The effect of a gastric bypass surgery on the absorption of acetylsalicylic acid and omeprazole after ingestion.

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON26757

Source
Nationaal Trial Register

Brief title
ERY-PAO study

Health condition

Roux-en-Y gastric bypass surgery (RYGB)

Sponsors and support

Primary sponsor: Department of Hospital Pharmacy
Medical Centre Haaglanden
Source(s) of monetary or material Support: Investigator initiated research.
Financial contribution by 'Wetenschapsfonds' of Medical Centre Haaglanden, Central Hospital Pharmacy the Hague and Dutch Obesity Clinic West.

Intervention

Outcome measures

Primary outcome

The primary study parameters are drug blood concentrations on the selected test days and times: 0 (before intake of the drugs), 30 minutes after intake, 1 hour, 2 hours and 4 hours after intake. With these concentrations the following pharmacokinetic parameters will be determined: Time to peak concentration (Tmax), peak concentration (Cmax), area under the curve (AUC), and half-life (t ½) of salicylic acid and omeprazole.

Secondary outcome

No secondary study parameters are defined.

Study description

Background summary

Rationale:

Roux-en-Y Bariatric (RYGB) surgery is asuccessful approach to morbid obesity. In this procedure, the stomach is reducedto a small 'gastric pouch'. The duodenum is bypassed by connecting the jejunumthis gastric pouch. The duodenum is then connected to a later part of thejejunum to ensure the passage of bile salts and pancreatic enzymes.

After oral intake, food and drugs firstpass the created gastric pouch before passing directly into the shortenedjejunum. Literature shows that this results in problems regarding vitamin andnutrient absorption. In contrast, little literature is available on theabsorption of orally administered drugs. The available literature consistsmainly of case reports or small studies. Several authors have tried to build amodel in which the change in absorption after RYGB surgery can be predicted,unfortunately without success. As there is no model available for predictingchanges in drug absorption after the surgery, research is necessary for drugs frequentlyused in this population.

We investigated the medication use of 115 patients in our center to obtain insight into the types of medicationfrequently used by this group of patients. Results showed that aspirin andomeprazole are two commonly used drugs.

In order to prevent arterial thromboticdisease in high-risk patients such as our population, treatment withacetylsalicylic acid is commonly prescribed for life-long use. A dosage of75-150 mg is proven to be an efficient dose in preventing mortality, myocardialinfarction or stroke.

This is not proven for a dose of less than 75 mg per day,except for stroke. Acetylsalicylic acid is mainly absorbed in the acidicenvironment of the stomach and partly in the duodenum. Changes in pH andgastric volume after RYGB surgery could affect the extent of absorption of ASA.Until now, no data are available on absorption of ASA in RYGB surgery patients.Reduced absorption of aspirin could have long term implications for theeffectiveness in the prevention of thromboembolic events and death. For thisreason, it is important to investigate the impact of RYGB surgery on theabsorption of acetylsalicylic acid. We hypothesize that the absorption ofacetylsalicylic acid after oral administration will be reduced by RYGB surgery.

As a proton pump inhibitor, omeprazoleinhibits the production of stomach acid, resulting in a less acidic stomach. Omeprazoleis prescribed after RYGB operation in a dosage of 20 mg twice daily to reducethe chance of development of anastomotic ulcerations and leakage. Omeprazole isan acid labile substance and is therefore always administered with an entericcoating. After passing the stomach this coating dissolves and omeprazole israpidly absorbed in the small intestine. Due to a higher pH in the stomachafter RYGB surgery, the enteric coating around the tablet can disappear fasterand omeprazole could be more rapidly absorbed. An in vitro experiment indeedshowed an accelerated uptake of omeprazole after the procedure, with no effecton the overall absorption of omeprazole. It is of great importance that theabsorption of omeprazole is sufficient to prevent complications after RYGBsurgery. For this reason we want to confirm previous results and investigatethe influence of RYGB surgery on the absorption of omeprazole in this study Wehypothesize that the absorption of omeprazole after oral administration will befaster but equivalent after RYGB surgery.

Objective:

The primary objective of the ERY-PAOstudy is to investigate the pharmacokinetics of acetylsalicylic acid (ASA) and omeprazolein morbidly obese subjects before and after RYGB surgery and to compare thesedata to study if there aredifferences in pharmacokinetics due to thisprocedure.

Study design:

Single centre, longitudinal open labelrepeated measures study.

Study population:

The study population will consist ofmorbidly obese subjects approved by the Dutch Obesity Clinic (NOK) West to undergo RYGB surgery. Approximately 350patients per year are approved for this surgery. Approximately 80% of the patientsapproved for surgery are female; mean age is 40 to 45 years. Patients aremostly of Caucasian, Hindu or African ethnicity. The study group consist ofhighly motivated study subjects. In order to get approved for surgery a longtrajectory, including guidance in diet, physical exercise and psychosocialcounselling has been completed.

Intervention:

The subjects will be asked to takeomeprazole 20 mg for a total duration of 2 weeks (day 1 * 14) before the RYGB surgery. After surgery, administration of omeprazole 20 mg twice daily is standard carefor the duration of 6 months. In addition, the subjects will be asked to take asingle dose of ASA 80 mg on 2 ‘test’ days: day 7 of omeprazole treatment beforesurgery, and day 7 of study medication omeprazole treatment after RYGB surgery.Test days will be planned at least 2 weeks before and 6 weeks after thesurgery. During the intervention periods, the subjects will be asked to fillout a medication diary to check adherence.

Primary studyparameters/outcome of the study:

The primary study parameters are drugblood concentrations on the selected test days and times: 0 (before intake of thedrugs), 30 minutes after intake, 1 hour, 2 hours and 4 hours after intake. Withthese concentrations the following pharmacokinetic parameters will be determined:Time to peak concentration (Tmax), peak concentration (Cmax), area under thecurve (AUC), and half-life (t ½) of salicylic acid and omeprazole.

Study objective

Roux-en-Y Bariatric (RYGB) surgery is a successful approach to morbid obesity. In this procedure, the stomach is reduced to a small 'gastric pouch' . The duodenum is bypassed by connecting the jejunum this gastric pouch. The duodenum is then connected to a later part of the jejunum to ensure the passage of bile salts and pancreatic enzymes. After oral intake, food and drugs first pass the created gastric pouch before passing directly into the shortened jejunum. Literature shows that this results in problems regarding vitamin and nutrient

absorption. In contrast, little literature is available on the absorption of orally administered drugs. The available literature consists mainly of case reports or small studies. Several authors have tried to build a model in which the change in absorption after RYGB surgery can be predicted, unfortunately without success. As there is no model available for predicting changes in drug absorption after the surgery, research is necessary for drugs frequently used in this population. We investigated the medication use of 115 patients in our center to obtain insight into the types of medication frequently used by this group of patients. Results showed that aspirin and omeprazole are two commonly used drugs. In order to prevent arterial thrombotic disease in high-risk patients such as our population, treatment with acetylsalicylic acid is commonly prescribed for life-long use. A dosage of 75-150 mg is proven to be an efficient dose in preventing mortality, myocardial infarction or stroke. This is not proven for a dose of less than 75 mg per day, except for stroke. Acetylsalicylic acid is mainly absorbed in the acidic environment of the stomach and partly in the duodenum. Changes in pH and gastric volume after RYGB surgery could affect the extent of absorption of ASA. Until now, no data are available on absorption of ASA in RYGB surgery patients. Reduced absorption of aspirin could have long term implications for the effectiveness in the prevention of thromboembolic events and death. For this reason, it is important to investigate the impact of RYGB on the absorption of acetylsalicylic acid. We hypothesize that the absorption of acetylsalicylic acid after oral administration will be reduced by RYGB surgery. As a proton pump inhibitor, omeprazole inhibits the production of stomach acid, resulting in a less acidic stomach. Omeprazole is prescribed after RYGB operation in a dosage of 20 mg twice daily to reduce the chance of development of anastomotic ulcerations and leakage. Omeprazole is an acid labile substance and is therefore always administered with an enteric coating. After passing the stomach this coating dissolves and omeprazole is rapidly absorbed in the small intestine. Due to a higher pH in the stomach after RYGB surgery, the enteric coating around the tablet can disappear faster and omeprazole could be more rapidly absorbed. An in vitro experiment indeed showed an accelerated uptake of omeprazole after the procedure, with no effect on the overall absorption of omeprazole. It is of great importance that the absorption of omeprazole is sufficient to prevent complications after RYGB surgery. For this reason we want to confirm previous results and investigate the influence of RYGB surgery on the absorption of omeprazole in this study We hypothesize that the absorption of omeprazole after oral administration will be faster but equivalent after RYGB surgery.

Study design

Test days will be mostly clustered and will take place before and after the surgery.

Blood sampling will be solely for study purposes and will be done on test day 1 and 2 in intervals during a period of 4 hours. Volumes of 4 ml are required for every analysis on drug concentrations. For genotyping, one sample with a volume of 7 ml is required.

In total, this results in 27 ml blood sample on test day 1 and 20 ml blood sample on test day 2.
Blood sampling will be done by venapunction on the designated test times by qualified health care professionals. Body length will be registered at inclusion. Determination of body weight and body fat percentage is part of the regular pre and aftercare for RYGB surgery. For the study the most recently measured weight and fat percentage compared with the test day will

be registered. Subjects will be asked to fill out a diary during the intervention periods to assess adherence to the study medication and use of other medication.

Intervention

The subjects will be asked to take omeprazole 20 mg for a total duration of 2 weeks (day 1 – 14) before the RYGB surgery. After surgery, administration of omeprazole 20 mg twice daily is standard care for the duration of 6 months. In addition, the subjects will be asked to take a single dose of ASA 80 mg on 2 ‘test’ days: day 7 of omeprazole treatment before surgery, and day 7 of study medication omeprazole treatment after RYGB surgery. Test days will be planned at least 2 weeks before and 6 weeks after the surgery. During the intervention periods, the subjects will be asked to fill out a medication diary to check adherence.

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Eligibility criteria

Inclusion criteria

1. Male or female aged between 18 and 65 years at the time of informed consent;

2. Written informed consent;

3. Scheduled to undergo RYGB surgery and approved to undergo this procedure according to the inclusion criteria of NOK West (Dutch Obesity Clinic West);

4. Ability to swallow whole medication tablets.

Exclusion criteria

1. Ulceration or leakage of the anastomosis post-surgery, to be determined 6 weeks after the RYGB surgery by the surgeon. This is an exclusion criterium for the second testday, to be determined during the study) - ‘Redo’ patients: patients previously treated for morbid obesity with a gastric sleeve or gastric banding;

2. Contra-indication to use ASA or omeprazole, e.g. known or suspected allergy;

3. Present use or use of drugs within 4 times the half-life of that drug before the start of the study that might interfere with the metabolism of the investigational drugs (inducers/inhibitors of CYP2C19);

4. Concurrent disease or increased risk of bleeding which may compromise safety of the administration of the study medication (e.g. Von Willebrands disease) according to the judgement of the investigator;

5. Gastro-intestinal disorders which may impair drug absorption (e.g. Crohn's disease or previous stomach or bowel surgery) according to the judgement of the investigator;

6. Treatment with any unlicensed drug during the previous month.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-05-2013
Enrollment:	40

Type:	Anticipated

Ethics review

Positive opinion Date:	07-04-2013
Application type:	First submission

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
NTR-new	NL3774
NTR-old	NTR3939
Other	METC Zuidwest Holland : 13-011
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
N/A