Proton Pump Inhibitor Induced Hypomagnesemia

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Malabsorption conditions
Study type	Observational invasive

Summary

ID

NL-OMON35945

Source
ToetsingOnline

Brief title
PPI induced hypomagnesemia

Condition

- Malabsorption conditions

Synonym
hypomagnesemia, low magnesium level

Research involving
Human

Sponsors and support

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

Intervention

Keyword: hypomagnesemia, magnesium, Omeprazole, PPI

Outcome measures

Primary outcome

(a) Primary blood variable: Serum magnesium in clot- or haparin-blood.

Measurement via calorimetric xylidyl blue method (Roche).

- a value < 0.65 mmol/l is considered to be hypomagnesemia

- a value between 0.66-0.84 mmol/l is considered to be normomagnesemia

- a value > 0.84 mmol/l is considered to be hypermagnesemia

(b) Genetic analysis:

This analysis is a "whole genome SNP array". Possible variations in the SNiPs may be unveiled by a comparison with a standard database. A limit value that identifies a variation to be significant is dependent on the analysis method.In general correlation peaks with a hight > 0.5 indicate possible interesting areas of the genome and may be closer investigated in further in vitro or in vivio models.

The SNP analysis will be performed as soon as a number of hypomagnesemic PPI users are identified.

Secondary outcome

(a) Secondary blood variabele: Serum calcium in clot- or heparin-blood

- a value < 1,83 mmol/L is considered to be hypocalcemia

- a value 1,83-2,31 mmol/L is considered to be normocalcemia

- a value > 2,31 mmol/L is hypercalcemia

Study description

Background summary

(a) Relevancy
At least 2 million people in the Dutch population make use of gastric acid blockers (PPI's) on a regular basis. PPIs are the first line treatment drug for gastric acid related diseases in human. These diseases include dyspepsia, inflammatory processes in esophagus, stomach and duodenum, and chronic diseases like Morbus Cron and others.

(b) Mode of action of PPI's
PPIs are potent and specific inhibitors of the gastric H-K-ATPase which is centrally involved in gastric acid production. All known PPIs (a group of related molecules) form inhibitory complexes with the H-K-ATPase. This complex formation results in the restriction proton secretion into the lumen of the stomach and a concomitant raise in pH. This change in pH is the desired effect that supports the treatment of priorly mentioned diseases.
The use of PPI's is considered to be safe. PPI's have a low toxicity and the rate and severeness of adverse reactions in general is low. These facts contributed to the release of PPI's for retail marketing without need for prescription by the physician.

(c) Subject
However, this study investigates on a rather rare but in some cases severe adverse effect of PPI usage. In the literature several cases (± 30) of PPI induced hypomagnesemia are discribed. In these cases there was a causative link between the hypomagnesmic status of the patient and the intake of PPIs. These patients more or less show common symptoms of a severe ion imbalance. The hypomagnesemia is often accompanied by hypocalcemia and hypokalemia. The combination of these is responsible for the symptoms seen in affected persons, like severe arrythemia of the heart and other neuromuscular pathies.

(d) Causes
The exact molecular and physiological causes of PPI induced hypomagnesemia still are not known. However, it can be assumed that this type of hypomagnesamia develops due to malabsorbtion of magnesium in the intestinal tract. This assumption is supported by the fact, that in the case reports the affected individuals do not show any renal leakage of magnesium.

Study objective

The knowledge on PPI induced hypomagnesemia is restricted. For that reason, this study has two key objectives which investigate on the frequency and the causes of PPI induced hypomagnesemia:

1. The investigation of the prevalence of PPI induced hypomagnesemia.
- This is an important factor for the estimation of the clinical relevance of this deviation.

2. A genetical screening of patients with PPI induced hypomagnesemia.
- This is important part to facilitate the generation of new knowledge on the aetiology of the deviation and for gaining insight in possibly unknown regulatory mechanisms of the magnesium homeostasis.

Study design

This study is of exploratory character and can be divided into two steps (a+b):

(a) Selection of participants
All potential participants is are recruited from regular visitors of the departments internal medicine UMC St Radboud and the CWZ (Canisius Wilhelmina-Ziekenhuis) Nijmegen. The participants with dyspepsia and PPI use are the target group for this selection, because of having a restricted amount of comorbidity. This is important to rule out disease parameters that might interfere with serum magnesium.

(b) Measurements
Selected participants that signed the informed consent agreement will undergo a bimodal blood screening with a single vena puncture. Two different blood samples will be collected.
1. One sample clot-blood or heparin-blood of approximately 5 ml volume.
- This sample is used to determine the serum magnesium concentration (and eventually also serum calcium). This analysis is performed to identify hypomagnesemic individuals and give an indication for the prevalence within the complete study population.
2. One sample EDTA blood of approximately 10 ml volume.
- This sample is intended for the whole genome SNP array. This is performed to identify a possible genetic variation that may make individuals prone to the development of PPI induced hypomagnesemia.

(c) Usage of proton pump inhibitors
At patient visit the following information will be collect over the patient's useage op the PPI's:
- The name and the doage of the durg.
- The frequency of PPI intake.
- The total period/history of PPI use.

Study burden and risks

The cumulative risk or burden that the participants undergo is low.

(a) Aim is it to work within a regular blood-withdrawal to prevent unnecessary vena puntures.
(b) However the participant admits an vena puncture for only for the benefit of the study if the participant would not undergo an otherwise indicated puncture. De risk of a single vena puncture and the withdrawal of a small amount of blood (approximately 15 ml) can be reasonably considered to be very small. There is a 5% chance of a fully reversible haematome resulting from the vena puncture.
(c) All blood sampling is performed in clinical context by professionally trained and experienced personnel from the daily practice.
(d) This study has the chance to gain new scientific knowledge on a possibly relevant subject within the healthcare of human. Considering the minimal burden for the participant it can be reasonably argued that this study in this sense is justified.

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

Usage of gastric acid blockers of the class of PPI's (Proton Pump Inhibitors).
These are mainly the group of the so called "Dyspepsia" patients.

Exclusion criteria

(a) Short bowel patients are excluded, because they have a malabsorptional status of their intestinal tract.
(b) Individuals with known alcoholism, because alcohol abuse can produce hypomagnesemia.
(c) Individuals with: Unregulated diabetes mellitus, syndrome of Gitelman, syndrome of Bartter, anemia, strong adipositas or strong anorexia.
(d) For a more exact list please refer to the study protocol

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	15-03-2012
Enrollment:	200
Type:	Actual

Ethics review

Approved WMO Date:	07-10-2011
Application type:	First submission
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
CCMO	NL37289.091.11