Multimodal treatment of perianal fistulas in Crohn's Disesase: seton versus anti-TNF versus advancement plasty

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON22680

Source
Nationaal Trial Register

Brief title
PISA-trial

Health condition

perianal fistulas, Crohn's disease
perianale fistels, ziekte van Crohn

Sponsors and support

Primary sponsor: Academic Medical Center
Source(s) of monetary or material Support: Zon MW

Intervention

Outcome measures

Primary outcome

The primary objective of this study is to analyse the number of patients that need a re-intervention due to fistula-related complications (abscesses, recurrent or new tract

formation).

Secondary outcome

The secondary outcomes parameters will be the number of patients with closed fistulas (based on MRI findings) after 18 months, Perianal Disease Activity Index (PDAI score) and number of necessary antibiotics courses during fistula treatment, quality of life (EQ-5D and IBDQ), and costs (KEA and BIA).

Study description

Background summary

Rationale: Currently, there is no guideline for the treatment of Crohn's patients with perianal fistulas. Most patients receive anti-TNF medication, but no long-term results of this expensive medication have been described, nor has its efficiency been compared to surgical strategies.
Objective: With this study, we hope to provide treatment consensus for daily clinical practice with reduction in costs.
Study design: The design of the study is a multicenter prospective randomised study.
Study population: All Crohn’s patients with newly diagnosed high perianal fistula (inter-, trans-, and suprasphincteric fistula with involvement of upper 2/3 of external sphincter), not on anti-TNF for 3 month, will be considered. Patients will be excluded if they have proctitis, recto-vaginal fistula, anal stenosis or anti-TNF allergy.

Intervention: The following groups will be compared:

Group I: chronic seton (seton drainage for 1 year)

Group II: anti-TNF (seton for 6 weeks under anti-TNF medication, followed by seton removal with continuation of medication for 1 year)

Group III: advancement plasty (seton drainage under anti-TNF). After 8-10 weeks, surgical closure of internal opening with advancement plasty under anti-TNF for 4 months)

Main study parameters/endpoints: The primary outcome parameter is the number patients needing fistula-related re-intervention(s). Secondary outcomes are the number of patients with closed fistulas (based on an evaluated MRI-score) after 18 months, disease activity by Perianal Disease Activity Index (PDAI), quality of life and costs.

Nature and extent of the burden and risks associated with participation: All patients will receive one of the three standard treatment approaches that are currently used for fistula treatment. Since there is no experimental study-arm, there are no additional risks associated with participation. During the study, the medical staff and trial nurses will monitor the necessity of surgical interventions and hospitalisations. Secondary outcome parameters

(number of draining fistulas and PDAI score) will be assessed during visits to the outpatient clinic at baseline and at intervals of 6 months for the duration of the study period. Health related quality of life will be measured by the EQ-5D and IBDQ questionnaires, both will be mailed to the patients every 3 months. Data on out-of-hospital care, and productivity losses resulting from sick-leave will be retrieved from tailored patient questionnaires.
Sample size calculation: Based on the available literature with re-interventions in 50% of patients on anti-TNF medication and after advancement plasty, a reduction with 30% to 20% of patients needing a re-intervention in the chronic seton group is considered clinically relevant and feasible. The sample size needed to detect this difference with a Chi-square test equals 42 patients per group, or 126 patients overall (alpha 0.05, power 80%, and 5% drop-out).

Study objective

It is hypothesised that after 18 months no differences will be found in the number of patients with draining fistulas for medical
and surgical treatment strategies. Since surgical seton drainage is the only treatment preventing recurrences or abscesses, we expect this strategy to be highly cost-effective.

Study design

N/A

Intervention

Group 1: chronic seton drainage

Group 2: anti-TNF

Group 3: Advancement plasty

All patients start at T=0 with the insertion of a seton(s) in day care setting. This will be done under antibiotics prophylaxis that will be continued for 2 weeks (ciproxin). In the chronic seton group treatment wil be combined with 6MP for 1 year, Both the anti-TNF group and the advancement plasty group will start with medication, anti-TNF and 6MP, after 2 weeks. If 6MP is contraindicated thiopurine or methotrexate can be added. The anti-TNF choice (infliximab or adalimumab) will be left to the discretion of the treating gastroenterologists. The anti-TNF agent consists of infliximab 5mg/kg at the beginning of treatment, which will be repeated at 2 and 6 weeks as a loading dose. After this, treatment will be scheduled every 8 weeks. If a patient is non-responsive to the treatment dose escalation is permitted to 5mg/kg every 6 weeks. When adalimumab is the preferable anti-TNF agent a loading dose of 160mg at the start of treatment is required. After 2 weeks the dosage will be reduced to 80mg and then continued with 40mg every 2 weeks. If a patient is non-responsive dose escalation is allowed

as far as 40mg a week. In case of a previously demonstrated allergy or adverse reaction, the patient should be randomised to the other drug. After 6 weeks, the seton will be removed in the anti-TNF group, while these patients continue their medication for up to one year. In the advancement group, the advancement plasty will be performed in day care setting (with seton removal at the same time) within eight to ten weeks after randomisation, when the anti-TNF has reached therapeutic levels. The anti-TNF medication will be continued until four months after randomisation.

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Eligibility criteria

Inclusion criteria

- ≥ 18 years

- Written informed consent

- High tract (intersphincteric, transsphincteric, suprasphincteric) perianal fistula located in the upper two-thirds of the external sphincter

- Fistula with one internal opening (based on MRI imaging). The number of external fistulas does not have to be taken into account

- Both new fistulas or recurrent active fistula (defined as any producing fistula)

Exclusion criteria

- Proctitis (defined as any active mucosal inflammation or ulcer > 5mm in the rectum)

- Anorectal stenosis (defined as the impossibility to introduce a proctoscope)

- Submucosal fistulas & low intersphincteric fistulas (lower one-third of external sphincter)

- Rectovaginal fistula

- Multiple internal openings

- Seton in situ for more than 3 months

- Use of Anti-TNF medication during last 3 months

- Previous Anti-TNF medication without any effect on perianal fistulas

- Previously demonstrated allergy for anti-TNF medication. If this allergy only concerns the chimeric monoclonal mouse-antibody infliximab, the patient could be randomised for adalumimab

- Patients with a stoma

- Immunocompromised patients (i.e. haematological malignancies, HIV/AIDS, bone marrow transplantation, splenectomy, genetic disorders such as severe combined immunodeficiency, chemotherapy, dialysis, solid organ transplant and long term immunosuppressant use such as corticosteroids in patients with rheumatoid arthritis)

- Life expectancy < 2 years

- The inability of reading/understanding and filling in the questionnaires

- Dementia or altered mental status that would prohibit the understanding and giving of informed consent

Study design

Design

Study type:	Interventional
Intervention model:	Parallel

Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	29-08-2013
Enrollment:	126
Type:	Anticipated

Ethics review

Positive opinion

Date:	23-08-2013
Application type:	First submission

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	NL3957
NTR-old	NTR4137
Other	: 2013_201
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
N/A