Intestine, microbiome and osteoarthritis

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We hypothesize that treatment with Sustained Release Calcium Butyrate (SRCaBu) will ameliorate: 1) the intestinal microbiome, intestinal barrier function and immune tolerance: 2) lower systemic inflammation of OA of the hand.

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

Samenvatting

ID

NL-OMON28862

Bron
NTR

Verkorte titel
TBA

Aandoening

Hand osteoarthritis

Ondersteuning

Primaire sponsor: BirrBeheer B.V.
Overige ondersteuning: Sponsor

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Difference in compositional and functional microbiome parameters after 4 weeks of SRCaBu treatment. A positive treatment effect with respect to microbiome composition and function is an increase in alpha diversity and fraction of strict anaerobes.

Toelichting onderzoek

Achtergrond van het onderzoek

Rationale: Three major aspects of functioning of the intestine, intestinal barrier (1), intestinal associated immune tolerance (2) and intestinal microbiome (3) interact closely in a very controlled way. A deviant homeostasis contributes to endotoxemia, low chronic systemic inflammation, often with constipation. This deviant homeostasis is often associated with elevated systemic inflammation and localized chronic inflammatory diseases like osteoarthritis (OA) and cardiovascular diseases. Short chain fatty acids, acetate, propionate and especially butyrate, formed by fermentation of non-digestible dietary fibres by the intestinal microbiome are essential for the mentioned aspects of the functioning of the intestine. The association between impaired intestinal barrier function and OA have been described in various studies and it was postulated that amelioration of the impaired barrier function would ameliorate OA. Several studies suggest that the low-grade chronic systemic inflammation in OA is associated with local inflammation in the intestine and impaired intestinal barrier function. We hypothesize that treatment with Sustained Release Calcium Butyrate (SRCaBu) will ameliorate: 1) the intestinal microbiome, intestinal barrier function and immune tolerance: 2) lower systemic inflammation of OA of the hand.
The primary objectives of this study:
This proof of concept study is to estimate the effects of SRCaBu (600 mg daily for four weeks compared with placebo) on compositional and functional characteristics of the microbiome for future sample size calculation.

The secondary objectives:
1) To evaluate the short-term effects (i.e. 4 weeks) of SRCaBu (600 mg dd) compared with placebo on pain and functioning of the hands in hand OA patients.
2) To evaluate whether SRCaBu (600 mg dd) lowers systemic inflammation in hand OA.
3) To evaluate whether immune tolerance will improve as mediating factor for lowering inflammation by characterizing the phenotype of T-cells and monocytes and determining the response of activated peripheral blood mononuclear cells (PBMCs) of patients before and after intake of 600 mg dd SRCaBu.
4) To examine the preliminary safety profile of (600 mg dd) SRCaBu in patients with hand OA over 4 weeks.
5) To examine the association between intestine functioning and pain and functioning of the hands in hand OA patients.
6) To examine the effect of SRCaBu intake on stool behaviour.
Study design: proof of concept, randomized, (double-)blinded, placebo-controlled trial design with follow-up of 4 weeks.
Study population: People with OA of the hand (both hands), aged 50 to 75 years,
BMI ≥20 and ≤30 kg/m2, fulfilling ACR criteria for hand OA, OA in other joints will be allowed.
Assessments: Physical examination 2x (blood pressure, waist circumference, weight, length, number of tender and swollen joint hands (2x). clinical hallmarks (1x)), X-ray of the hands, (1x), vena puncture (2x), faecal sampling (at home) (2x). Questionnaires (2x): hand functioning (MHQ) , quality of life (SF12) patient’s global assessment. Electronic daily questionnaires on pain (NRS) and stool behaviour (Bristol stool behaviour questionnaire).

Medication adherence (pill count at 4 weeks).
Intervention and control group: treatment with placebo or SRCaBu (600mg dd) for a period of 4 weeks;
Main study parameters/endpoints: compositional and functional characteristics of the microbiome.
Secondary endpoints: change in intestinal barrier function, change in systemic inflammation parameters, immune tolerance and inflammatory response, tender and swollen joint count, pain, functioning of hands, patient's global assessment, quality of life, stool behaviour.
Nature and extent of the burden and risks associated with participation, benefit and group relatedness: Burden; 2 visits to Sint Maartenskliniek (consultation and physical examination; blood pressure, blood sampling (2x 53 mL), faecal sampling (at home 2x)). Online questionnaires (daily). Daily intake of 4x 150 mg SRCaBu or placebo for four weeks.
Group relatedness:
There is no disease modifying agent available for OA. The now used medicines, non-steroidal anti-inflammatory agents and corticosteroids can have unwanted side effects. New is the treatment with Tanezumab, a humanized murine monoclonal antibody to nerve growth factor. Tanezumab is a completely new approach for the treatment of pain, but has drawbacks that it sometimes accelerates the process of joint degradation, and is expensive.

Doel van het onderzoek

We hypothesize that treatment with Sustained Release Calcium Butyrate (SRCaBu) will ameliorate: 1) the intestinal microbiome, intestinal barrier function and immune tolerance: 2) lower systemic inflammation of OA of the hand.

Onderzoeksopzet

Assessments will be performed at baseline and after 4 weeks of follow-up.

Onderzoeksproduct en/of interventie

Sustained Release Calcium Butyrate (SRCaBu)

Contactpersonen

Publiek

Sint Maartenskliniek
Tim Pelle

024 365 9148

Wetenschappelijk

Sint Maartenskliniek
Tim Pelle

024 365 9148

Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

In order to be eligible to participate in this study, a subject must meet all of the following criteria:
- Age ≥ 50 year and ≤ 75 years,
- Hand OA according to the 1990 ACR diagnostic criteria for hand OA (31) in both hands operationalized as:
• Hand pain, aching, or stifness and 3 or 4 of the following:
o Hard tissue enlargement of 2 or more of 10 selected joints (Ten selected joints include bilateral second and third interphalangeal proximal joints, second and third distal interphalangeal joints, and first carpometacarpal joint)
o Hard tissue enlargement of 2 or more DIP joints
o Fewer than 3 swollen MCP joints
o Deformity of at least 2 of 10 selected joints.
- Pain (NRS) during hand activities of both hands ≥ 5 ≤ 8 (scale 0-10), during 15 of the last 30 days.
- Body Mass Index (BMI) > 20 and < 30 kg/m2,
- In possession of a smart phone to use the app to assess stool behaviour on a daily basis
- Can operate a computer to fill in online questionnaires via CastorEDC.
- Able to read, write and sufficiently communicate in Dutch
- Have an email address

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

- Recent use of antibiotics (last three months)
- Previous surgery of one of the hands
- Recent cerebro- or cardiovascular incident (past 6 months)
- Diabetes
- Other chronic inflammatory disease
- Other musculoskeletal diseases than OA with possible hand localisation
- Cognitive deficits affecting the scoring process

- Received intramuscular of intra-articular corticosteroid injections in the previous 4 weeks
- Fibromyalgia according to the 2010 ACR diagnostic criteria for fibromyalgia (32)
- Any other syndrome(s) or condition(s) that could interfere with the assessment of pain
- Severe current psychiatric disorders assessed by physician
- Self-reported consumption of alcoholic drinks, > 2 units per day

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Dubbelblind
Controle:	Placebo

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	01-07-2021
Aantal proefpersonen:	33
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nee

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	NL9401
Ander register	METC : 2021-8175

Resultaten