Exploratory research into the effect of temporarily withdrawal of PPIs (Proton Pump Inhibitor) use, to reduce the stomach wall uptake of 99mTc-Sestamibi in a myocardial perfusion imaging

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4.1 The main questionWhat is the effect of temporarily stopping PPI use on the stomach wall uptake of Tc99m Sestamibi with a myocardial perfusion?4.2 Sub-questions:- What is the relative maagwanduptake a myocardial perfusion Tc99m Sestamibi with...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Myocardial disorders
Study type	Interventional

Summary

ID

NL-OMON42879

Source
ToetsingOnline

Brief title
The effect of shortterm withdrawal of PPI for myocardial perfusion imaging.

Condition

- Myocardial disorders
- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
cardiac research, myocardial perfusionscintigraphy

Research involving
Human

Sponsors and support

Primary sponsor: Rijnstate Ziekenhuis
Source(s) of monetary or material Support: niet van toepassing

Intervention

Keyword: 99mTc Sestamibi, Myocardial perfusion imaging, Proton Pump Inhibitor, Stomach wall

Outcome measures

Primary outcome

9.1 Quantitative data collection

Of each participant, the sex, age, height, weight, BMI and noted the breast size. The breast size is measured prior to the first study. Measured horizontally over the body over the largest parts of the breast in centimeters (cm). The breast size may have an influence on the detector - organ distance. Deviations in the quality and measurements can be thus explained. The quantitative data collection is carried out by means of placing ROIs. ROI's are placed by the operator on project planar images of the heart and stomach wall ROIs are with a size of 6 pixels placed, by means of the reconstruction computer, on the images from the raw data. To answer the main question of the relationship between maagwanduptake and myocarduptake to be determined. To the stomach wall, and the entire myocardium inferiorwand be able to assess best be used in the non-attenuation-corrected images, ROIs drawn. Specifically, on the left anterior oblique (LAO), slice 17, and the anterior recording, slice 33. Slice 17 and slice 33 are images to which the stomach wall to quantify is the best (21). Slice on 17 and 33 is for the entire heart also signed an ROI. If the stomach wall exhibits a higher uptake than the inferiorwand, the counts per

pixel in the inferiorwand are averaged, whereby the uptake of the actual inferiorwand may vary with the reality. By drawing an ROI in inferiorwand can be accurately determined whether stopping PPIs, affecting the uptake of inferiorwand. There calculate two ratios:

- Entire myocardium - stomach ratio
- Inferior wall of the myocardium - stomach wall ratio

From the slice 17 and 33 are calculated throughout the heart rate and stomach inferiorwand-stomach ratio. Of these two directions is calculated an average value of each ROI (21). The result is set forth in counts per pixel. To convert the result in counts per pixel calculation must be performed in relative activity. First, the actual administered activity of the radiopharmaceutical is determined. The administered activity is displayed in the application of research. If the investigation should not be carried out at the appointed time be performed Activity calculation for the decay in time.

The decay formula, the current dose is calculated: At = A0 x 0.5 ^ (t / HVT)

At = activity in MBq at start acquisition

A0 = activity in MBq at calibration time (indicated on sticker application form)

t = time difference in hours between the calibration time and start acquisition

HVT = the half-life of 99m technetium (6.0 hours) (43).

By dividing the result of the dose calculated by the body weight of the participant and counts per pixel is determined, the relative uptake in MBq / kg per counts / pixel. The relative uptake shows the measured relative uptake in the stomach wall, or the entire myocardium to inferiorwand.

The collected data is processed by the project executor in the validated data

management research manager system (DMRM) V 5.12.1.0. the Rijnstate hospital. For any publication data processing required in a validated database. Then the data from DMRM is exported and imported into IBM statistical Package for the Social Sciences (SPSS) version 23.0. SPSS is tested with the DMRM may not.

9.2 Visual data collection

The myocardial images are assessed by two nuclear medicine on the basis of a brief questionnaire. Using the questionnaire, the visual assessment of the level. After post-processing, patients in the PACS system in a separate folder automatically anonymous computer. On this anonymous data to find the visual assessment instead. The project supervisor fills the assigned anonymous names filled in the questionnaire. Because the evaluating nuclear medicine physicians do not know which participants PPIs have they may be regarded as blind continued or phased external readers. The questionnaire in Annex 5 aims to determine the ability to assess the inferiorwand of the myocardium. Another object of the questionnaire is to examine whether re-acquisition is necessary. The answers to the questionnaires are processed by the project executor in DMRM and SPSS.

9.4 Randomization and blinding

Blinding of participants for the nuclear medicine has the advantage of assessing the nuclear medicine as external blind readers. This increases the reliability of the examination. Patients are randomly by the investigator to the nuclear medicine submitted for review.

During this study is de-blinding will take place only in emergencies. A de-blinding can be done by the principal investigator, just in case: medical or

safety reasons.

9.5 Research pause or stop

Patients can take at any time waive the study without consequences or statements. The principal investigator is still often exclude patients after inclusion for a medical emergency.

Secondary outcome

The results of the qualitative measurements and the visual feedback of the participants in I.G. 1,compared with the results of the qualitative measurements and the visual feedback of the participants in I.G. 2. A similar comparison is applied at I.G. 1 in respect to C. G. 3. The outcome is to demonstrate or difference is present in maagwanduptake when PPI use is discontinued or continued. The outcome is unity expressed relative uptake in MBq / kg counts per pixel for the qualitative measurement. The outcome measure for the visual evaluation or re-acquisition is necessary.

The normal distribution is assessed by means of histograms. In a normal distribution of the quantitative results of the intervention groups are yellow with each other and tested with the unpaired t test. When the distribution is not normal, the Mann-Whitney U test offers an alternative. In all statistical analyzes a P *0.05 is considered to be statistically significant. With a p-value can be shown, or a difference in discontinuation or continuation of PPIs and the results are not coincidental if p is *0.05.

When the visual data is evaluated using histograms on a normal data distribution. To demonstrate consistency or independence of the subjective

image quality is tested using the chi-square test. The responses of the nuclear medicine are tested to demonstrate a statistically significant difference. The outcome of the Chi-square (X2)) is an absolute number. With the Chi-square test you can prove or selected values are based on chance or that a difference actually exists. The intraclass correlation coefficient (ICC) test, is tested to what extent the nuclear medicine match rate. The ICC values between 0 and 1, where 1 represents maximum agreement. An ICC value of 0.7 or higher is considered satisfactory agreement.

Study description

Background summary

In 2014, 5308 patients died in the Netherlands from a myocardial infarction (1). The mortality ratio is 55% male and 45% female (1). Atherosclerosis in the coronary arteries reduce blood flow to the heart (2). A total closure of the coronary artery can lead to a stroke (3-8). A result of a perfusion disorder is ischemia; oxygen deficiency of the underlying myocardial cells (8). The sooner diagnosed, the lower the mortality rate, and the higher is the life expectancy (9). In nuclear medicine, is diagnosed with the help of a myocardial perfusion scintigraphy (MPS), perfusion disorders.
The MPS visuals the myocardium, through the myocardial SPECT technique (3 to 8.10). The purpose of SPECT is the creation of cross-sections and 3-D images of the distribution of the administered radiopharmaceutical taken on a series of static images around the patient (11,12). During the investigation, multiple images from multiple directions with the gamma camera that rotates around the patient. (11). In addition to the images that have come into position by means of the myocardial SPECT technique can be carried out with the aid of an additional study a CT attenuation correction (attenuation correction) for the myocardial SPECT technique (13). The purpose of the attenuation correction is to correct for distance between the organs and the detector so as to give a real uptake of radioactive agent again. This reduces the sensitivity and specificity higher and perfusion disorders can be better visualized (13.14) .The myocardperfusieonderzoek has diagnostic value, with a sensitivity between 77% and 95%, and specificity between 78% and 83% is achievable (6 , 7,10,15-17).
The MPS consists of a research in stress and rest. To diagnose a stroke or ischemia, the images from the stress and rest were compared (11). An infarction

is characterized if the deviation is visible in the research effort and peace research (11). An ischemia is characterized if the deviation by stress testing is visible but not (11) at rest. For MPS is a radionuclide Technetium 99metastabiel (99mTc) Sestamibi tracer coupled specific to an organ. A radionuclide that is linked is referred to a radiopharmaceutical tracer (11).
For stress effort is maximum effort necessary for maximum uptake of the radiopharmaceutical. At maximum effort, deviations mapped optimally. With the aid of a cycling test or drug administration with the agents adenosine or regadenoson, the maximum effort of the myocardium is obtained. There is no difference detected in diagnostic value, if adenosine or regadenoson is used. (18-20). Approximately 1.2-1.5% of the administered dose of 99mTc-Sestamibi is taken up by the myocardium (11).

Not all of the radiopharmaceutical 99m Tc Sestamibi is incorporated into the myocardium, in addition, is also recording (uptake) of radiopharmaceutical in other parts of the body present. This is called external cardiac uptake and is often visible in organs below the diaphragm and liver, duodenum, gall bladder, intestines and stomach (21-27).
Extracardiac uptake may cause scattered radiation (scatter) and overlap, and change the uptake in the myocardium. (21,24,25,27-32). Extracardiac uptake can contribute to a bias in the distribution of the radiopharmaceutical, mainly in the inferiorwand myocardial (22,23,26,27,33,34). As a result, it becomes more difficult to assess the inferiorwand. It may seem that the inferiorwand shows perfusion disturbances, while the actual situation otherwise occur (33,34). A too high extra cardiac uptake can lead to a poor rating of the inferior wall, so that re-acquisition is required (21 to 23.34).
When a reduction of the additional cardiac uptake, the inferiorwand can be better assessed from milk and drinking water have an impact in order to reduce the interfering additional cardiac uptake (16-18,20-22,24,26-29). Milk stimulates peristalsis of the intestines and stimulates the liver for excretion of radiopharmaceuticals. Water reduces activity in the stomach because the stomach acid is diluted (21,23,25,26,31). The reduction of additional cardiac uptake by milk and water, is insufficient to be able to assess the myocardium well. It is clear from previous studies that the taking of stomach protective drugs also called proton pump inhibitors mentioned (PPIs), leads to an increased uptake of the radiopharmaceutical in the stomach wall (22,25,29,31). Patients who suffer from include heartburn, stomach problems encounter, dyspepsia have, or will use pain relief funds eligible to use proton pump inhibitors. PPI use reduced stomach acid (36.37) .Patiënten use PPIs chronic (> 90 days) or preventive (<90 days) (38).

The chronic use of pain control agents, the so-called non-steroidal anti-inflammatory drug (NSAID), the chronic use of PPIs often has the effect of (36-38). Chronic PPI users are excluded because risk of reflux symptoms, inflammation, heartburn and side effects are greater if this group of patients stopped using PPIs (37.38). Patients taking PPIs preventive use less risk of complications, because the PPI prevention is used. (37,38). When PPI users stop

immediately, often occur reflux disease, inflammation and heartburn at (36,38). This would limit participation in the study. When PPIs are stopped with a reduction schedules, enter reflux and heartburn symptoms less rapidly (36). Or the temporary stop of PPIs also leads to a better assessment MPS, is at this time still unknown.
Previous research has shown that the use of PPIs affects the stomach wall uptake (29,31) Both studies show if patients use PPI, this leads to an increased maagwanduptake. Rijnstate hospital in Arnhem would like to investigate the effect on stomach wall activity at MPS, as PPI use is discontinued in patients taking preventive PPIs. A valid assessment leads to less re-acquisitions and probably improve patient care. In this study answers the question: What is the effect of temporarily stopping PPI use on the stomach wall uptake of 99m Tc-Sestamibi in a myocardial perfusion imaging?

Study objective

4.1 The main question

What is the effect of temporarily stopping PPI use on the stomach wall uptake of Tc99m Sestamibi with a myocardial perfusion?

4.2 Sub-questions:

- What is the relative maagwanduptake a myocardial perfusion Tc99m Sestamibi with exertion Be it peace studies, in patients who have stopped taking PPIs, compared with patients who continue with PPIs?
- How stopping PPIs may affect the image quality and the ability to assess a myocardial perfusion

4.3 Hypothesis

It is expected that the temporary cessation of PPIs for myocardial perfusion imaging shows an equivalent image in patients not taking PPIs.

Study design

The study is a prospective quantitative research. Participants must give permission by signing an informed consent, can be found in Annex 4 to take part in the study. Participants will temporarily stop the use of PPI through the reduction schedule of the pharmacy. Examples of common PPIs are: Omeprazole, Esomeprazole and Pantoprazole. Annex One is a detailed overview of different properties and forms of administration by PPI. Reducing the PPIs take about two to three days (39). The cardiologist select patients taking PPIs and get a MPS.

In nuclear medicine is being investigated by the project promoter, or patients using chronic or preventive PPIs. With the aid of the following in and

exclusion criteria, patients are screened and selected. Selected patients will be contacted by telephone. To maintain overview to potential participants, just by lead investigator Dr. Schelfhout, a colleague or project executor contacted. In case participation is additional information, the reduction schedule, and the informed enclosed with the appointment confirmation. The secretariat will send two to three weeks prior to the survey by mail appointment confirmations. One week prior to the study, a second telephone consultation location. This consultation will be clarified ambiguities. A cooling-off period of at least one week is guaranteed in this way.

Because a MPS consists of a research effort and rest, participants will be placed in the intervention groups, schematic representation in Figure 1. In total, gives rise to three intervention groups:
I. G. 1: strike stress Research - continue rest Research
I. G. 2: continue stress Research - rest Research strike
I. G. 3: continue stress Research - continue rest Research
Intervention Group 3 continues with PPI use in both studies and forms the control group. Intervention group 3 from now control called abbreviated C. G.

By comparing two efforts or peace studies together, it can be shown, or a difference in gastric wall uptake exists when PPIs are discontinued or continued. Also, different data can be easily traced and corrected. The following groups are for both stress and rest were compared:

I. G. 1 - I.G. 2
I. G. 1 - C.G. 3
I. G. 2 - C.G. 3

With the aid of the control group it can be shown that the results are not due to chance. By comparing each intervention group with the control group taking PPI use is unchanged, it is shown that the effect occurred not due to chance. In Rijnstate hospital in Arnhem, the stress test will be examined first and one to four days later the rest research (11). This study will I.G. 1 as the rest research be carried out first, and from one to four days later, the stress test. In this way, the informed consent can be delivered / signed at the first examination. At that time, no reduction of PPIs yet occurred.

Intervention

-

Study burden and risks

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Contacts

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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Patients with a cardiology reference indication for myocardial perfusion imaging.
- Patients older than 18 years.
- Patients wherein for the myocardial perfusion preformed with etheir adenosine or regadenoson
- Patients taking preventive less than 90 days using PPIs
- Patients who have signed an informed consent.
- Patients in which the scan was performed on the scanner BrightView 1 in Nucleare department Rijnstate Arnhem.
- Patients who have no defects at the myocardal inferiorwall.

Exclusion criteria

- Patients with dyspepsia
- Patients with only uptake in the stomach cavity, thus no reliable measurement can be done and no visually assesment can be reliable preformed.
- Patients who are not prepared and tested according to the protocols
- Patients with the following well-known diseases, Zollinger Ellison Syndrome, a barrettoesofagus or a esophagitis with endoscopic grade C or D
- Patients partially been injectjet or underskin injection, no maximum uptake of radiopharmaceutical is can be reached.
- Patients that use medications that interact with PPIs.
- Patients with gastric resection or surgically treated for stomach problems.
- Patients with gastric ulcer prophylaxis.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)

Primary purpose: Diagnostic

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	60
Type:	Anticipated

Ethics review

Approved WMO Date:	27-06-2016
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Approved WMO

Date:	04-07-2016
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	26-01-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	EUCTR2016-001383-10-NL
CCMO	NL57340.091.16