Salivary pepsin for diagnosis of gastro-oesophageal reflux disease in infants (0-18 months)

Published: 20-10-2014
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To test the hypothesis that salivary pepsin is able to predict outcome of treatment in GERD suspected infants.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Gastrointestinal motility and defaecation conditions
Study type	Observational non invasive

Summary

ID

NL-OMON45027

Source
ToetsingOnline

Brief title
Salivary pepsin in infants

Condition

- Gastrointestinal motility and defaecation conditions

Synonym
gastroesophageal reflux disease, regurgitation, vomit

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Gastro esophageal reflux disease, Infants, Pepsin, Saliva

Outcome measures

Primary outcome

Primary outcome parameters:

1. Healthy controls: Salivary pepsin concentrations at day 1 to create reference values.
2. Symptomatic infants: correlation of baseline pepsin values and clinical outcome after initial conservative treatment (incl feed thickener) and (if applicable) PPI treatment.
3. Difference between salivary pepsin concentrations of healthy controls and symptomatic infants at baseline

Secondary outcome

Healthy controls:

Day to day variability between samples taken at day 1 and day 2.

Symptomatic infants:

1.Salivary pepsin concentrations after conservative treatment and feed thickeners compared to baseline and compared between responders/non responders

2.For non responders: salivary pepsin concentration after subsequent proton pump inhibitor treatment compared to baseline and after-conservative treatment pepsin levels.

3.Correlation between pH-MII parameters (below) and pepsin saliva

concentrations at baseline, after initial standard treatment and after 4 weeks PPI treatment.

a. Reflux index (% of the time the esophageal pH is < 4)

b. Symptom association probability (SAP): Calculation of the statistical relationship between symptoms and reflux episodes using Fisher*s exact test

c. Symptom index (SI): the percentage of symptom events that are temporally related to a reflux event. Defined as: (Number of reflux associated symptoms /Total number of symptoms) ×100%

d. Symptom sensitivity index (SSI): the percentage of reflux events that are temporally related to a symptom. Defined as: (Number of symptom associated reflux episodes/Total number of reflux episodes) ×100%

Study description

Background summary

Gastro-esophageal reflux is the involuntary movement of gastric contents into the esophagus and is referred to as GER disease (GERD) when causing troublesome symptoms and/or complications. GERD is common in infants with a prevalence of >12% in the western population. To prevent over- as well as under diagnosis and treatment of infant GERD, there is a clear need to distinguish mild GER related symptoms from pathological GERD in this large group of patients. Currently, the international guidelines propose combined pH and multichannel intraluminal impedance (pH-MII) as a diagnostic tool to assess GERD. However, normal values are lacking and it is unclear how the results of this test relate to treatment outcome. Salivary pepsin measurement has been shown a specific marker for GERD in adults and is a simple, non invasive test. The additional diagnostic and predictive value of pepsin measurement in saliva of symptomatic infants is unknown.

Study objective

To test the hypothesis that salivary pepsin is able to predict outcome of treatment in GERD suspected infants.

Study design

1. Cross sectional study in healthy control infants
2. Prospective outcome study in infants with GERD

Protocol:
1.Saliva samples from healthy controls will be collected one hour after a feed on two consecutive days (day 1 and day 2, min 2 max 5 samples per day).
2.Saliva samples from symptomatic infants will be collected one hour after a feed (min 2 max 5 samples per day) at presentation and after two weeks of standard conservative treatment including feed thickeners. If the infants do not respond to this therapy, a pH-MII is performed followed by a 4 weeks trial of proton pump inhibitor (PPI) treatment and a saliva samples will be taken a last time after PPI treatment.

Definitions gastro esophageal reflux disease and response
Asymptomatic: initial score on I-GERQ-R questionnaire <16 points and no troublesome signs and symptoms of GER as reported by parents or physician
Symptomatic: initial score on I-GERQ-R questionnaire >=16 points and reported troublesome signs and symptoms of GER as by parents and judged physician

Response:
A. No response: I-GERQ-R above symptomatic score (>=16 points) and no significant improvement (delta <5) in symptom score compared to baseline.
B. Partial response (partial treatment effect): I-GERQ-R above symptomatic score (>=16 points) but WITH significant improvement (delta >=5) in symptom score compared to baseline
OR
I-GERQ-R drops below symptomatic score (<16 points) but WITHOUT significant improvement (delta >=5) in symptom score compared to baseline .
C. Complete response (cured): I-GERQ-R drops below symptomatic score (<16) AND a significant improvement of symptom score compared to baseline .
Group A & B will be considered non responders and taken to the next phase of the study

Study burden and risks

Sampling saliva for pepsin measurement is a non invasive possible new diagnostic tool for GERD in infants. The saliva is collected via a blunt, disposable transfer pipet that is placed under the tongue and is completely harmless to the infant. Therefore, burden and risks associated with participation are estimated minimal. All diagnostic and treatment approaches in this study are according to current guidelines for suspected GERD in infants.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

Healthy controls
- Informed consent signed by caregiver(s)
- >=34wks gestational age- 24 months postnatal age
- Negative score in I-GERQ-R questionnaire (<16);Symptomatic infants
- Informed consent signed by caregiver(s)
- >=34wks GA - 18 months PNA
- Attending either a general pediatric outpatient clinic or specific pediatric gastroenterology department for gastro esophageal reflux related symptoms
- Positive score on I-GERQ-R questionnaire (>=16 points)

Exclusion criteria

Valid for both healthy subjects and symptomatic infants:
- Known structural gastro-intestinal abnormalities
- Previous gastro-intestinal surgery
- Neurological syndromes and development disorders
- Any condition that would make it unsafe for the subject to participate determined by the treating physician.
- Use of anti gastro esophageal reflux medications (prokinetics, erythromycin, proton pump inhibitors, H2 receptor antagonists, antacida) in the last 5 days before inclusion.

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	23-02-2015
Enrollment:	150
Type:	Actual

Ethics review

Approved WMO

Date:	20-10-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC

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
Other	4578
CCMO	NL49655.018.14