Expression of factors involved in bile acid metabolism throughout the gastrointestinal tract
Amendement: Expression of HIF-1alpha protein in upper GI tractus

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To obtain insights into the diverse nuclear receptors involved in the regulation of the bile acid cycle across the entire human gastrointestinal tract. Amendement:The aim of our study is to investigate the expression and amount of expression of HIF-...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Gastrointestinal signs and symptoms
Study type	Observational invasive

Summary

ID

NL-OMON33749

Source
ToetsingOnline

Brief title
GIBAM (=gastrointestinal bile acid metabolism)

Condition

- Gastrointestinal signs and symptoms

Synonym
indirect Crohn's Disease, no direct abberations are invistigated

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: bile acid, double balloon enteroscopy, GI-tract, nuclear receptor

Outcome measures

Primary outcome

To obtain insight in the expression of several nuclear receptors across the

entire human gastrointestinal tract.

Amendement: To obtain insight in the expression and amount of HIF-1 alpha in

normal tissue of upper gastrointestinal tract

Secondary outcome

Possible association between nuclear receptors and pathologic diagnosis (i.e.

Crohn*s disease)

Study description

Background summary

Disruptions of the bile acid cycle causes an accumulation or a deficit of bile acids, which may lead to a great variety of diseases of th egastrointestinal tract, including cholestatic liver disease and Barrett's esophagus [1, 2]. In this process nuclear receptors (NRs) play an essential role. They function as bile acid sensors and influence genes including enzymes and transporters of the bile acid cycle. Hereby, they change the composition of circulating bile acids as well as the toxicity and function of bile acids [1, 3].
Molecular biologic techniques have made it possible to clarify the role and function of NRs. Although the presence of these NRs in different parts of the gastrointestinal tract has been studied in murine models, in humans little is known. Recent studies in human have shown that NRs such as the Farnesoid X

receptor (FXR) and Pregnane X receptor (PXR) are associated with Barrett's esophagus and inflammatory bowel disease [4, 5]. To understand the role and function of NRs in the development of these and other disease of the gastrointestinal tract, knowledge of NRs and the genes that they influence that are involved in the regulation of bile acid metabolism in the entire human gastrointestinal tract is necessary.

Amendement: Hypoxia inducible factor 1 alpha (HIF-1 alpha) is a transcriptional factor which is induced by hypoxia. Increased concentrations of intracellular HIF-1 alpha molecules occur after hypoxia as a result of reduced degradation by the ubiquitin proteasome pathway. Binding of HIF-1 alpha to the hypoxia response element of several *HIF regulated genes* results in the increased transcription of several proteins involved in angiogenesis, glycolysis and erythropoiesis.1 The presence of HIF-1 alpha has been demonstrated in the surface epithelium of normal colon and adenomas and in areas associated with peri-necrotic areas of colon adenocarcinomas.1 In addition, HIF-1 alpha overexpression has been shown in colon of patients with ischemic colitis2, ulcerative colitis and Crohn*s disease3. Rather, until now the expression of HIF-1 alpha has not been investigated in normal tissue of upper gastrointestinal tract.

Study objective

To obtain insights into the diverse nuclear receptors involved in the regulation of the bile acid cycle across the entire human gastrointestinal tract.

Amendement:
The aim of our study is to investigate the expression and amount of expression of HIF-1 alpha in normal tissue of upper gastrointestinal tract

Study design

For this study we obtain material at eight specified locations of the gastrointestinal tract of patients (± 50), which is stored for the design of several molecular as well as immunological experiments. Herefore, we use small pieces of tissue (biopsy specimen) of patients, which are taken during standard double balloon enteroscopy at the department of Gastroenterology of the Erasmus MC University Medical Center Rotterdam. Formalin fixed biopsies that are taken standard for diagnostics will be used. This paraffin fixed materiaal serves to determine the location of the targeted bile acid factors using immunologic techniques. Also, extra biopsies will be transferred in a special buffer, encoded and stored in a -80°C freezer to, at a later moment, isolate RNA from to determine the expression levels of several bile acid genes, ie nuclear

receptors.

Amendement:
Formalin fixed biopsies that are taken standard for diagnostics will be used. This paraffin fixed materiaal serves to determine the location of HIF 1 alpha using immunologic techniques.

Study burden and risks

In general, the duration for taking the extra biopsies will be no longer than 5 min (duration of a standard DBE is 90 min). The scopy itself is a very low risk intervention (less than 1 in 3000 scopies leads to complications).

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

Subjects undergoing double balloon enteroscopy

Exclusion criteria

Uncorrected coagulopathy at moment of enteroscopy. Subjects that do not fully understand the patient information folder (p.e due to insufficient comprehension of Dutch language)

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	23-01-2008
Enrollment:	50
Type:	Actual

Ethics review

Approved WMO

Date:	06-11-2007
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL19263.078.07