The effect of body composition on the farmacokinetiek IFX in patients with inflammtoy bowel disease;

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The aim of the studie is to determine the correlation between fat mass end the IFX concentration. Primary research question:What is the effect of fat mass percentage, measured by a validated scale, and secundaire skinfold measurement, waist...

Ethical review	Approved WMO
Status	Suspended
Health condition type	Gastrointestinal inflammatory conditions
Study type	Observational invasive

Summary

ID

NL-OMON46317

Source
ToetsingOnline

Brief title
FLINX (Farmacokinetics and body composition in IBD patients with IFX)

Condition

- Gastrointestinal inflammatory conditions

Synonym
Colitis ulcerosa, Crohn's disease, Inflammatory Bowel Disease

Research involving
Human

Sponsors and support

Primary sponsor: Zuyderland Medisch Centrum
Source(s) of monetary or material Support: Reguliere zorg; de extra meting zal (zoals het er nu naar uit ziet) door onszelf worden uitgevoerd gezien alle aanwezige apparatuur

geen extra kosten hebben. Mocht dit niet zo zijn is er vanuit eigen geldstroom binnen de comic mogelijkheid tot financiering.

Intervention

Keyword: Body composition, farmacokinetics, Inflammatory bowel disease, Infliximab

Outcome measures

Primary outcome

The primary outcome measure is the correlation between fat mass, measured by an validated scale, and the IFX level. This will be measured prior to the IFX infusion. The IFX concentration will be measured and analysed in blood. Prior to de IFX infusion the trough level will be measured (according to regular health care). 30 minutes after the end of the infusion the top level will be measured

Secondary outcome

Secondarily, the body composition; measured by skinfold thickness, waist circumference, hand grip strength, BMI and body composition will be correlated to the IFX concentration.

Furthermore, de disease activity, inflammation parameters and the amount of adverse effects will be measured en corelated to the fat mass.

Study description

Background summary

Patients with inflammatory bowel disease (IBD), with ulcerative colitis and Crohn*s disease as most important types, suffer from chronic recurrent inflammatory processes in the intestine. The treatment of IBD consist, in

10-30% of the population, of anti-TNFalfa (TNFi), such as infliximab (IFX). TNFi belongs to the biologicals, a relative new group of medication. They are effective in the treatment of IBD, but there are also some side effects known. The primary therapy failure rate is approximately 10-40% and the secondary annual loss of response (LOR) is approximately 10% (1). Besides, biologicals have high investment costs. In the current clinical practise the dose of most of the TNFi medications are based on bodyweight, in particular infliximab.
In the study of Dotan Et al (2) the researchers investigated the effect of several patient characteristics on the pharmacokinetic characteristics of IFX in the treatment of IBD. They showed that there was no linear relation between body weight and the clearance of IFX. Patients with a lower bodyweight, had a 35% lower IFX level in the serum at all tie with a fixed dosage of 5mg/kg in comparison with patients with a weight twice as high. Due to research in the field of the pharmacokinetics and dynamics in the past, nowadays the dosage of IFX is based on mg/kg bodyweight. The writers of the study of Dotan et al. (2) seems to conclude that the dosage of IFX is not optimal, and can therefore possibly be optimized. It seems that an individual patient with a higher body weight does not need the same amount mg/kf medication in comparison with an individual with a lower bodyweight in order to get the same level of IFX in the blood. Other studies also describe the fact that body composition might be a better tool to determine the dose of IFX medication. (3,4) Body Mass Index (BMI) is often used to describe body composition. However, BMI does not seems to be the an ideal method for IFX dose optimization. (3,4) Nutritional status, measured by measuring the body composition in fat mass and fat free mass, might be a better biomarker in order to optimize the dose of IFX in comparison with weight or possibly with BMI (2-4). Body surface, calculated from bodyweight and height, might also be a tool in order to optimize the dosage, and is currently used in the oncology field for the determination of pharmaceuticals.
The study of Scaldaferri et al (5), describe that patients with a high BMI, has a higher serum level IFX 30 minutes after infusion (toplevel), in comparison with patients with a low BMI. This difference was not seen previous to the IFX infusion (trough level). This higher top level in patients with a higher BMI does not seems to lead to a better response to the medication. When taking body fat into account, there was no significant difference between top level in patients with a high or low bodyfat percentage. From this can be hypothesized that body composition may be a better method in order to determine the dose of IFX.
In patients with IBD, the nutritional status is often suboptimal. The aetiology is multifactorial, and malnutrition and malabsorption of nutrients play a role. (6). The literature also describe a reduced muscle mass (cachexia) in these patients (3,7). Body composition is underexposed in patients with IBD.

Given that it is described in the literature that determining the dosage of IFX based on body weight does not seems ideal, other methods must be investigated in order to determine a more optimal dosage. An advantage of body bodyweight is that it is easily applicable in daily clinical practise. Therefore, it is important that possible new methods, such as body composition, is also easily

applicable in daily clinical practise. A more optimal dose might also lead to less side effects and a lower LOR rate. Besides, a more optimal dose might also lead to a lower dose for some IBD patients, reducing the costs and is thereby also interesting for financial aspects.
Therefore, the aim of this study is to investigate the effect of body composition, body surface and BMI on the IFX serum level compared to just determining the body weight. Besides, there will be investigated if body composition and BMI, and their possible pharmacokinetic consequences influence the effectiveness of the IFX medication in the IBD population.

Study objective

The aim of the studie is to determine the correlation between fat mass end the IFX concentration.

Primary research question:
What is the effect of fat mass percentage, measured by a validated scale, and secundaire skinfold measurement, waist cirucmference, hand grip strength, BMI and body surface on the IFX level, with IFX dose based on the body weight, in an IBD population using IFX medication?

Secondary research question(s)
The secondary research is question is; Is the effectiveness of IFX and the safety (advere effects) related to the body composition in IBD patients starting with IFX medication?

Study design

In this observational study, patients treated with IFX or patients that will start with IFX for the treatment of IBD will be included in de study. A transversal study design will be used in order to investigate the relation between body composition and the IFX concentration. This will be measured in patients already treated with IFX. Besides, patients starting with IFX during the study period will be included. In this patients, a steady state need to be reached in order to measure a reliable measure. Therefore the IFX concentration will be measured after the third IFX infusion in these patients. In this population we will also measure the effect of the IFX in a prospective setting.
All patients will be recruited from the IBD population from Zuyderland Medical Centre location Sittard and Heerlen.

Study burden and risks

The measurements to determine the body composition, are not-invasive methods. There are no risk or negative effects expected. Blood collection can hurt or cause haemorrhage. The blood collection is taken from an already placed infusion. All together, we collect 1 tube of 6 ml blood extra, above regular

care. This amount does not cause problems for adults. All other measurements (IFX trough level, inflammation parameters in blood and calprotectine) and the medication gifts will be done according to regular care. Therefore, there are no extra risk here. Patients do not have to visit the hospital more often than normal. The extra measurements fort the study will take approximately 2 hours above regular care. The study load and risks for the participants is therefore low.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Inclusion criteria:
Patiënt are eligible to participate in the study if all of the following criteria are met:
1. Patient, male or female, is aged above 18 years

2. Patient has an established diagnosis of ulcerative colitis or Crohn*s disease
3. Patients is being treated with, or start with the treatment IFX for a period of at least 12 weeks, or for the first time during the study period.
4. Patiënt must be able to understand the patient information and the explanation of the investigator
5. Patient must be able to undergo the study measurements and understand the instructions of the investigator
6. Patient is informed about the intention and nature of the study including the possible risks and has signed the informed consent before inclusion.

Exclusion criteria

Exclusion criteria
Patients are not eligible if one or more of the following criteria are met:
1. Patient is mentally or physically not able to participate to the study, including severe mental illness.
2. Patient has had a change in the dosage of the IFX during the last 5 weeks.
3. Patients who is currently pregnant, breastfeeding, or is planning to become pregnant during the study period.
4. Patients suffering from severe comorbidities which can influence the body composition of the pharmacokinetics of IFX;
a. Current malignancy or a malignancy in the recent history (<5 years), except cutaneous basal cell carcinoma and cutaneous squamous cell carcinoma.
b. (history of) Liver/renal failure
c. Short Bowel Syndrome
d. Heart failure defined as; New York Heart Association (NYHA) Class III or IV
5. Patients participating in other studies, or participated I another study with an intervention in de last 4 months.

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Suspended
Start date (anticipated):	23-01-2019
Enrollment:	33
Type:	Actual

Ethics review

Approved WMO Date:	29-10-2018
Application type:	First submission
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)
Approved WMO Date:	19-12-2018
Application type:	Amendment
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 28109
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL66944.096.18
OMON	NL-OMON28109