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INTERACCIONES FÁRMACO-ALIMENTO

Mar Blanco Rogel

Julio 2021

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INTERACCIONES

FÁRMACO- ALIMENTO/NUTRIENTE

MALDIGESTIÓN/MALABSORCIÓN

INTERACCIÓN INTRALUMINAL FC-NUTRIENTE	**SOLUBILIZACIÓN** Aceite mineral **QUELACIÓN** Tetraciclinas **PRECIPITACIÓN** Antiácidos	 Vitaminas liposolubles Calcio, magnesio Fosfato
ALTERACIÓN DE LOS MECANISMOS DE ABSORCIÓN DEL NUTRIENTE	Biguanidas	Vitamina B12 Folatos
ENTEROPATÍA INDUCIDA POR FC	Neomicina Colchicina Antineoplásicos	Malabsorción de grasas y vit liposolubles. Malabsorción de lactosa Vit B12 y electrolitos

MALDIGESTIÓN/MALABSORCIÓN

ALTERACIÓN DE LA FISIOLOGÍA DEL TRACTO DIGESTIVO	**ACELERACIÓN DEL TRÁNSITO** Laxantes Procinéticos	Malabsorción de vit liposolubles, calcio, electrolitos
	MODIFICACIONES DEL pH Anti H2 Antiprotones Antiácidos	Malabsorción de hierro, calcio, folatos, vit B12, tiamina
	ALTERACIÓN DE LA FUNCIÓN PANCREÁTICA Neomicina Orlistat	Malabsorción de grasas, vit liposolubles y calcio
	ALTERACIÓN DE LAS SALES BILIARES Colestiramina	Malabsorción de grasas, vit liposolubles y calcio
	ALTERACIÓN DE LA FLORA Antibióticos	↓ prod vit K y biotina Diarrea, intolerancia a la lactosa

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INHIBIDORES DE LA BOMBA DE PROTONES

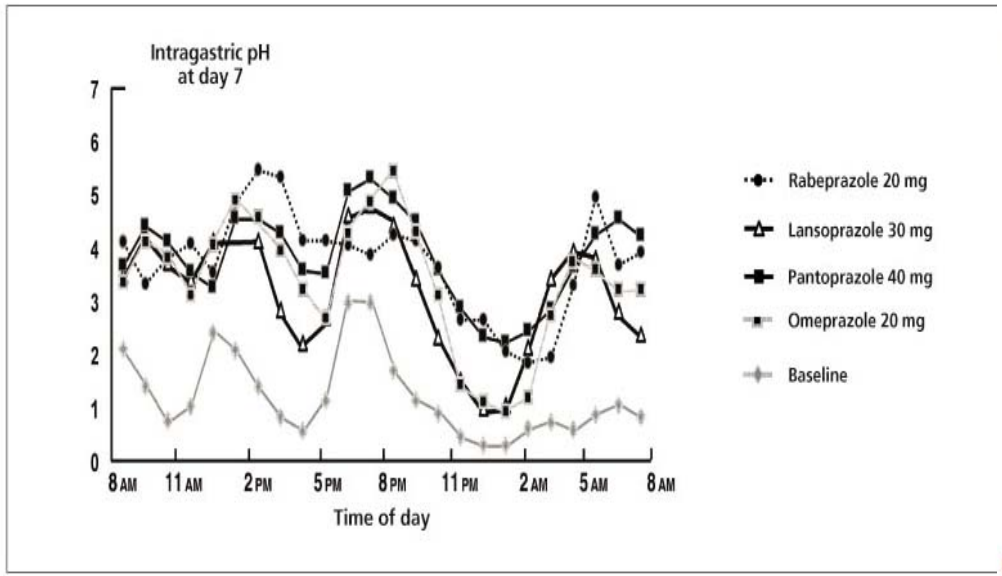
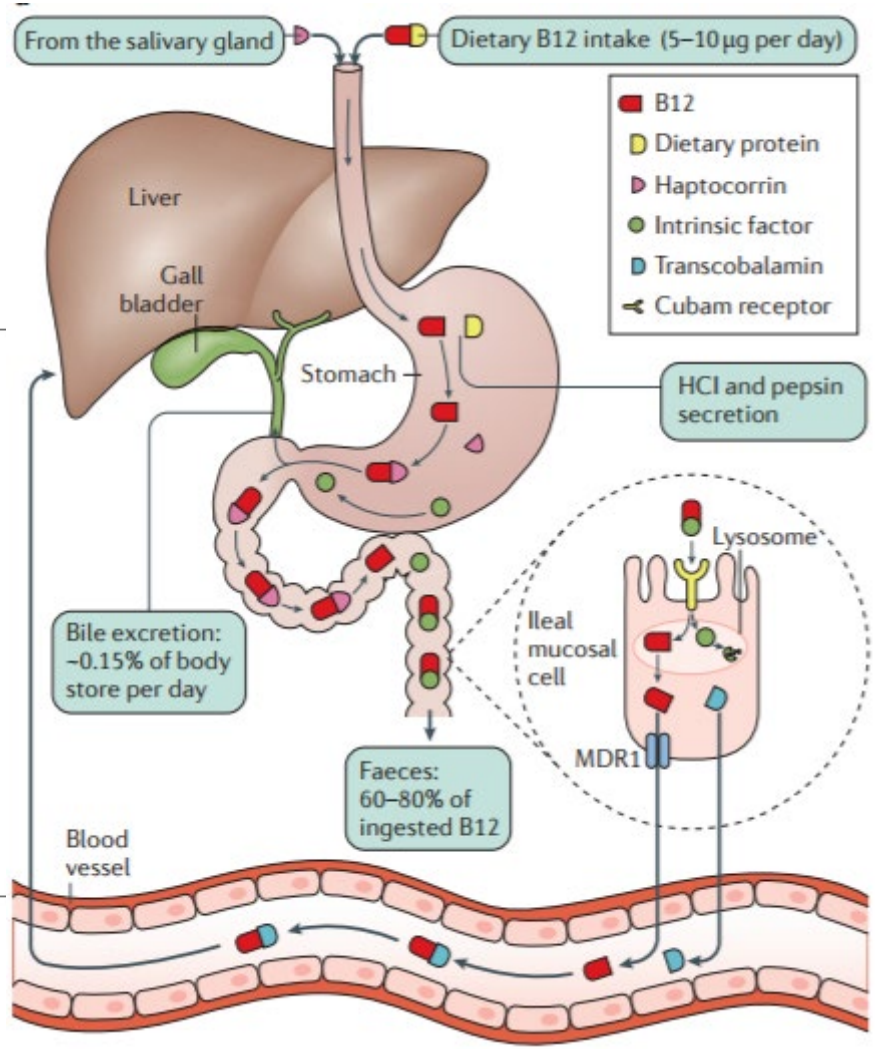


Fig. 1. Comparison of the intragastric pH profile of different PPIs. Mean 24-h intragastric pH with 4 PPIs *versus* baseline (49).



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INHIBIDORES DE LA BOMBA DE PROTONES

↓

CALCIO, HIERRO, B12, MAGNESIO….

↓

OSTEOPOROSIS, FRACTURAS, ANEMIA, INFECCIONES BACTERIANAS, DEMENCIA ….

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JAMA. 2013 Dec 11;310(22):2435-42. doi: 10.1001/jama.2013.280490.

Proton pump inhibitor and histamine 2 receptor antagonist use and vitamin B12 deficiency.

Lam JR[1], Schneider JL, Zhao W, Corley DA.

Author information

Abstract

IMPORTANCE: Proton pump inhibitors (PPIs) and histamine 2 receptor antagonists (H2RAs) suppress the production of gastric acid and thus may lead to malabsorption of vitamin B12. However, few data exist regarding the associations between long-term exposure to these medications and vitamin B12 deficiency in large population-based studies.

OBJECTIVE: To study the association between use of PPIs and H2RAs and vitamin B12 deficiency in a community-based setting in the United States.

DESIGN, SETTING, AND PATIENTS: We evaluated the association between vitamin B12 deficiency and prior use of acid-suppressing medication using a case-control study within the Kaiser Permanente Northern California population. We compared 25,956 patients having incident diagnoses of vitamin B12 deficiency between January 1997 and June 2011 with 184,199 patients without B12 deficiency. Exposures and outcomes were ascertained via electronic pharmacy, laboratory, and diagnostic databases.

MAIN OUTCOMES AND MEASURES: Risk of vitamin B12 deficiency was estimated using odds ratios (ORs) from conditional logistic regression.

RESULTS: Among patients with incident diagnoses of vitamin B12 deficiency, 3120 (12.0%) were dispensed a 2 or more years' supply of PPIs, 1087 (4.2%) were dispensed a 2 or more years' supply of H2RAs (without any PPI use), and 21,749 (83.8%) had not received prescriptions for either PPIs or H2RAs. Among patients without vitamin B12 deficiency, 13,210 (7.2%) were dispensed a 2 or more years' supply of PPIs, 5897 (3.2%) were dispensed a 2 or more years' supply of H2RAs (without any PPI use), and 165,092 (89.6%) had not received prescriptions for either PPIs or H2RAs. Both a 2 or more years' supply of PPIs (OR, 1.65 [95% CI, 1.58-1.73]) and a 2 or more years' supply of H2RAs (OR, 1.25 [95% CI, 1.17-1.34]) were associated with an increased risk for vitamin B12 deficiency. Doses more than 1.5 PPI pills/d were more strongly associated with vitamin B12 deficiency (OR, 1.95 [95% CI, 1.77-2.15]) than were doses less than 0.75 pills/d (OR, 1.63 [95% CI, 1.48-1.78]; P = .007 for interaction).

CONCLUSIONS AND RELEVANCE: Previous and current gastric acid inhibitor use was significantly associated with the presence of vitamin B12 deficiency. These findings should be considered when balancing the risks and benefits of using these medications.

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J Bone Miner Res. 2014 May 13. doi: 10.1002/jbmr.2279. [Epub ahead of print]

Long-Term Proton Pump Inhibitor Therapy and Falls and Fractures in Elderly Women: A Prospective Cohort Study.

Lewis JR[1], Barre D, Zhu K, Ivey KL, Lim EM, Hughes J, Prince RL.

Author information

Abstract

Proton pump inhibitors (PPIs) are widely used in the elderly. Recent studies have suggested that long-term PPI therapy is associated with fractures in the elderly however the mechanism remains unknown. We investigated the association between long-term PPI therapy ≥ 1 year and fracture risk factors including bone structure, falls and balance related function in a post hoc analysis of a longitudinal population-based prospective cohort of elderly postmenopausal women and replicated the findings in a second prospective study of falling in elderly postmenopausal women. Long-term PPI therapy was associated with increased risk of falls and fracture-related hospitalizations; adjusted odds ratio (AOR) 2.17; 95% CI, 1.25-3.77; P = 0.006 and 1.95; 95% CI, 1.20-3.16; P = 0.007 respectively. In the replication study, long-term PPI use was associated with an increased risk of self-reported falling; AOR, 1.51; 95% CI, 1.00-2.27; P = 0.049. No association of long-term PPI therapy with bone structure was observed; however questionnaire-assessed falls-associated metrics such as limiting outdoor activity (P = 0.002) and indoor activity (P = 0.001) due to fear of falling, dizziness (P < 0.001) and numbness of feet (P = 0.017) and objective clinical measurement such as Timed Up and Go (P = 0.002) and Romberg eyes closed (P = 0.025) tests were all significantly impaired in long-term PPI users. Long-term PPI users were also more likely to have low vitamin B12 levels than non-users (50% vs. 21%, P = 0.003). In conclusion, similar to previous studies, we identified an increased fracture risk in subjects on long-term PPI therapy. This increase in fracture risk in elderly women, already at high risk of falling, appears to be mediated via increased falls risk and falling rather than impaired bone structure and should be carefully considered when prescribing long-term PPI therapy.

World J Nephrol. 2012 Dec 6;1(6):151-4. doi: 10.5527/wjn.v1.i6.151.

Proton pump inhibitor-induced hypomagnesemia: A new challenge.

Florentin M[1], Elisaf MS.

Author information

Abstract

Proton pump inhibitors (PPIs) are commonly used in clinical practice for the prevention and treatment of peptic ulcer, gastritis, esophagitis and gastroesophageal reflux. Hypomagnesemia has recently been recognized as a side effect of PPIs. Low magnesium levels may cause symptoms from several systems, some of which being potentially serious, such as tetany, seizures and arrhythmias. It seems that PPIs affect the gastrointestinal absorption of magnesium. Clinicians should be vigilant in order to timely consider and prevent or reverse hypomagnesemia in patients who take PPIs, especially if they are prone to this electrolyte disorder.

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RENAL FAILURE

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Ren Fail, Early Online: 1–5
 DOI: 10.3109/0886022X.2015.1057800

informa
healthcare

BRIEF REPORT

Proton pump inhibitors linked to hypomagnesemia: a systematic review and meta-analysis of observational studies

Wisit Cheungpasitporn[1], Charat Thongprayoon[1], Wonngarm Kittanamongkolchai[1], Narat Srivali[2], Peter J. Edmonds[3], Patompong Ungprasert[4], Oisin A. O'Corragain[5], Sira Korpaisarn[6], and Stephen B. Erickson[1]

[1]Division of Nephrology and Hypertension, Mayo Clinic, Rochester, MN, USA, [2]Division of Pulmonary and Critical Care Medicine, Mayo Clinic, Rochester, MN, USA, [3]Department of Medicine, SUNY Upstate Medical University, Syracuse, NY, USA, [4]Division of Rheumatology, Mayo Clinic, Rochester, MN, USA, [5]Department of Medicine, University College Cork, Cork, Ireland, and [6]Department of Medicine, MetroWest Medical Center, Framingham, MA, USA

Abstract

Background: The reported risk of hypomagnesemia in patients with proton pump inhibitor (PPI) use is conflicting. The objective of this meta-analysis was to assess the association between the use of PPIs and the risk of hypomagnesemia. *Methods*: A literature search of observational studies was performed using MEDLINE, EMBASE and Cochrane Database of Systematic Reviews from inception through September 2014. Studies that reported odd ratios or hazard ratios comparing the risk of hypomagnesemia in patients with PPI use were included. Pooled risk ratios (RRs) and 95% confidence interval (CI) were calculated using a random-effect, generic inverse variance method. *Results*: Nine observational studies (three cohort studies, five cross-sectional studies and a case-control study) with a total of 109,798 patients were identified and included in the data analysis. The pooled RR of hypomagnesemia in patients with PPI use was 1.43 (95% CI, 1.08–1.88). The association between the use of PPIs and hypomagnesemia remained significant after the sensitivity analysis including only studies with high quality score (Newcastle–Ottawa scale score $\geq$ 8) with a pooled RR of 1.63 (95% CI, 1.14–2.23). *Conclusions*: Our study demonstrates a statistically significant increased risk of hypomagnesemia in patients with PPI use. The finding of this meta-analysis of observational studies suggests that PPI use is associated with hypomagnesemia and may impact clinical management of patients who are taking PPIs and at risk for hypomagnesemia related cardiovascular events.

Keywords

Electrolyte, hypomagnesemia, magnesium, meta-analysis, proton pump inhibitors

History

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Published online 25 June 2015

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MEDICATION GUIDE
PRILOSEC® (pry-lo-sec)
(omeprazole)
delayed-release capsules
PRILOSEC (pry-lo-sec)
(omeprazole magnesium)
for delayed-release oral suspension

Read this Medication Guide before you start taking PRILOSEC and each time you get a refill. There may be new information. This information does not take the place of talking with your doctor about your medical condition or your treatment.

What is the most important information I should know about PRILOSEC?
PRILOSEC may help your acid-related symptoms, but you could still have serious stomach problems. Talk with your doctor.
PRILOSEC can cause serious side effects, including:

- **Diarrhea**. PRILOSEC may increase your risk of getting severe diarrhea. This diarrhea may be caused by an infection (*Clostridium difficile*) in your intestines.
  Call your doctor right away if you have watery stool, stomach pain, and fever that does not go away.
- **Bone fractures**. People who take multiple daily doses of proton pump inhibitor medicines for a long period of time (a year or longer) may have an increased risk of fractures of the hip, wrist, or spine. You should take PRILOSEC exactly as prescribed, at the lowest dose possible for your treatment and for the shortest time needed. Talk to your doctor about your risk of bone fracture if you take PRILOSEC.

PRILOSEC can have other serious side effects. See **"What are the possible side effects of PRILOSEC?"**

What are the possible side effects of PRILOSEC?
PRILOSEC can cause serious side effects, including:

- **See "What is the most important information I should know about PRILOSEC?"**
- **Vitamin B-12 deficiency.** PRILOSEC reduces the amount of acid in your stomach. Stomach acid is needed to absorb vitamin B-12 properly. Talk with your doctor about the possibility of vitamin B-12 deficiency if you have been on PRILOSEC for a long time (more than 3 years).
- **Low magnesium levels in your body.** This problem can be serious. Low magnesium can happen in some people who take a proton pump inhibitor (PPI) medicine for at least 3 months. If low magnesium levels happen, it is usually after a year of treatment.

You may or may not have symptoms of low magnesium. **Tell your doctor right away if you develop any of these symptoms:**

- seizures
- dizziness
- abnormal or fast heart beat
- jitteriness
- jerking movements or shaking (tremors)
- muscle weakness
- spasms of the hands and feet
- cramps or muscle aches
- spasm of the voice box

Your doctor may check the level of magnesium in your body before you start taking PRILOSEC or during treatment if you will be taking PRILOSEC for a long period of time.
The most common side effects with PRILOSEC in adults and children include:

- headache
- stomach pain
- nausea
- diarrhea
- vomiting
- gas

In addition to the side effects listed above, the most common side effects in children 1 to 16 years of age include:

- respiratory system events
- fever

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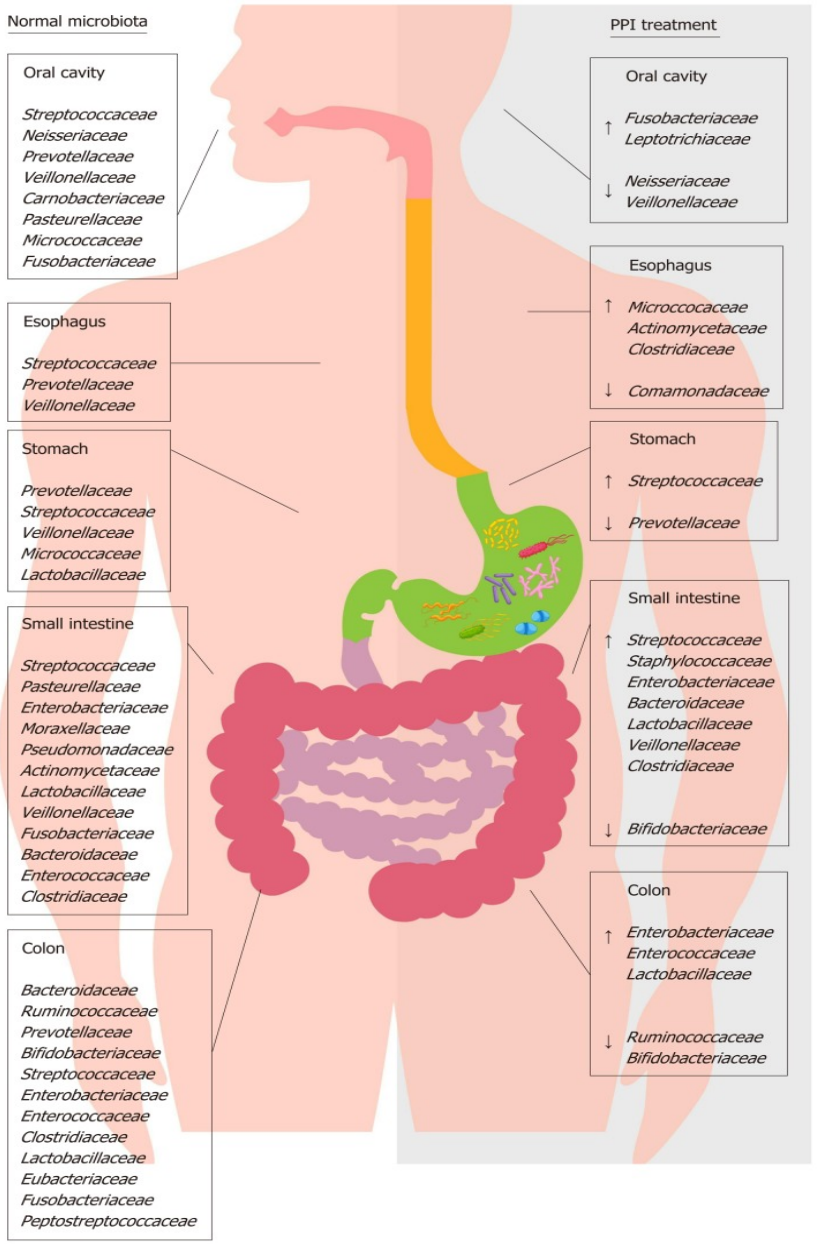
World Journal of Gastroenterology

Submit a Manuscript: https://www.f6publishing.com World J Gastroenterol 2019 June 14; 25(22): 2706-2719

Proton pump inhibitors and dysbiosis: Current knowledge and aspects to be clarified

Giovanni Bruno, Piera Zaccari, Giulia Rocco, Giulia Scalese, Cristina Panetta, Barbara Porowska, Stefano Pontone, Carola Severi

The evidence indicates that PPIs which are widely used in gastroenterology clinical practice likely through their acid-antisecretory effects, ***are able to modify the host microbiota*** *in each segment of the GI tract and can contribute to dysbiosis development; this dysbiosis can, in turn, facilitate the onset of certain GI disorders. Moreover, the gastric* ***hypochlorhydria*** *caused by PPIs* ***favors the survival and migration of oral bacteria in lower areas*** *of the GI tract, with a possible establishment of a pro-inflammatory microenvironment.*



IBP + AINES

J Pain Res. 2018; 11: 361–374.
Published online 2018 Feb 14. doi: 10.2147/JPR.S156938
PMCID: PMC5817415
PMID: 29491719

Coprescribing proton-pump inhibitors with nonsteroidal anti-inflammatory drugs: risks versus benefits

Kok Ann Gwee,[1] Vernadine Goh,[2] Graca Lima,[3] and Sajita Setia[4]

MAYO CLINIC

REVIEW

Nonsteroidal Anti-inflammatory Drugs, Proton Pump Inhibitors, and Gastrointestinal Injury: Contrasting Interactions in the Stomach and Small Intestine

Wojciech Marlicz, MD, PhD; Igor Łoniewski, MD, PhD; David S. Grimes, MD, FRCP; and Eamonn M. Quigley, MD, FRCP, FACP, FACG, FRCPI

*"**Probiotic preparations** are able to prevent NSAID-induced mucosal damage in the small intestine"*

ARTICLE HIGHLIGHTS

- Nonsteroidal anti-inflammatory drugs (NSAIDs) and proton pump inhibitors (PPIs) are among the most frequently prescribed and used medications worldwide.
- Current guidelines from major professional medical societies advocate prescribing PPIs along with NSAIDs in all patients at risk of upper gastrointestinal tract bleeding. The clinical benefit of such coadministration is regarded as obvious and safe and has come to be viewed as standard medical practice.
- Recent scientific evidence points toward unwanted adverse effects in the small intestine if PPIs are combined with NSAIDs. PPIs, by altering the small intestine microbiome, can augment the injurious effects of NSAIDs on the intestinal mucosa.
- Medical practitioners should be aware of potential short- and long-term risks of combined PPI/NSAID therapy in high-risk patients and its effect on small-bowel mucosa.
- Strategies aimed at modulating the gut microbiota may offer the potential of lowering the risk of intestinal mucosal injury related to NSAID/PPI cotherapy.

ANTIÁCIDOS + AINES

Drug Category	Name	Nutrient	Effect on Nutrient Status or Function	Human Studies [1]	Risk Factors
Acid-Suppressing Drugs	Proton Pump Inhibitors	Vitamin B12 Vitamin C Iron CalciumMagnesium Zinc β-Carotene	Decrease Decrease Decrease Decrease Decrease Decrease Decrease	5 observational 5 intervention 1 observation 4 intervention 2 case reports 1 observational 2 intervention >10 observational 4 intervention 30 case reports 2 intervention 1 intervention	Advanced age *H. pylori* infection Genetics (slow metabolizers Low dietary intake (vegetarians) *H. pylori* infection Pre-existing iron deficiency Vegetarians Advanced age Women Advanced age Duration of drug use Women Undetermined Undetermined
Non-Steroidal Anti-Inflammatory Drugs	Aspirin	Vitamin C Iron	Decrease Decrease	1 observational 4 intervention 6 observational 8 intervention	Absence of cold virus Advanced age *H. pylori* infection

pharmaceutics

MDPI

Review

Evidence of Drug–Nutrient Interactions with Chronic Use of Commonly Prescribed Medications: An Update

Emily S. Mohn [1], Hua J. Kern [2], Edward Saltzman [1], Susan H. Mitmesser [2] and Diane L. McKay [1,*]

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Original Investigation

Association of Proton Pump Inhibitors With Risk of Dementia
A Pharmacoepidemiological Claims Data Analysis

Willy Gomm, PhD; Klaus von Holt, MD, PhD; Friederike Thomé, MSc; Karl Broich, MD; Wolfgang Maier, MD; Anne Fink, MSc; Gabriele Doblhammer, PhD; Britta Haenisch, PhD

RESULTS A total of 73 679 participants 75 years of age or older and free of dementia at baseline were analyzed. The patients receiving regular PPI medication (n = 2950; mean [SD] age, 83.8 [5.4] years; 77.9% female) had a significantly increased risk of incident dementia compared with the patients not receiving PPI medication (n = 70 729; mean [SD] age, 83.0 [5.6] years; 73.6% female) (hazard ratio, 1.44 [95% CI, 1.36-1.52]; *P* < .001).

CONCLUSIONS AND RELEVANCE The avoidance of PPI medication may prevent the development of dementia. This finding is supported by recent pharmacoepidemiological analyses on primary data and is in line with mouse models in which the use of PPIs increased the levels of β-amyloid in the brains of mice. Randomized, prospective clinical trials are needed to examine this connection in more detail.

BIGUANIDAS

Acta Med Port. 2017 Oct 31;30(10):719-726. doi: 10.20344/amp.8860. Epub 2017 Oct 31.

[Vitamin B12 Deficiency in Type 2 Diabetes Mellitus].

[Article in Portuguese; Abstract available in Portuguese from the publisher]

Tavares Bello C[1], Capitão RM[1], Sequeira Duarte J[1], Azinheira J[2], Vasconcelos C[1].

Tomkin *et al*. (1971) fue el primero en describer la malabsorción de B12 en pacientes con metformina.

Dosis usuales comprendidas entre 1000mg-3400 mg.

Las **dosis altas tienen mayor probabilidad** de interacción. Ingesta del fármaco después de las comidas.

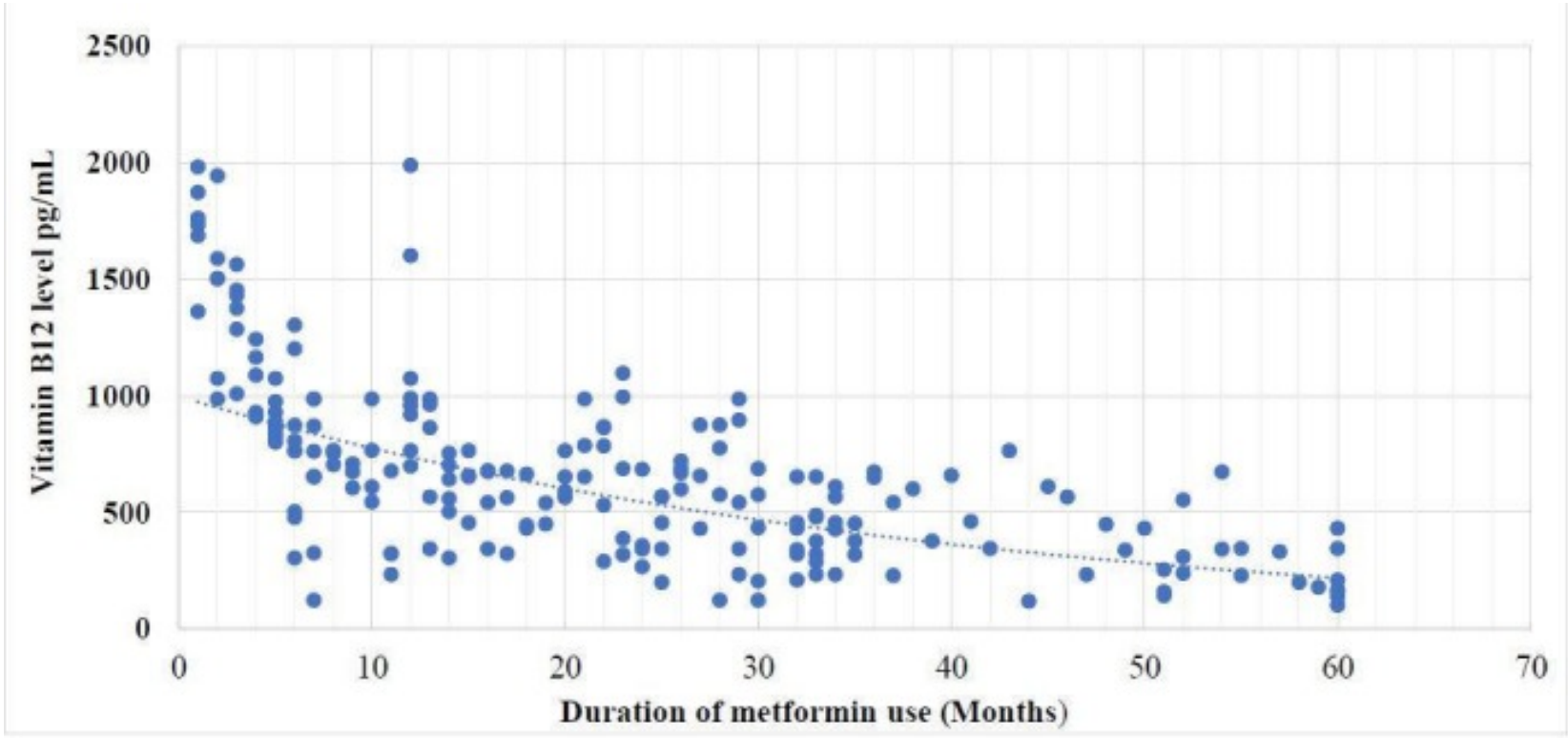
En consumo crónico más del **30% de pacientes muestra deficiencia de B12.**

Mayor riesgo gente mayor, hipotiroidismo y con larga duración de la enfermedad.

Personas afectadas:

DM tipo 2
SOP

BIGUANIDAS: METFORMINA



Khan A (2017) Prevalence of Vitamin B12 Deficiency in Patients with Type II Diabetes Mellitus on Metformin: A Study from Khyber Pakhtunkhwa. Cureus 9(8): e1577

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Clinical Care/Education/Nutrition
ORIGINAL ARTICLE

Increased Intake of Calcium Reverses Vitamin B_{12} Malabsorption Induced by Metformin

WILLIAM A. BAUMAN, MD
SPENCER SHAW, MD
ELIZABETH JAYATILLEKE, MS
ANN M. SPUNGEN, EDD
VICTOR HERBERT, MD, JD

OBJECTIVE — Of patients who are prescribed metformin, 10–30% have evidence of reduced vitamin B_{12} absorption. B_{12}-intrinsic factor complex uptake by ileal cell surface receptors is known to be a process dependent on calcium availability. Metformin affects calcium-dependent membrane action. The objective of this study was to determine the magnitude and mechanism of the reduction in serum vitamin B_{12} after metformin administration.

RESEARCH DESIGN AND METHODS — A comparative study design was employed using 2 groups (metformin and control). A total of 21 patients with type 2 diabetes received sulfonylurea therapy; 14 of these 21 patients were switched to metformin. Monthly serum total vitamin B_{12} measurements and holotranscobalamin (holoTCII) (B_{12}-TCII) were performed. After 3 months of metformin therapy, oral calcium supplementation was administered.

RESULTS — Serial serum vitamin B_{12} determinations revealed a similar decline in vitamin B_{12} and holoTCII. Oral calcium supplementation reversed the metformin-induced serum holoTCII depression.

CONCLUSIONS — Patients receiving metformin have diminished B_{12} absorption and low serum total vitamin B_{12} and TCII-B_{12} levels because of a calcium-dependent ileal membrane antagonism, an effect reversed with supplemental calcium.

Diabetes Care 23:1227–1231, 2000

These considerations prompted us to hypothesize a metformin-induced decrease in vitamin B_{12} absorption because of altered intestinal calcium metabolism.

RESEARCH DESIGN AND METHODS

Subjects

A total of 21 subjects with known type 2 diabetes who were receiving therapy with an oral sulfonylurea and followed as outpatients in the diabetes clinic of the Veterans Affairs Medical Center, Bronx, New York, were recruited for study. The subjects' ages were restricted to 30–60 years. Patients were excluded if they had a history of alcoholism or other drug abuse, psychiatric disease, chronic renal failure, liver disease, cardiopulmonary disease, pernicious anemia, bowel surgery, stomach or bowel disease, acid-based disturbance, or cancer, or if they were receiving antibiotics or any medications known to influence gastrointestinal motility. An initial blood sample was obtained to exclude the possibility of

Med Clin (Barc). 2010 Jul 17;135(6):287-8. doi: 10.1016/j.medcli.2009.06.035. Epub 2009 Aug 14.

[Vitamin B12 deficiency secondary to metformin therapy].

[Article in Spanish]

Esteban Jiménez O, González Rubio F, Buñuel Granados JM, Navarro Pemán C.

PMID: 19683315 [PubMed - indexed for MEDLINE]

Posible mecanismo de la depleción

J Pharm Pharm Sci (www.cspsCanada.org) 19(3) 382 - 398, 2016

Metformin and Vitamin B12 Deficiency: Where Do We Stand?

Marwan Awad Ahmed

Protein bounded vitamin B_{12}
(nutrition)

Proton pump inhibitors → Hydrochloric acid, pepsin: **Proteolysis** → stomach

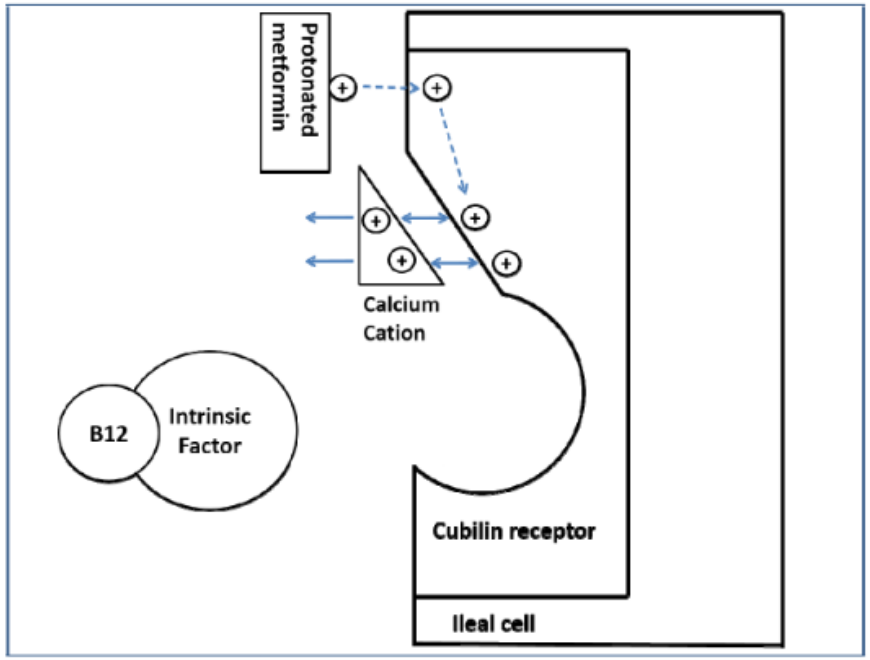
vitamin B_{12}

Proton pump inhibitors → Gastric mucosa: **Intrinsic Factor (IF)** → stomach

IF-Vitamin B_{12}-complex

Metformin → pH > 6: **Calcium ionized** → terminal ileum)

Binding to IF-B_{12}-receptor
(endocytosis → blood)



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Endocrine Journal 2013, **60** (12), 1275-1280

ORIGINAL

Relationship between metformin use, vitamin B12 deficiency, hyperhomocysteinemia and vascular complications in patients with type 2 diabetes

Yuka Sato[1)], Kenjiro Ouchi[2)], Yoshiko Funase[1)], Keishi Yamauchi[1)] and Toru Aizawa[1)]

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[2)] *Medical Research and Education Center, Aizawa Hospital, Matsumoto, Japan*

Abstract. Aim of the study was to clarify the relationship between metformin-induced vitamin B12 (B12) deficiency, hyperhomocysteinemia and vascular complications in patients with type 2 diabetes. Serum B12 concentrations, homocysteine plasma levels, the presence of retinopathy and history of macroangiopathy (stroke or coronary heart disease) were analyzed in patients without renal dysfunction (serum creatinine<115 μmol/L). Firstly, B12 status was analyzed in 62 consecutive metformin-treated patients. Secondly, the relationship between B12, homocysteine and vascular complications was analyzed in 46 metformin-treated and 38 age- and sex-matched non-metformin-treated patients. Among the 62 consecutive metformin-treated patients, B12 was deficient (<150 pmol/L) in 8 (13%) and borderline-deficient (150-220 pmol/L) in 18 (29%): the larger the metformin dosage, the lower the B12 (P=0.02, Spearman's ρ=-0.30). There were independent correlations between metformin use and B12 lowering (P=0.02, r=-0.25), and B12 lowering and elevation of homocysteine (P<0.01, r=-0.34). Elevation of homocysteine was a risk for retinopathy (P=0.02, OR 1.26, 95%CI 1.04-1.52). There was no significant relation between homocysteine and macroangiopathy. Correlation between B12 and homocysteine was stronger in metformin-treated (P<0.01, r=-0.48) than non-metformin-treated (P=0.04, r=-0.38) patients. In ten B12 deficient patients, B12 supplementation (1,500 μg/day) for 2.2±1.0 months with continued use of metformin raised B12 levels: 152±42 and 299±97 pmol/L before and after treatment, respectively (P<0.01). Metformin-induced B12 lowering in diabetes was associated with elevation of homocysteine, and hyperhomocysteinemia was independently related to retinopathy. Metformin-induced B12 deficiency was correctable with B12 supplementation.

Key words: Metformin, Homocysteine, Diabetes, Retinopathy

ANTICONCEPTIVOS ORALES

J Reprod Med. 1980 Oct;25(4):150-6.

Nutritional effects of oral contraceptive use: a review.

Webb JL.

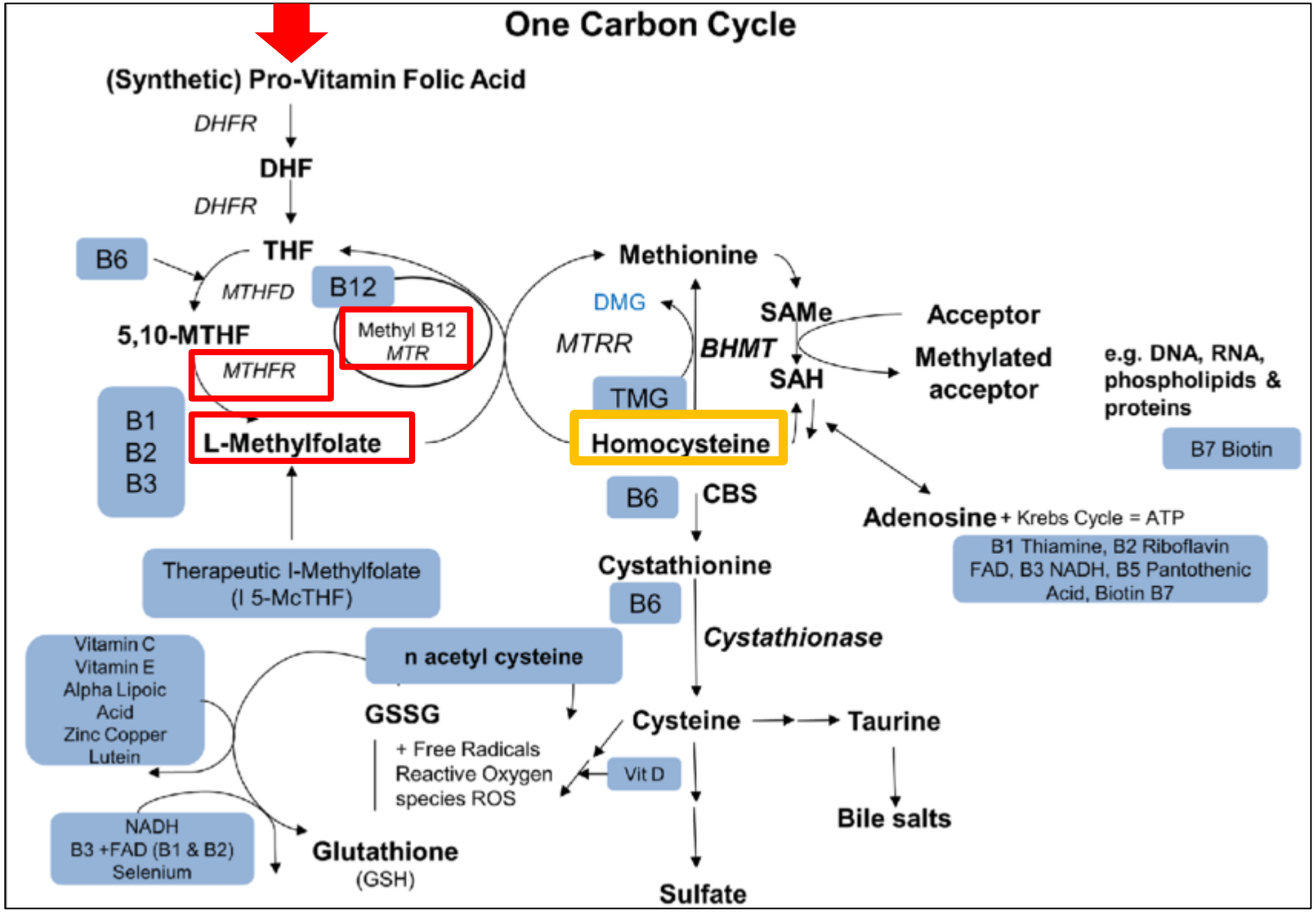
Abstract

Oral contraceptives agents (OCA) have been in use for more than two decades, and at the present time, 150 to 200 million women are using the preparations. Apart from their gynecologic influence, the hormones have been shown to affect a number of metabolic and nutritional processes, some advantageously and others disadvantageously. Concern over the nutritional status of females consuming OCA prompted this review. Eight vitamins and three minerals were investigated. Contraceptive steroid ingestion was shown to depress the physiologic levels of six nutrients (riboflavin, pyridoxine, folacin, vitamin B12, ascorbic acid and zinc), elevate the levels of three others (vitamin K, iron and copper) and provide little or no change in one (alpha tocopherol) and questionable increases in another (vitamin A). It was concluded that females consuming OCA should pay particular attention to vitamin and mineral intake and, if warranted, consume physiologic supplements of needed nutrients.

Evidence **shows a fall in folate and vitamin B12 levels in women taking oral contraceptives.** These levels do not return to normal **until about three months after usage has stopped**, but many women become pregnant during this time.

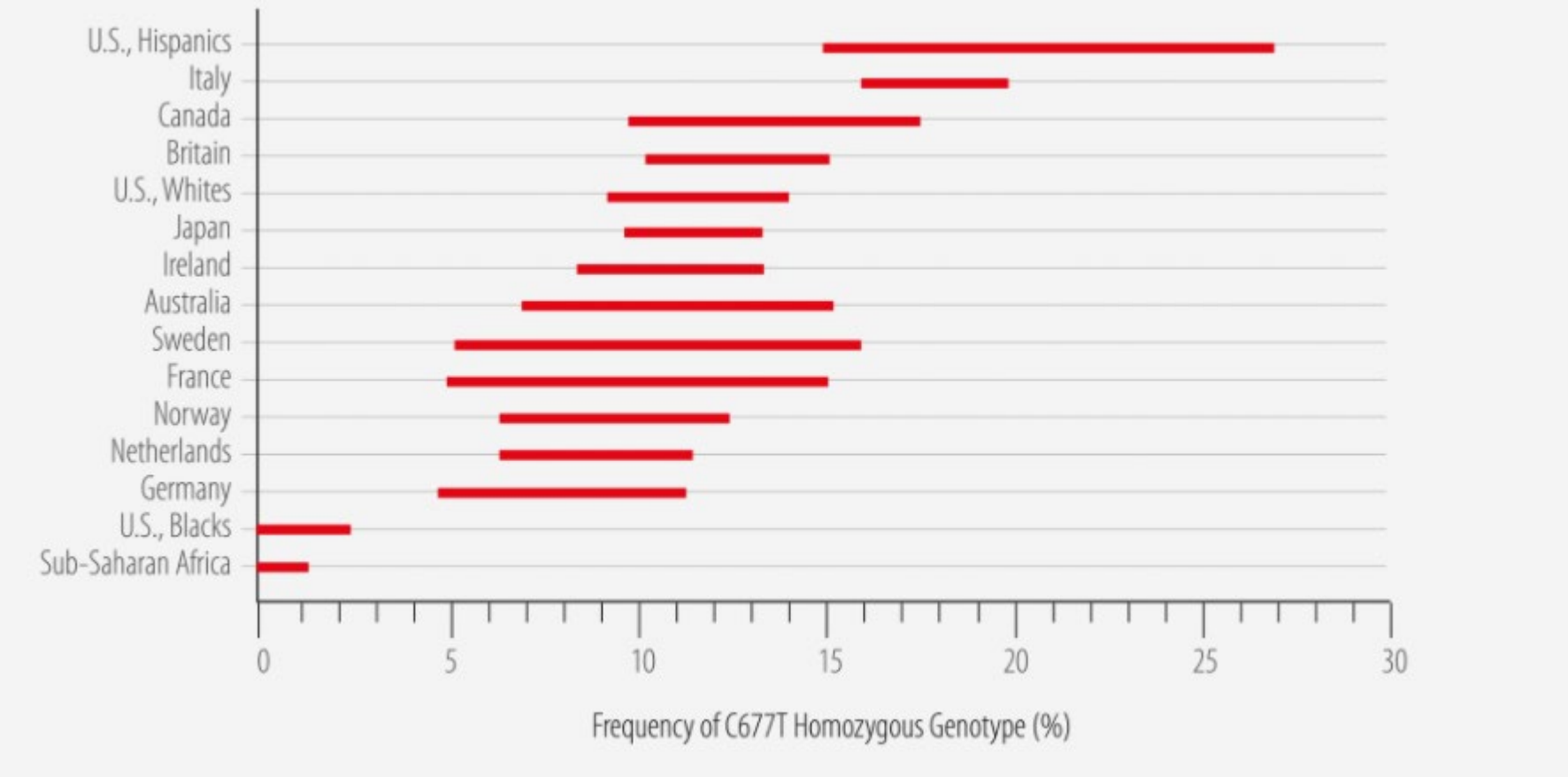
Mountifield JA. Effects of oral contraceptive usage on b(12) and folate levels. *Can Fam Physician*. 1985;31:1523-1526.

ANTICONCEPTIVOS ORALES



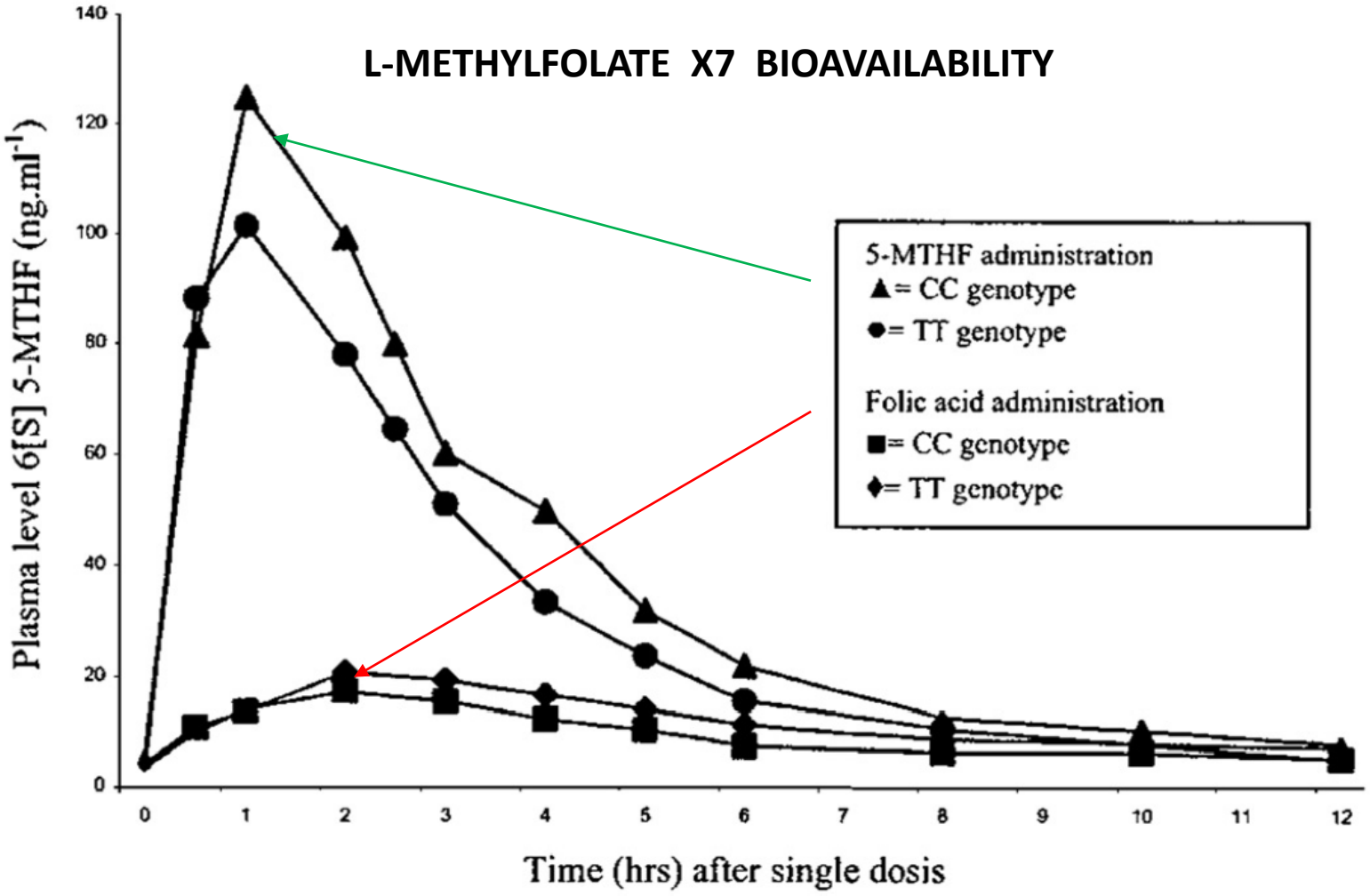
EPHEDRA
FORMACIÓN

POPULATION FRECUENCY MTHFR POLYMORPHISM



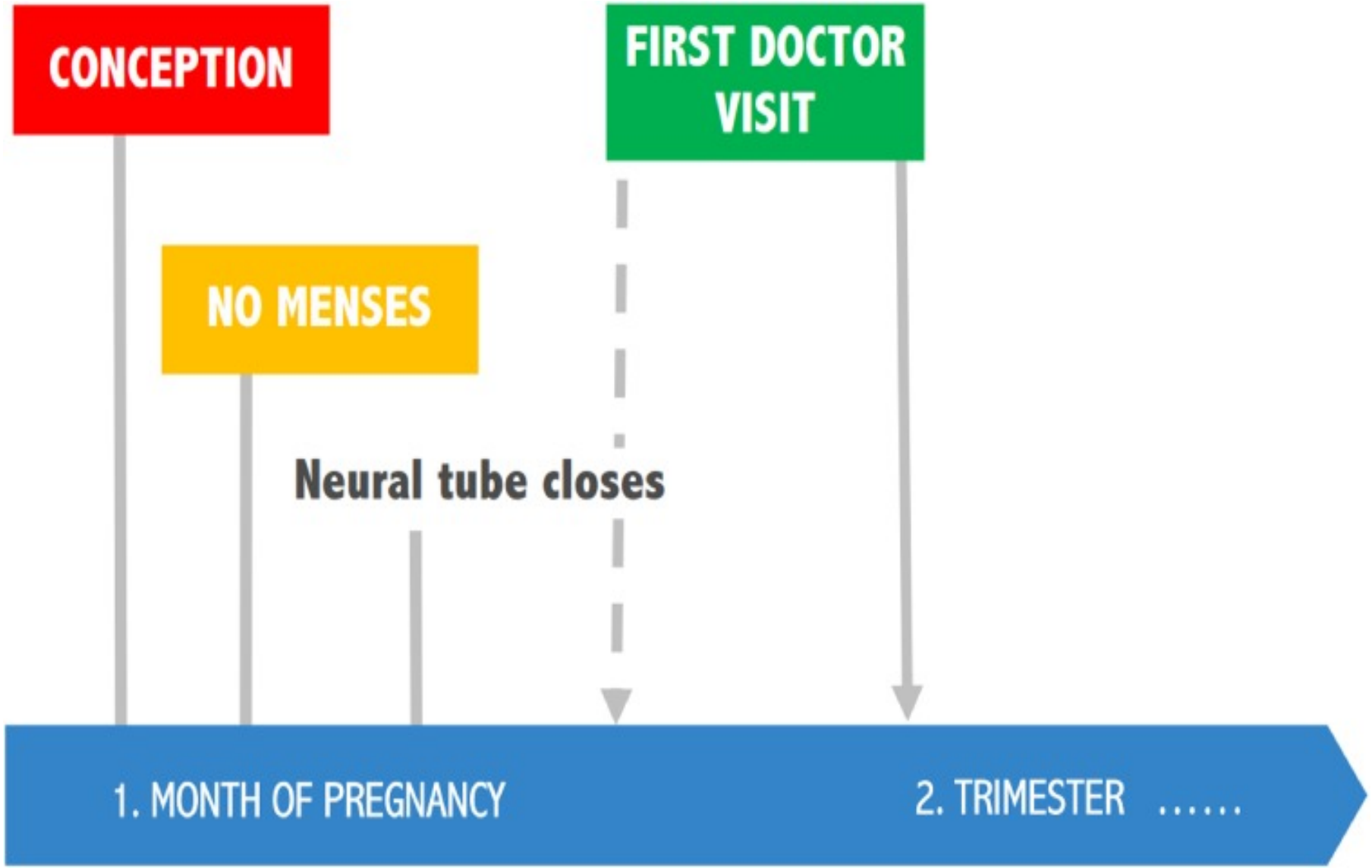
Wilcken B et al. Geographical and ethnic variation of the 677C>T allele of 5,10 methylenetetrahydrofolate reductase (MTHFR): findings from over 7000 newborns from 16 areas worldwide. J Med Genet. 2003

FOLATE, FOLIC ACID, L-METHYLFOLATE



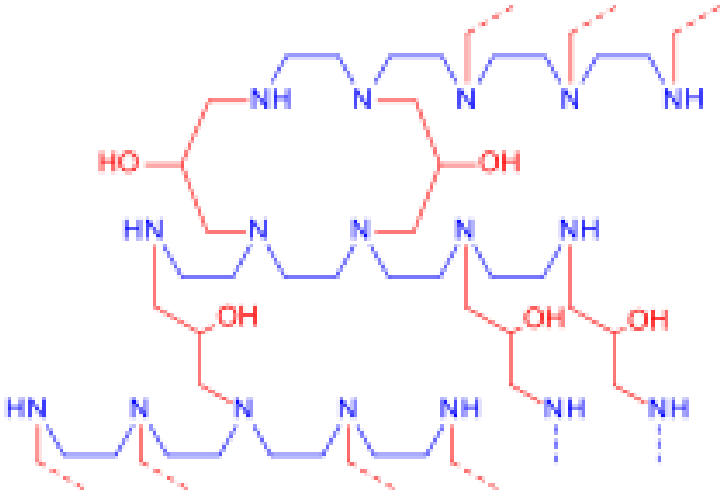
Scaglione F, Panzavolta G. Folate, folic acid and 5-methyltetrahydrofolate are not the same thing. Xenobiotica. 2014 May;44(5):480-8.

EPHEDRA
FORMACIÓN



HIPOLIPEMIANTES

- **RESINAS DE INTERCAMBIO IÓNICO**
  - Colestipol, colestiramina

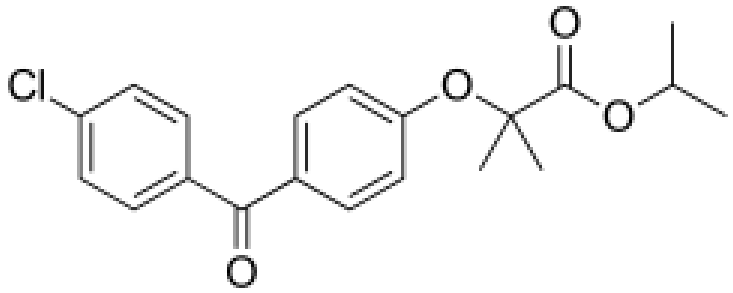


NUTRIENTES AFECTADOS:
VITAMINAS Y MINERALES

FIBRATOS

- Gemfibrozilo, clofibrato, fenofibrato

NUTRIENTES AFECTADOS:
CoQ10, vitamina E



Estatinas + fibratos: >10 % de los pacientes aumentan los valores de creatinina. Mayor riesgo de toxicidad muscular (rabdomiólisis).

Sarter B. Coenzyme Q10 and cardiovascular disease: a review. J Cardiovasc Nurs. 2002 Jul;16(4):9-20. Review.

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Gracias ;)