total of 16 patients and patients will be allocated to two treatment-groups:
• CC-group: 8 patients will receive ciprofloxacin (750mg) together with clindamycin (600mg) (both suspension) followed by a low dose intravenous administration of the same drugs (10 ul) 2 hours later.
• FF-group: 8 patients will receive flucoxacillin (1000mg) together with fluconazol (400mg) (both tablets) followed by a low dose intravenous administration (10 ul) of the same drugs 2 hours later.

2. Most of the patients will be included when they are admitted for HPN training.
3. Plasma concentrations will be assessed 4 times during hospital stay for pharmacokinetic

analysis: baseline, 1, 2 and 4 hours after ingestion.
The choice for these compounds was based on their frequent use, favourable bioavailability propfile, and high cost of the i.v. product.

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

- Patients with current use of long-term home parenteral nutrition (> 3 consecutive months) and clinically stable
- Diagnosed with SBS (total small bowel length 200cm or less after Treitz ligamentum)
- Age 18 years of older
- Signed Informed Consent
- Patient is fully able to understand the nature of the proposed intervention.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

- Active vomiting, worsening or new diarrhea
- Contra-indications (for example allergies or interfering co-medication) for any of the study treatments
- Impaired renal function (creatinin clearance <30ml/min/1,73m2)

- Pregnancy
- Morbid obesity (BMI >35)
- Any current or prior medical condition that may interfere with the conduct of the study or the evaluation of its results in the opinion of the investigator

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	Geneesmiddel

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	01-11-2019
Aantal proefpersonen:	16
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	NL7796
Ander register	CMO Arnhem-Nijmegen : 2019-5561

Resultaten