Prevention of severe infectious complications after colorectal surgery using antimicrobial decontamination of the digestive tract

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To determine the effect of Pre-OP, in addition to perioperative intravenous antimicrobial prophylaxis on the cumulative incidence of deep surgical site infections (SSI) and/or mortality within 30 days after surgery in patients undergoing elective...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Bacterial infectious disorders
Study type	Interventional

Summary

ID

NL-OMON47368

Source
ToetsingOnline

Brief title
PreCaution

Condition

- Bacterial infectious disorders
- Gastrointestinal therapeutic procedures

Synonym
Surgical site infection, wound infection

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Antibiotic prophylaxis, Colorectal surgery, Surgical site infection

Outcome measures

Primary outcome

The primary objective is to determine the effect of Pre-OP, in addition to standard perioperative intravenous antimicrobial prophylaxis, in patients undergoing elective colorectal surgery, on the cumulative incidence of deep SSI and/or mortality within 30 days after colorectal surgery.

Secondary outcome

1. To determine the effect of Pre-OP, in addition to standard perioperative intravenous antimicrobial prophylaxis, in patients undergoing elective colorectal surgery on:

- The cumulative incidence of deep SSI within 30 days after surgery

- The all-cause mortality within 30 days after surgery

- The cumulative incidence of superficial incisional SSI within 30 days after surgery

- The cumulative incidence of anastomotic leakage

- The all-cause mortality within 6 months after surgery

- The cumulative incidence of relaparotomy within 30 days after surgery

- The cumulative incidence of bacteraemia within 30 days after surgery

- The cumulative incidence of infections within 30 days after surgery with

highly-resistant Enterobacteriaceae (HRE) or Clostridium difficile

- The presence of HRE in the intestinal flora 30 days after surgery

- The postoperative length of hospital stay, including readmissions within 6

months after surgery

- The postoperative length of ICU stay, including readmissions within 6 months

after surgery

- The in-hospital use of antibiotics within 30 days after surgery

- The in-hospital costs up to 6 months after surgery

- The quality of life up to 6 months after surgery

2. To identify risk factors for SSI and assess whether these are dependent on:

- The type of surgery (e.g. colon versus rectum)

- The use of Pre-OP (active study medication versus placebo)

Study description

Background summary

Gastrointestinal surgical procedures, including colorectal surgery, are important therapeutic interventions. They are performed approximately 40,000 times each year in the Netherlands and surgical site infections (SSI) are relatively frequent complications. The main consequences of SSI are a prolonged stay (average prolongation 10-16 days) in the hospital and increased mortality (attributable mortality 10-15%). The proposed intervention, preoperative oral antimicrobial prophylaxis (Pre-OP), is expected to prevent half of these complications at a low cost and with minimal adverse effects. If the intervention is as effective as expected the estimated benefits are huge: approximately 470 lives and ¤70 million per year, at a low cost and with hardly any side effects.
There are only few well-designed studies supporting this strategy. In addition, the few studies with a good design, combine oral antibiotics with mechanical bowel preparation. The latter has been abandoned recently because there is

evidence that it is associated with a worse outcome. In conclusion, there is no good scientific evidence supporting the use of Pre-OP. Current guidelines consider Pre-OP in addition to perioperative intravenous antimicrobial prophylaxis an unresolved issue, and, therefore, it is hardly applied at present in The Netherlands.

Study objective

To determine the effect of Pre-OP, in addition to perioperative intravenous antimicrobial prophylaxis on the cumulative incidence of deep surgical site infections (SSI) and/or mortality within 30 days after surgery in patients undergoing elective colorectal surgery.

Study design

Double blind, randomised placebo-controlled multicentre clinical trial

Intervention

Pre-OP consists of a solution (5ml) of colistin sulphate 20 mg/ml and tobramycin 16 mg/ml. The intervention starts 3 days prior to elective surgery and is administered four times daily for 3 consecutive days. The treatment ends on the night before surgery. Patients in the control group will receive a placebo solution without active ingredients, with an identical taste and colour.

Study burden and risks

The intervention consists of non-absorbable antibiotics. When administered orally, there is virtually no uptake of antibiotic components in the bloodstream. It is therefore expected that the occurrence systemic side effects is negligible. The development of antibiotic resistance might be a concern of the use of Pre-OP. Previous studies using decontamination strategies with comparable antimicrobial composition were unable to detect development of antibiotic resistance, even though the duration of treatment in these studies exceeded the timeframe of 3 days. Studies on long-term (ecological) effects of antibiotic decontamination did not detect an increase in antibiotic resistance either. Based on these previous studies we expect the risk of developing antibiotic resistance to be limited.

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

1. Adult patients (18 years of age or older)
2. Patients undergoing elective colorectal surgery.;Abovementioned patients may not meet any of the exclusion criteria

Exclusion criteria

Patients who meet one or more of the following criteria will not be eligible to participate in this study:;1. Patients younger than 18 years of age
2. Legally incapacitated patients or patients who refuse to sign informed consent.
3. Patients with an inability to take oral medication
4. Patients who have undergone abdominal surgery within 30 days before randomisation
5. Patients who have a known and documented allergy to any of the medications or agents used (i.e. colistin, tobramycin or other aminoglycoside antibiotics)
6. Patients diagnosed with myasthenia gravis
7. Pregnant women and nursing mothers
8. Patients undergoing colorectal surgery in an emergency setting (i.e. not elective)
9. Patients with a stoma

10. Patients who already participated in the PreCaution trial

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	19-04-2017
Enrollment:	966
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	niet van toepassing
Generic name:	Colistin sulphate
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	niet van toepassing
Generic name:	Tobramycin
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	27-06-2016
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	20-09-2016
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	03-01-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	26-04-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	03-05-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	14-09-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	10-04-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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: 20443
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EudraCT	EUCTR2015-005736-17-NL
CCMO	NL56697.041.16
OMON	NL-OMON20443