A randomised, open label, placebo controlled exploratory study in healthy volunteers, to characterise the acid neutralisation activity of sodium alginate oral suspension in the fasted state, using a custom-designed intragastric and oesophageal pH catheter

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The objective of this exploratory study is to investigate the acid neutralisation action of sodium alginate oral suspension versus placebo liquid, within the stomach and to assess suitability and robustness of the pH monitoring methodology.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON41075

Source
ToetsingOnline

Brief title
Acid neutralisation exploratory pH monitoring study

Condition

- Other condition

Synonym
gastric acid reflux, heartburn

Health condition

GORD

Research involving
Human

Sponsors and support

Primary sponsor: Reckitt Benckiser Healthcare (UK) Ltd
Source(s) of monetary or material Support: Reckitt Benckiser Healthcare (UK);Ltd

Intervention

Keyword: acid neutralisation, healthy volunteers, placebo controlled, randomised

Outcome measures

Primary outcome

The primary endpoint will be the mean percentage of time that pH >= 4 over 0-30 minutes post-dose across electrodes 3 to 10. The primary analysis will be the comparison of this endpoint between Sodium alginate oral suspension versus placebo liquid.

Secondary outcome

• The mean percentage of time that pH >= 4 over the interval 30-60 minutes post-dose across electrodes 3 to 10.

• The mean percentage of time that pH >= 3 over the intervals 0-30 minutes and 30-60 minutes post-dose across electrodes 3 to 10.

• The mean percentage of time that pH >= 3 and pH >= 4 over the 10 minute intervals post-dose across electrodes 3 to 10.

• The percentage of time that pH >= 3 and pH >= 4 over the 10 minute and 30 minute intervals at each electrode.

These endpoints will be compared between Sodium alginate oral suspension and placebo. For calcium carbonate / magnesium carbonate chewable tablets, these endpoints will be assessed non-comparatively.

For all treatments, the following will be displayed non-comparatively:

• The pH level at each 4 second time point during each monitoring period at each electrode.

Study description

Background summary

This exploratory study is being conducted to characterise the acid neutralisation activity of Sodium alginate oral suspension versus a liquid placebo, in order to confirm robustness of the methodology being used and to develop appropriate endpoints for a future confirmatory study.
In addition, to confirm that the methodology is suitable, a small cohort of subjects will receive a single maximum dose of calcium carbonate / magnesium carbonate chewable tablets (two tablets). The results from this cohort will be used to confirm robustness of the methodology in order to enable preparations for a further exploratory study in Sodium alginate tablets.

The effects of acid neutralisation can be observed in a healthy stomach, therefore, to minimise risk to patients, healthy volunteers of both genders will be used. Previous research within this field has successfully demonstrated the effects of acid neutralisation in vivo. To align with previous research and reduce variablility caused by the post prandial gastric buffering effect, a fasted stomach will be investigated in this study. A single, maximum dose of Investigational Medicinal Product (IMP) should be sufficient to demonstrate the antacid activity of the product and therefore only a single maximum dose will be given in the study. Subjects will be randomised to receive either liquid or tablet, they will not receive both medications.

The liquid cohort of the study uses a cross-over design to minimise an individual*s variation in stomach response, so each subject of this group will receive in a randomised order 20 mL Sodium alginate oral suspension or 20 mL placebo liquid in each treatment period. The tablet cohort will only receive 2 calcium carbonate / magnesium carbonate chewable tablets orally. These routes

of administration and dosages are approved in the summary of product characteristics (SmPC).

This study will use a custom-designed CE marked catheter that has been specifically designed and made for this study, containing 10 pH electrodes. This catheter will measure pH from 5 cm above to 16 cm below the Squamocolumnar Junction (SCJ).

Study objective

The objective of this exploratory study is to investigate the acid neutralisation action of sodium alginate oral suspension versus placebo liquid, within the stomach and to assess suitability and robustness of the pH monitoring methodology.

Study design

There will be two groups in this study.

Group I will be a randomised, crossover, open label, single-dose, placebo controlled study, to characterise the antacid activity of Sodium alginate oral suspension (20 mL) in healthy volunteers, using a custom-designed intragastric and oesophageal pH catheter. Subjects and clinic staff will remain open label to medications administered, with the consultant gastroenterologist blinded to medication allocation, in order to be unbiased when assessing catheter positioning during pH recording periods.

In addition, a separate, small cohort of subjects (Group II) will be used to assess the suitability of the pH monitoring methodology. These subjects will receive a single maximum dose of calcium carbonate / magnesium carbonate chewable tablets (2 tablets) and will undergo the same pH monitoring procedures as subjects of Group I.

Sodium Alginate Oral Suspension Cohort (Group I)
Subjects will attend the clinic for four visits (one screening, two dosing and one follow up visit). There will be a minimum 5 days and a maximum 14 days washout period between dosing in the two treatment visits. The follow up will be performed 3-7 days after the second dosing day.

Calcium Carbonate / Magnesium Carbonate Chewable Tablet Cohort (Group II)
As there will be no cross-over element to this part of the study subjects will only attend the clinic for three visits (one screening, one dosing and one follow up visit). The follow up will be performed 3-7 days after the dosing day.

Intervention

The study will start with a screening visit. During the screening visit standard medical assessments including safety laboratory tests (blood draw, urine collection), an alcohol breath test, urine drug screen, a physical examination and a vital signs measurement will be performed.

After the subject passes all above mentioned tests, the subject will be enrolled in the study.

During study the subjects will enter the clinic and will receive 1 or 2 medication formulations (pending enrollment group 1 or 2), subjects will be asked on a regular basis for possible side effects and the vital signs will be checked on a regular basis.

On day 1 of each period a pH catheter (a thin flexible tube containing sensors to measure the acidity in the stomach) will be inserted. in addition an endoscopy will performed confirming correction positioning of the catheter. Movement of the subject is restricted during the pH monitoring procedure.

Finally a follow-up examination will be performed. During this visit the subjects will be asked for possible side effects, blood will be drawn for safety, the vital signs will be checked and a physical examination will be performed.

Study burden and risks

There have been side effects reported with the study medications. The side-effects that are reported and are possibly related to administration of sodium alginate or calcium carbonate products include allergic manifestations such as urticaria (hives), bronchospasm (difficulty in breathing), angioedema (swelling of the skin), abdominal pain/discomfort, pruritus rash (itchy skin), diarrhoea, nausea, vomiting, an allergic-like reaction and acute very severe allergic reactions in the whole body as a result of hypersensitivity to any of the active substances (sodium alginate, sodium bicarbonate and calcium carbonate) or to any of the excipients (e.g. hydroxybenzoates). Other side effects include muscular weakness, hypermagnesaemia (increased levels of magnesium in the blood), hypercalcaemia (increased calcium levels in the blood), alkalosis (disturbance in acidity in the body), acid rebound or constipation. Furthermore, milk alkali syndrome (excessive calcium amount in blood) can cause ageusia (loss of taste functions of the tongue), headache, azotemia (an increase in urea or creatinine in the blood), asthenia (weakness) and calcinosis (formation of calcium deposits in soft tissue).

The risks are limited in healthy participants, but you may experience one of the above mentioned side-effects or other symptoms not previously reported. To keep the risks as low as possible, your health will be closely monitored during the trial to minimize these risks.

In total, two blood samples will be drawn. The total blood volume will be 16 mL. The blood collection procedure is not dangerous, but may cause discomfort or bruising. Occasionally, fainting or an infection at the blood sampling site can occur.

The nasal endoscopy and catheter insertion procedures are not painful. In general, it is described as an uncomfortable feeling. During the procedure there is a small risk to develop bleeding and perforation of the oesophagus, stomach or duodenum. In addition, reactions to drugs administered as part of the procedure can occur, for example to the local anaesthetics. The risk of one of these side-effects to occur is considered to be low, as the insertion of the catheter can be verified visually by a small camera.

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) Informed consent has been obtained.
2) Age: >= 18 years <= 50 years.
3) Sex: male or female subjects.
4) Status: healthy subjects.
5) Body Mass Index (BMI): >= 18.5 and <= 24.9

Exclusion criteria

1) A history of gastro-oesophageal reflux or active gastrointestinal disease (gastroduodenal ulcer, gastrointestinal haemorrhage, mechanical obstruction or perforation) within the last year.
2) Clinically significant allergic, pulmonary, neurological, renal, hepatic, cardiovascular, psychiatric, metabolic, endocrine, or haematological disease.
3) A history of basal skull fracture or who have undergone trans-sphenoidal surgery.
4) Have been hospitalised within the previous three months for major surgery or medical illness.
5) A clinically significant illness within the 4 weeks prior to screening.
6) Have taken any prescription medication or non-prescription medication within the last seven days, prior to the screening visit, which the Principal Investigator considers may interfere with the study.
7) Have taken antacids, H2 antagonists, motility stimulants (e.g. prokinetics, macrolide antibiotics such as erythromycin and azithromycin, and 5HT agonists such as sumatriptan) or other medicines for relief of symptoms of acid reflux disease 2 weeks prior to enrolment in the study and during the study and/or have taken proton pump inhibitors 4 weeks prior to enrolment into the study and during the study. Enrolment is defined as the date of informed consent signature.
8) Are taking any of the following medications: antihistamines, tetracyclines, digoxin, fluoroquinolone, iron salt, neuroleptics, thyroxine, penicillamine, beta-blockers (atenolol, metoprolol, propranolol), glucocorticoid, chloroquine, and biphosphonates.
9) Have a drug hypersensitivity, which in the opinion of the Principal Investigator might interfere with the study.
10) Any previous history of allergy or known intolerance to any of the Investigational Medicinal Product*s (IMP) or following formulation constituents: e.g. sodium alginate, parabens (methyl and propyl), glucose syrup, carbomer, and xanthan gum
11) Those with known hypophosphataemia.
12) Those on a highly restricted salt diet.
13) Those with, or a history of, hypercalcaemia, nephrocalcinosis and recurrent calcium containing renal calculi.
14) A current or recent (within one year) history of alcohol abuse or significant abuse of any legal or illegal drugs, substances and solvents.
15) Regularly (weekly) consume excessive amounts of alcohol (> 8 units for men and > 6 units for women in one consumption, excessive amounts as defined by the UK National Office

of Statistics).
16) Have consumed more than 2 units of alcohol per day in the 7 days prior to the screening visit.
17) Regular consumption of excessive quantities of caffeine (> 6 cups of tea, coffee or cola per day), according to the Investigator*s judgement.
18) Tobacco use is > 6 cigarettes per day or equivalent or unable to refrain from tobacco/ nicotine use during the study periods.
19) Any clinically significant abnormal laboratory result, in the opinion of the Principal Investigator.
20) Female subjects of childbearing potential who, for the duration of the study, are either unwilling or unable to take adequate contraceptive precautions (as defined in the protocol or are unwilling to be sexually abstinent (as defined in the protocol).
21) Pregnancy or lactating mother.
22) Are unable to communicate well with the Investigator (i.e. language problem, poor mental development or impaired cerebral function) in the opinion of the Investigator.
23) Those previously randomised into this study.
24) Employee at study site.
25) Partner or first-degree relative of the Investigator.
26) Participation in a clinical study in the previous 3 months.
27) Those unable in the opinion of the Investigator to comply fully with the study requirements.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Placebo
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	10-10-2014
Enrollment:	24

Type:	Actual

Medical products/devices used

Generic name:	pH catheter
Registration:	Yes - CE intended use
Product type:	Medicine
Brand name:	Gaviscon Double Action Liquid Sachets
Generic name:	-
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Rennie Chewable Tablets
Generic name:	-
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	28-08-2014
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
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Application type:	First submission
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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	EUCTR2014-003158-15-NL
CCMO	NL50419.056.14