Endoscopic Balloon Dilatation of stenotic ileocecal anastomosis in Crohn*s disease with or without additive local steroid injection and oral Budenofalk* a double-blind, randomized, parallel group trial

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The primary objective of this study is to evaluate whether adding intensive local anti-inflammatory therapy (Triamcinolone injection therapy combined with 9 mg oral BudenoFalk once daily for 24 weeks) to routine enteric balloon dilatation reduces...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Gastrointestinal stenosis and obstruction
Study type	Interventional

Summary

ID

NL-OMON38167

Source
ToetsingOnline

Brief title
ENDO ACE TRIAL

Condition

- Gastrointestinal stenosis and obstruction

Synonym
Gut obstruction, stenosis

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Tramedico,Tramedico bv

Intervention

Keyword: Anastomosis, Crohn, Dilatation, Endoscopic

Outcome measures

Primary outcome

To evaluate whether the addition of intensive local anti-inflammatory therapy reduces the recurrence of stenosis and/or need for surgical intervention in routine enteric balloon dilatation in Crohn*s disease patients with symptomatic stenosis of the anastomosis.

Secondary outcome

To assess the feasibility and value of radiologic imaging of the anastomosis in the endoscopy suite, and validating Radiological Crohn*s Disease Anastomotic Index (RCDAI).

Study description

Background summary

Crohn*s disease may affect the entire digestive tract but is mostly located in the ileocecal region (1). In 30% percent of the cases the disease is characterized by formation of strictures leading to bowel obstruction (2,3,4). Up to 80% of CD patients will eventually require at least one surgical resection within the first ten years after diagnosis (5,6). Most of these patients require multiple resections during the course of their disease, which may eventually result in short bowel syndrome. Stenosis of the anastomotic site as a cause of inflammation and fibrosis is a frequent long term complication (50-70%) after an ileocecal resection (10).
When a stenotic anastomosis is present there are several treatment options. Surgical resection or stricturoplasty of the strictured segment is often

required. Research has shown that an operation can efficiently and safely be postponed or even prevented by Endoscopic Balloon Dilatation (EBD)(11-18). When EBD of a stenotic enteral anstomosis is performed a balloon catheter is guided through the lumen of an endoscope to the anastomosis. Here the balloon is inflated until enduring adequate dilatation is reached. Often multiple dilatation sessions are required for the desired result.
Retrospective studies have shown that additive local anti-inflammatory therapy (by injection of a long acting steroid at the site of the anastomosis and/or a locally acting steroid) is safe and may decrease the need for redilatation and/or surgical intervention (19,20). In these studies a Triamcinolone solution (8 mg/mL or 40 mg/mL) was used, whereby four-quadrant injections of 0,5-1 mL were performed at the most inflamed and narrowed area*s. There is only one prospective study on the benefit of local injection of Triamcinolon (21). The authors concluded from this pilot study that there is no benefit for Triamcinolon injection. However, a low dose of Triamcinolon was used (8 mg/mL). Furthermore, it may be hypothised that adding oral anti-inflammatory drugs may cause more enduring results.
The standard approach for assessing the extend of a stenotic segment was the Enteric Follow Through examination (EFF). This is a radiological procedure in which a fluid contrast medium is injected through a catheter into the enteric lumen. Nowadays, EFF has largely been replaced by MR Enteroclysis and MR Enterography, both using non-ionizing magnetic resonance. The latter has been shown to be equally effective in assessing intestinal stenoses and is better tolerated by patients since there is no need to position a nasogastric tube (22). Fluoroscopic imaging is another option for assessing stenoses in the intestinal lumen. Fluoroscopy uses a contrast medium that is applied with a through-the-scope catheter during colonoscopy. Fluoroscopy gives a real-time image of the stenotic anastomosis and a possible pre-stenotic dilatation. There are no standardized scoring systems for stenoses using fluoroscopy. A radiological index would be very practical in clinical routine (Radiological Crohn*s Disease Anastomotic Index, RCDAI).

Study objective

The primary objective of this study is to evaluate whether adding intensive local anti-inflammatory therapy (Triamcinolone injection therapy combined with 9 mg oral BudenoFalk once daily for 24 weeks) to routine enteric balloon dilatation reduces the recurrence of stenosis and/or need for surgical intervention in Crohn*s disease patients with a symptomatic anastomosis.

Study design

This is a randomized, double blind, clinical trial. The study will be conducted with two arms in the form of a parallel group comparison and will serve to compare two different approaches to dilating a stenosised anastomosis in Crohn*s disease. Patients with a symptomatic stenosis will be treated.

Patients will undergo an ileocolonoscopy for mucosal assessment of the anastomosis, and radiologic assessment (MR enterography and abdominal ultrasound).
During screening colonoscopy a fluoroscopy will also be performed. The images will be compared to the images from the former EFF by an experienced radiologist together with the gastroenterological department.

Intervention

Group A:
Triamcinolone injection therapy (0,5 - 1 ml 40 mg/mL solution in four kwadrants) combined with 3 capsules (9 mg) oral BudenoFalk once daily for 20 weeks. At week 20 patients have to start tapering Budenofalk with 3 mg (1 capsule) per 2 weeks.
Group B:
Placebo injection therapy combined with 3 placebo capsules once daily for 20 weeks. At week 20 patients have to start tapering the placebo with 1 capsule per 2 weeks.

Study burden and risks

Burden for the patient:
- IBDQ and VAS score
- 7 UMU visits
- Adverse events:During treatment with drugs one can experience adverse reactions. The most reported reactions of Budenofalk are tremors, diarrhea, dermal reactions, itching, intestinal symptoms, nausea, muscle cramps and flatulance.
- Risks of procedures:
The possible risks of endoscpy are swelling of the abdomen and fainting. Seldomly other complications occur, namely damaging of the intestine possibly acquiring surgical intervention, internal bleeding, problems with the haert or bloedvessels, respiratory problems and/or infections.
The risks of an endoscopic balloon dilatation are damaging of the intestine possibly acquiring surgical intervention and internal bleeding possibly necessitating blood transfusion. .
The risks of injection of Triamcinolon in the intestinal wall are not investigated properly. Risk of damaging of the intestine possibly acquiring surgical intervention and internal bleeding should be taken into acount possibly necessitating blood transfusion.

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

• Informed consent
• Man or woman 18 years or older
• Established diagnosis of Crohn*s disease
• Negative stool culture (at screening visit, for exclusion of infectious ileocolitis and Clostridium Difficile infection)
• History of ileocecal resection
• >= 2 Symptoms of intestinal obstruction
- Intermittent abdominal pain
- Abdominal distension
- Nausea
- Vomiting
- Anorexia
• Significant stenotic segment (defined as a decrase in calibre of the intestinal lumen with or without a pre-stenotic dilatation) located at the anastomosis as diagnosed with MR enterography and transabdominal ultrasound

Exclusion criteria

• A stenotic segment of more than 5 cm
• Rutgeerts score i4 inflammation at the site of stenosis
• Fistulas at the site of stenosis or in the near proximity
• A stenosis that cannot be properly endoscopically visualized
• A significant stenosis proximal to the stenosis at the site of the anastomosis`
• The concomitant use of other oral drugs containing budesonide. A washout period of four weeks is applied.
• Pregnancy, lactation, or intended pregnancy within 9 months
• Serious secondary illnesses of an acute or chronic nature (e.g., acute cardiovascular disease, active infection)
• Known intolerance/hypersensitivity to the study drug
• Well-founded doubt about the patient*s cooperation

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	07-05-2009
Enrollment:	42
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Budenofalk
Generic name:	Budesonide

Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Kenacort
Generic name:	triamcinolonacetonide
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	18-09-2008
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	26-02-2009
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	21-10-2009
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	07-11-2011
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	10-11-2011
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	05-07-2012
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	18-07-2012
Application type:	Amendment

Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	20-02-2013
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	28-02-2013
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

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
EudraCT	EUCTR2007-005455-42-NL
CCMO	NL19976.058.08