The effect of Roux-en-Y gastric bypass surgery in morbidly obese patients on Pharmacokinetics of (Acetyl)salicylic acid and Omeprazole.

Published: 06-02-2013
Last updated: 24-04-2024

The primary objective of the ERY-PAO study is to investigate the pharmacokinetics of acetylsalicylic acid (ASA) and omeprazole in morbidly obese subjects before and after RYGB surgery and to compare these data to study if there are differences in...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Gastrointestinal therapeutic procedures
Study type	Interventional

Summary

ID

NL-OMON39934

Source
ToetsingOnline

Brief title
ERY-PAO

Condition

- Gastrointestinal therapeutic procedures

Synonym
gastric bypass surgery, Roux-en-Y gastric bypass surgery

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Centrum Haaglanden

Source(s) of monetary or material Support: Het onderzoek betreft een investigator initiated onderzoek. Financiering zal plaatsvinden door bijdragen van de Nederlande Obesitas Kliniek West;Apotheek Haagse Ziekenhuizen en het Wetenschapsfonds van Medisch Centrum Haaglanden (aanvraag in behandeling)

Intervention

Keyword: Aspirin, Gastric Bypass, Omeprazole, Pharmacokinetics

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

*) of salicylic acid and omeprazole.

Secondary outcome

No secundary study parameters are defined.

Study description

Background summary

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 objective

The primary objective of the ERY-PAO study is to investigate the pharmacokinetics of acetylsalicylic acid (ASA) and omeprazole in morbidly obese subjects before and after RYGB surgery and to compare these data to study if

there are differences in pharmacokinetics due to this procedure.

Study design

Single centre, longitudinal open label repeated measures study.

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.

Study burden and risks

The medicinal intervention will gain no direct benefit for the study subjects. However, the results of the study will definitely be beneficial to the study subjects. Available information on oral absorption of medication after RYGB surgery is limited. Most study subjects will be relatively young, but already eligible to use multiple drugs. When they get older even more medicines, possibly including ASA and omeprazole, will be prescribed to patients who underwent RYGB surgery.
Any information about the oral uptake of drugs can provide new insights on how to treat these patients in a safe and effective way. For omeprazole, administration during 6 months is standard care for the study subjects. The results of the ERY-PAO study will determine whether this standard care is sufficient and, if necessary, standard protocols can be adapted for future patients.

ASA has been used in clinical practice since 1899. The most important side effect of low dose ASA is stomach ache. Complications can include gastro-intestinal bleeding or ulceration. The absolute risk of upper gastro-intestinal complications in low dose ASA use is approximately 2 to 3 per 1000 person-years (51). The relative risk of high gastro-intestinal bleeding in low dose ASA use varies between 1,4 and 5,3 (52). In order to prevent these complications, co-administration of a proton pump inhibitor is recommended (52;53). This reduces the relative risk for gastro- intestinal bleeding in low dose ASA users from 3,8 [2,8-5,2] to 1,1 [0,5-2,6]. In the ERY-PAO study, 2 single doses of ASA will be administered in combination with a proton pump inhibitor. Hence, for our subjects, there will be no extra risk of stomach complications.

Another potential risk for ASA use is a prolonged bleeding time. This effect will continue during the life time of the thrombocyte, so one week after discontinuation of ASA 90% of the thrombocytes will have normal function (55). Hence, it is recommended to discontinue use of ASA a week before some surgeries (56). In cardiac patients undergoing RYGB surgery, continuation of ASA 80 mg proved to be safe for use until the day of the surgery (57). In the ERY-PAO study, administration of a single dose of ASA will be given at least two weeks before the RYGB surgery and at least 6 weeks after the surgery to rule out a prolonged bleeding time due to ASA during surgery.

For omeprazole, no serious side effects have been described since the regular use of this drug in clinical practice (since 1988). Common side effects include nausea, flatulence and diarrhea

Contacts

Public
Medisch Centrum Haaglanden

Lijnbaan 32
Den Haag 2512 VA
NL
Scientific
Medisch Centrum Haaglanden

Lijnbaan 32
Den Haag 2512 VA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Male or female aged between 18 and 65 years at the time of informed consent.
- Written informed consent
- Scheduled to undergo RYGB surgery and approved to undergo this procedure according to the inclusion criteria of NOK West (Dutch Obesity Clinic West)
- Ability to swallow whole medication tablets

Exclusion criteria

- 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.
- Contra-indication to use ASA or omeprazole, e.g. known or suspected allergy
- 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)
- 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.
- 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.
- Treatment with any unlicensed drug during the previous month.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	06-08-2013

Enrollment:	40
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Acetylsalicylic acid
Generic name:	Acetylsalicylic acid
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Losec
Generic name:	Omeprazole
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	06-02-2013
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	27-03-2013
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	EUCTR2012-005387-10-NL
CCMO	NL42835.098.13