Inulin * a potential preventive dietary supplement against PPI induced hypomagnesemia

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Objective: The primary objective is to determine if the dietary fructan-fiber inulin is applicable in PPIH. More specific, it aims to (i) improve the magnesium balance in cases of hypomagnesemic PPI users and (ii) to evaluate if the use of inulin is...

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

Summary

ID

NL-OMON38331

Source
ToetsingOnline

Brief title
Inulin rescue trial

Condition

- Malabsorption conditions
- Electrolyte and fluid balance conditions

Synonym
hypomagnesemia, magnesium shortage, PPI induced hypomagmagnesemia

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, Inulin, PPI, PPIH

Outcome measures

Primary outcome

Main study parameters/endpoints: Main study parameter is serum Mg2+. PPI*s exert their negative effect on serum Mg2+ in brisk manner and is influenced by the overall Mg2+ status of the patient. Mg2+ depleted individuals react to PPI-challenge within 4-5 days and gradually develop hypomagnesemia (serum Mg2+ < 0.7mmol/L). (6) Serum Mg2+ is measured twice in one two weeks (first trial period at t=0d and t=14d, subsequently at t=28d, t=42d and t=56). t=0d gives the start value and t=14d the end value (for the first trial period).

The primary endpoint is defined in two ways: First if the end value at t=14d is 20% reduced compared to start value at t=0d or, second, if the end value drops to 0.55 mmol/L. The latter is important to prevent symptomatic hypomagnesemia and to initiate appropriate supplementation (not expected). Vice versa, hypomagnesemia (defined as serum Mg2+ > 1.1mmol) is second endpoint because it can be indicative for renal failure or the use of antacids. (7)

Moreover, severe adverse reactions within trial periods irrespective of origin will lead to immediate stop of intervention or alternative treatment.

Secondary outcome

na

Study description

Background summary

Rationale: Proton pump inhibitors (PPI*s) are used by millions of patients. They are the mainstay of choice for several gastric acid related diseases like GERD, peptic ulcers and H. Pylori eradication. PPIs have an excellent safety profile, however, since 2006 case reports started to emerge that describe some patients that develop symptomatic hypomagnesemia due to PPI use (Proton pump inhibitor induced hypomagnesemia * PPIH). This led to an increase in clinical attention to PPIH and the understanding about the epidemiology and contributing risk-factors is improving. Data from an ongoing study (not published) shows that the actual prevalence of hypomagnesemia in PPI-using outpatients is 12% showing that there is a considerable proportion of patients at risk. Moreover, polymorphisms present in the magnesium transporter TRPM6 (transient receptor potential 6) increased the chance of PPI users to develop hypomagnesemia by 4 times. It is anticipated that PPIH is caused by the intestinal malabsorption of Mg2+, but the exact molecular mechanism is speculative. There is some evidence that PPI*s induce a raise of the pH in the large intestine. This reduces the fraction of ionized Mg2+ available for uptake by the magnesium transporting channel TRPM6 which is apically expressed in the colon, the final intestinal segment absorbing Mg2+.

Study objective

Objective: The primary objective is to determine if the dietary fructan-fiber inulin is applicable in PPIH. More specific, it aims to (i) improve the magnesium balance in cases of hypomagnesemic PPI users and (ii) to evaluate if the use of inulin is accompanied with any unwanted side-effects.

Study design

Study design: This is an observational study that will follow patient serum Mg2+ values over a period of 57 days. In the study period a number of 4 individual n=1 trials will be conducted with a duration of 14 days each (2 x trial period with PPI + inulin AND 2 x trial period with PPI only). Each trial period follows the last suit without a lag phase (please refer to figures 1a + b).

Study burden and risks

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: Patients will be addressed individually and informed about this study. Patients will receive the written information on the inulin trial and in individual interviews the background and procedures will be explained. Patients willing to participate, need to sign the standard common consent form which is included as part of this study protocol.
Burdens:

First: Participants will need to visit the Radboudumc for intake and blood-withdrawal over a period of 57 days (figures 1a & 1b). The frequency is 2 times in the first 15 days (at t=0d and at t=14d). Each subsequent trial follows the preceding directly and blood is sampled then subsequently at t=28d, t=42d t=56). In total the patient will need to visit the Radboudumc 5 times for blood sampling (if indicated or wanted patients can also donate blood at their native place/physician to prevent unnecessary travels). Additionally, patients will be asked to collect 24 hrs urine for Mg2+ and Ca2+ measures. Collected urine can be delivered at blood sampling or can be sent. Serum Mg2+ surveillance is a prerequisite to join and stay in this study.

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

The use of PPIs (protonpump inhibitors, type omeprazol) and having hypomagnesemia as defined by serum Mg2+ < 0.7 mmol/L.

Exclusion criteria

Unstable health conditions, patients that have stopped the PPI, acutely ill patients.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-01-2014
Enrollment:	22
Type:	Anticipated

Ethics review

Approved WMO

Date:	27-02-2014
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	NL47262.091.13