Human colon ischemia and reperfusion

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

Summary

ID

NL-OMON38684

Source
ToetsingOnline

Brief title
Colon IR

Condition

- Gastrointestinal inflammatory conditions

Synonym
Colon ischemia/reperfusion; 'colon infarction'

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Colon, Human, Ischemia/reperfusion

Outcome measures

Primary outcome

The primary objective of this study is to determine the pathophysiology of colonic ischemia and reperfusion in vivo in man.

Secondary outcome

* To examine cellular changes and inflammatory alterations in the human colon induced by IR.

* To study the barrier function and permeability of the human colon after IR exposure.

* To study the early macroscopic mucosal changes that occur as a consequence of colonic IR.

* To study the consequences of human colon IR on gene expression patterns.

* Identification of targets for diagnostic, preventive and therapeutic strategies.

* To determine the maximum tolerable ischemia time for the colon.

Study description

Background summary

Gastrointestinal ischemia-reperfusion (IR) remains a common, major clinical problem. Colon ischemia is the most common form of intestinal ischemia and carries high morbidity and mortality because of the high bacterial density in the intraluminal milieu and ischemia-associated intestinal barrier loss, bacterial translocation and subsequent systemic inflammatory responses. Next to that, colon ischemia is a major risk factor for anastomotic dehiscence, a serious complication with great impact on morbidity, mortality, length of hospitalization and costs. At the same time there are no optimal diagnostic tools or preventive and therapeutic strategies available, which also contributes to the high morbidity and mortality rates in patients suffering

from this condition. In contradiction to the human small intestine, hardly anything is known about colonic IR. Therefore we use a new human experimental model for colonic IR, to gain insight in the pathophysiology of colonic IR in man.

Study objective

This study aims at revealing the pathophysiology of colonic IR in man, with a specific interest for cellular and inflammatory changes, barrier function and intestinal permeability, macroscopic mucosal changes, gene expression patterns and identification of targets for diagnostic, preventive and therapeutic strategies. The information and knowledge obtained after completion of this study will be helpful in the improvement of diagnostic, preventive and therapeutic strategies in patients suffering colonic IR.

Study design

During colonic surgery a small colonic segment, to be removed for surgical reasons, is isolated and selectively subjected to 30 (30I), 45 (45I) or 60 minutes of ischemia (60I), followed by 30 (30R) and 60 minutes of reperfusion (60R). The supplying small arterial branches and draining venous structures of the specific colonic segment are identified in the mesentery and subsequently clamped to halt circulation. Release of the clamps will allow for reperfusion. In a subgroup of patients a sterile saccharide solution (sucralose and erythritol) will be injected intraluminally just before initiation of ischemia. Blood and tissue will be sampled at all time points for further analysis of intestinal permeability, barrierfunction, cellular and inflammatory changes and gene expression patterns. These analysis will be carried out by means of different techniques such as High Performance Liquid Chromotography Mass Spectrometry (HPLC-MS), immunohistochemistry, immunofluorescence, western blot, qPCR, laser capture microdissection (LCM) and subsequent genome wide expression analysis, electron microscopy and other techniques which seem to be useful during the course of the study. In another subgroup of patients a sterile video capsule will be inserted in the isolated colon segment, before applying ischemia and reperfusion. The images can be used to visualize macroscopic mucosal changes during IR.

Study burden and risks

The patients enrolled in this study will all undergo major abdominal surgery with duration of about 2-3 hours. Because IR is applied on intestinal tissue which will be resected anyway during the surgical procedure, this will not interfere with standard surgical care. The only actions undertaken by the surgeon solely related to this research proposal, are the isolation of 3-6 cm of gut, application of the clamp (followed by 30, 45 or 60 minutes of ischemia), administration of the saccharides or video capsule (just before de

start of ischemia) and blood sampling from the vein of the isolated gut segment. These actions will not add substantially to the total duration of the operation.

There are no specific benefits for the participating patients, however in the future the results of our study will likely be useful for patients suffering from intestinal ischemia and reperfusion. The additional risks for the patients in this study are minimal and they will not increase the total risk of the operation. Studies carried out in the human small intestine and colon according to a similar design show no negative effects or increased risk for the participating patients

Contacts

Public
Academisch Medisch Centrum

Universiteitssingel 50
Maastricht 6229 ER
NL
Scientific
Academisch Medisch Centrum

Universiteitssingel 50
Maastricht 6229 ER
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Adult patients (18 years of age and older) undergoing major open colonic surgery in the MUMC+ / OMC
o Right hemicolectomy
o Left hemicolectomy
o Low Anterior resection
o Hartmann*s procedure
• Patients who have given an informed consent

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
< 18 years of age
* Inflammatory Bowel Disease (IBD)
* Acute major colonic procedures
* Patients who have refused informed consent
* Laparoscopic colonic procedures

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-09-2013
Enrollment:	198
Type:	Anticipated

Ethics review

Approved WMO Date:	06-11-2013
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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
CCMO	NL42918.068.12