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INTERACCIONES FÁRMACO-ALIMENTO

Mar Blanco Rogel

Julio 2021

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INTERACCIONES

FÁRMACO- ALIMENTO/NUTRIENTE

ALTERACIÓN DEL METABOLISMO

- **Aceleración del catabolismo** de algunas vitaminas y formación de formas inactivas.
    - Fenobarbital-vit D
- **Inhibición de la producción de las formas activas** de determinadas vitaminas
    - Isoniacida – vit B6 (inhibición piridoxal Kinasa)

FÁRMACOS ANTIEPILÉPTICOS

FÁRMACO	DEFICIENCIA DE VITAMINAS	CONSECUENCIAS
CARBAMAZEPINA	B6, B9, B12	INCREMENTO DE LA HOMOCISTEÍNA -> MAYOR RIESGO CARDIOVASCULAR
FENOBARBITAL*	D*	
FENITOÍNA*	Ca	ALTERACIONES ÓSEAS E INMUNES

Posible mecanismo de acción: inhibición de la absorción intestinal del folato, inhibición de las enzimas del ciclo del carbono-1.

H. Ono, A. et al.- . Concentraciones de homocisteína total en plasma en pacientes epilépticos que toman anticonvulsivos. Rev. Elsevier.

T. Kishi, N. Fujita, T. Eguchi, K. Ueda. Mecanismo para la reducción del folato sérico por los fármacos antiepilépticos durante el tratamiento prolongado. Rev. Elsevier .

Hahn TJ, Birge SJ, Scharp CR, Avioli LV. Phenobarbital-induced alterations in vitamin D metabolism. J Clin Invest. 1972 Apr;51(4):741-8.

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Available online at www.sciencedirect.com
ScienceDirect

Epilepsy & Behavior 12 (2008) 317–323

Epilepsy & Behavior

www.elsevier.com/locate/yebeh

Erythrocyte and plasma fatty acid profiles in patients with epilepsy: Does carbamazepine affect omega-3 fatty acid concentrations?

Se desconoce el mecanismo subyacente a la ***muerte súbita inexplicada en la epilepsia (SUDEP);*** *La arritmia cardíaca es un mecanismo potencial. Si* ***CBZ reduce las concentraciones de FA omega-3****, esto podría hacer que el paciente sea más susceptible a las arritmias cardíacas, y puede ayudar a explicar las observaciones de que los usuarios de CBZ o las altas concentraciones sanguíneas de CBZ parecen estar sobrerrepresentadas en algunas series de SUDEP .*

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Nutritional Aspects of Treatment in Epileptic Patients

How to Cite This Article: Soltani D, Ghaffar pour M, Tafakhori A, Sarraf P, Bitarafan S. Nutritional Aspects of Treatment in Epileptic Patients. Iran J Child Neurol. Summer 2016; 10(3): 1-12.

The proposed mechanism is that EIAEDs may increase the function of the cytochrome p-450 enzymes which induce production of **inactive form from the active form of vitamin D** (vit D). In this way, **absorption of the calcium** (Ca) from gastrointestinal tract will be **reduced**. The reduction of the serum vit D and Ca absorption stimulate the release of parathyroid hormone (PTH) which results in higher uptake of Ca from bone. EIAEDs disturb Ca homeostasis and decrease serum level of Ca. This result is due to the effect of long-term therapy with anticonvulsant drugs on vitamin D metabolism.

EIAEDs **increase catabolism of pyridoxine or vitB6** because of increasing activity of the oxidizing enzyme in the liver, inducing vitB6 deficiency and **polyneuropathy** consequently in patients with seizure. In addition, EIAEDs **reduce the transsulfuration** pathway which is effective in PLP synthesis

EIAEDs disturb the normal function of **folate conjugase in intestine**. Mentioned enzyme has key role in conversion of dietary folatepolyglutamates to folatemonoglutamate for better absorption. As a result, EIAEDs reduce folate absorption from **folatepolyglutamates in foods** (62). Among NEIAED, valproic acid inhibits glutamate formyltransferase enzyme and decrease the formation of active metabolite of folic acid that is named folinic acid

nutrients

MDPI

Perspective

Italian Association of Clinical Endocrinologists (AME) and Italian Chapter of the American Association of Clinical Endocrinologists (AACE) Position Statement: Clinical Management of Vitamin D Deficiency in Adults

Table 2. Vitamin D and drugs interaction.

Mechanism of Action	Drugs
Drugs that interfere with vitamin D absorption	Bile acid sequestrants (Cholestyramine) Lipase inhibitors (Orlistat)
Drugs that interfere with vitamin D metabolism	Antiepileptic drugs (phenobarbital, phenytoin) Corticosteroids Statins Antimicrobials (Rifampicin, Isoniazid, Hydroxychloroquine) Immunosuppressive agents (cyclosporine, tacrolimus) Chemotherapeutic agents Highly active antiretroviral agents Histamine H2-receptor antagonists
Drug-vitamin D interactions that may induce side effects	Thiazides

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Alfa tocoferol bajo en RBC, pero normal en plasma. DHA bajo

J Nutr Sci Vitaminol (Tokyo). 1988 Dec;34(6):627-31.

Alpha-tocopherol and fatty acid levels in red blood cells in patients treated with antiepileptic drugs.

Tamai H[1], Wakamiya E, Mino M, Iwakoshi M.

Author information

1 Department of Pediatrics, Osaka Medical College, Japan.

Abstract

Red blood cell (RBC) alpha-tocopherol and fatty acid levels in children undergoing long-term antiepileptic therapy were examined. Antiepileptic drugs included diphenylhydantoin (PHT), valproic acid (VPA), phenobarbital (PB), and carbamazepine (CBZ). RBC alpha-tocopherol levels were low in patients receiving multi-drug combination therapy, as compared with children receiving no treatment (controls), but plasma alpha-tocopherol levels were the same in both groups. With respect to fatty acid composition in RBCs, docosahexaenoic acid (DHA) level was decreased in children receiving antiepileptic therapy, while no changes were documented in the other fatty acids.

Naunyn Schmiedebergs Arch Pharmacol. 2015 Oct;388(10):1029-38. doi: 10.1007/s00210-015-1135-0. Epub 2015 May 29.

Synergistic effect of docosahexaenoic acid on anticonvulsant activity of valproic acid and lamotrigine in animal seizure models.

Gavzan H[1], Sayyah M, Sardari S, Babapour V.

Author information

1 Department of Basic Science, Faculty of Veterinary Medicine, University of Tehran, Tehran, Iran.

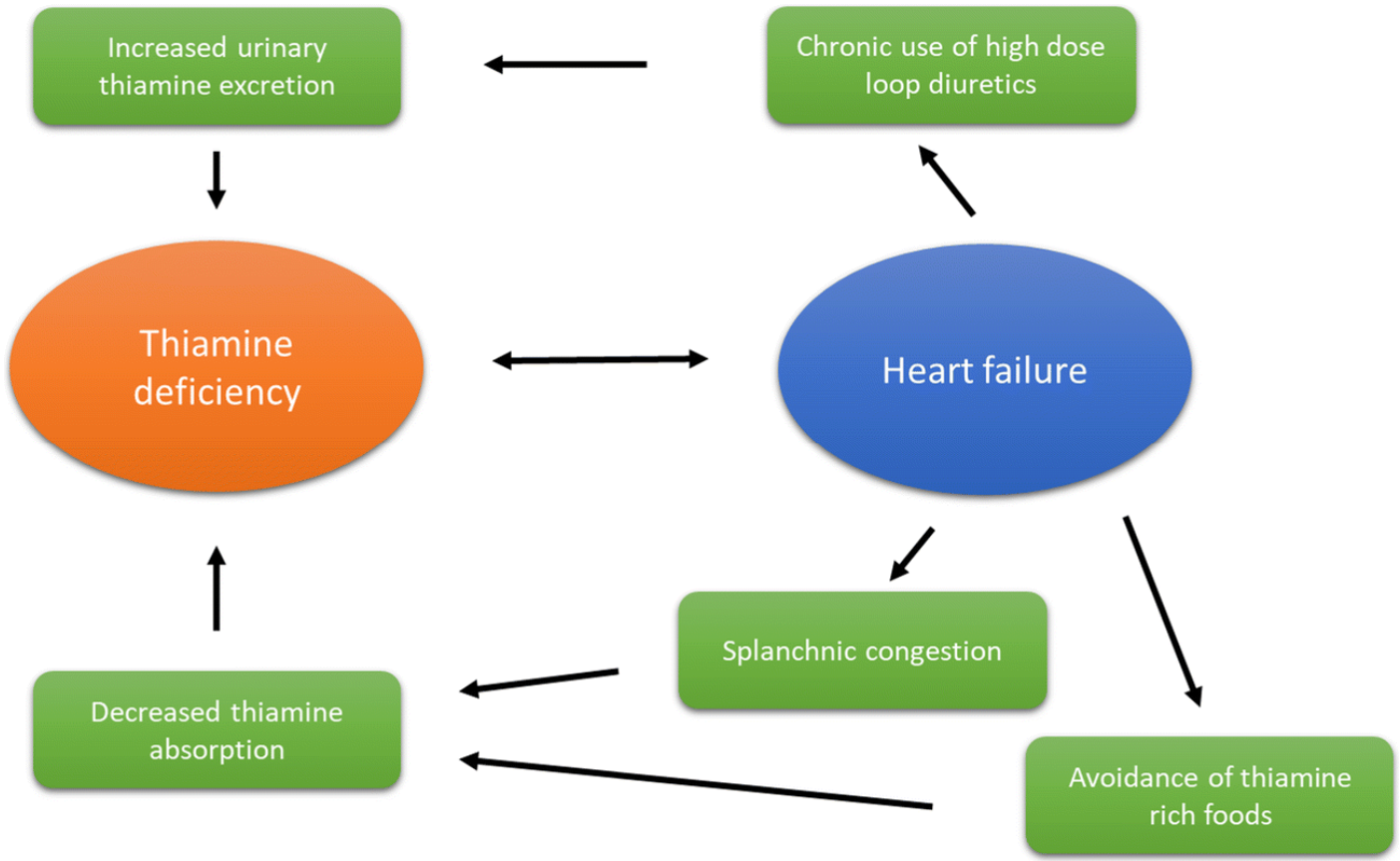
Abstract

Add-on therapy is a common strategy to improve efficacy and tolerability of antiepileptic drugs (AEDs). Anticonvulsant potential and appropriate safety of docosahexaenoic acid (DHA) makes it a promising candidate for combination therapy. We evaluated influence of DHA on anticonvulsant activity of AEDs phenytoin, valproate, and lamotrigine in maximal electroshock (MES), pentylenetetrazole (PTZ), and kindling models of epilepsy. The dose-response to DHA was obtained 15 min after intracerebroventricular (i.c.v.) injection in PTZ model of clonic seizures in mice, MES model of tonic seizures in mice, and kindling model of complex partial seizures in rats. The dose-response curve of valproate (30 min after i.p. injection to mice) in PTZ, phenytoin (60 min after i.p. injection to mice) in MES, and lamotrigine (60 min after i.p. injection to rats) in kindling models were obtained. Dose-response curves of the AEDs were then achieved in the presence of ED25 of DHA. DHA had no anticonvulsant effect in the MES model. However, it showed a dose-dependent protective effect against PTZ (ED50 = 0.13 μM) and kindled seizures (ED50 = 1.08 mM). DHA at ED25 caused a 3.6-fold increase in potency of valproate as its ED50 value from 117.5 (98.3-135.3) decreased to 32.5 (21.6-44.1) mg/kg. Moreover, a 4.9-fold increase in potency of lamotrigine occurred, as its ED50 value from 13.10 (11.50-14.9) decreased to 2.65 (0.8-5.6) mg/kg. CompuSyn analysis indicated synergistic anticonvulsant interaction between DHA and both valproate and lamotrigine. Co-administration strategy of the safe and inexpensive anticonvulsant compound DHA with AEDs should be favorably regarded in clinical studies of epilepsy treatment.

ALTERACIÓN DE LA ELIMINACIÓN

MECANISMO	FÁRMACO	NUTRIENTE AFECTADO
RIÑÓN	Diuréticos	
	Tiazidas	Na, K, Mg, Zn (↓ elim Ca)
	Furosemida	Na, K, Mg, Zn, Ca, tiamina
	Ahorradores de K	Na, Mg, Zn
	Mineralocorticoides	↑ K ↓Na
	Gentamicina	K, Mg
	Cisplatino	K, Mg
	Anfotericina	K, Mg
INTESTINO	Aspirina AINEs	Hierro, Vit C

INSUFICIENCIA CARDÍACA-TIAMINA



Kattoor AJ, Goel A, Mehta JL. **Thiamine Therapy for Heart Failure: a Promise or Fiction?** Cardiovasc Drugs Ther. 2018 Aug;32(4):313-317.

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Can J Clin Pharmacol. 2003 Winter;10(4):184-8.

Thiamine deficiency in congestive heart failure patients receiving long term furosemide therapy.

Zenuk C[1], Healey J, Donnelly J, Vaillancourt R, Almalki Y, Smith S.

Author information

1 Ottawa Hospital, Civic Campus Pharmacy Department.

Abstract

98% de los pacientes con IC tienen deficiencia de tiamina con 80 mg de furosemida/día

57% de los pacientes con IC tienen deficiencia de tiamina con 40 mg de furosemida/día

OBJECTIVE: To assess the p ...nide therapy.

DESIGN: Prospective, bioche ... University of Ottawa Heart Institute.

SUBJECTS: Thirty-two patier ...e included. Patients were then separated into two grou ...g/day.

METHODS: The primary measure was actual thiamine status as assessed by the erythrocyte transketolase enzyme activity and the degree of thiamine pyrophosphate effect.

RESULTS: Biochemical evidence of severe thiamine deficiency was found in 98% (24 of 25) patients receiving at least 80 mg/day of furosemide and in 57% (four of seven) of patients taking 40 mg furosemide daily, odds ratio (OR) 19.0 (1.13<OR<601.29). Thiamine status was not associated with any other clinical variables.

CONCLUSIONS: These findings suggest that thiamine deficiency occurs in a substantial proportion of congestive heart failure patients being treated with furosemide.

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Int J Clin Pract. 2013 Aug;67(8):717-25. doi: 10.1111/ijcp.12040. Epub 2012 Dec 26.

Pharmaco-nutrient interactions - a systematic review of zinc and antihypertensive therapy.

Braun LA[1], Rosenfeldt F.

Author information

Abstract

BACKGROUND: Antihypertensive medicines are to known to cause diverse disturbances to electrolyte homeostasis; however, their potential to affect zinc is less well known. The primary aim was to explore whether antihypertensive medicines have the potential to affect zinc status.

METHODS: A review of electronic databases was undertaken. Full-length English language articles describing clinical trials involving antihypertensive medicines and reporting on zinc measurements were reviewed.

RESULTS: Eight eligible studies were identified which involved the use of ACE inhibitors, thiazide diuretics, beta blockers, or ARB drugs of which five included a control group Studies used urinary zinc excretion, plasma zinc levels or erythrocyte zinc as key measures of zinc status. Studies reported increased urinary zinc losses for captopril (from 50 mg/day), enalapril (20 mg/day), losartan (50 mg/day), losartan (50 mg/day) together with hydrochlorothiazide (12.5 mg/day), captopril (75 mg/day) together with frusemide (40 mg/day) and stand-alone hydrochlorothiazide (25 mg/day). Serum levels of zinc decreased with captopril (50-150 mg/day), verapamil (240 mg/day), atenolol (50-150 mg/day) and the combination of losartan (50 mg/day) and hydrochlorothiazide (12.5 mg/day), eryrthrocyte levels decreased with use of valsartan (80 mg/day) and in some studies for captopril, but not for metoprolol (100 mg/day), atenolol (50-150 mg/day), verapamil (240 mg/day), doxazosin (4 mg/day) or amlodipine 10 mg/day). Major limitations were that most studies were small and did not report on dietary zinc intake.

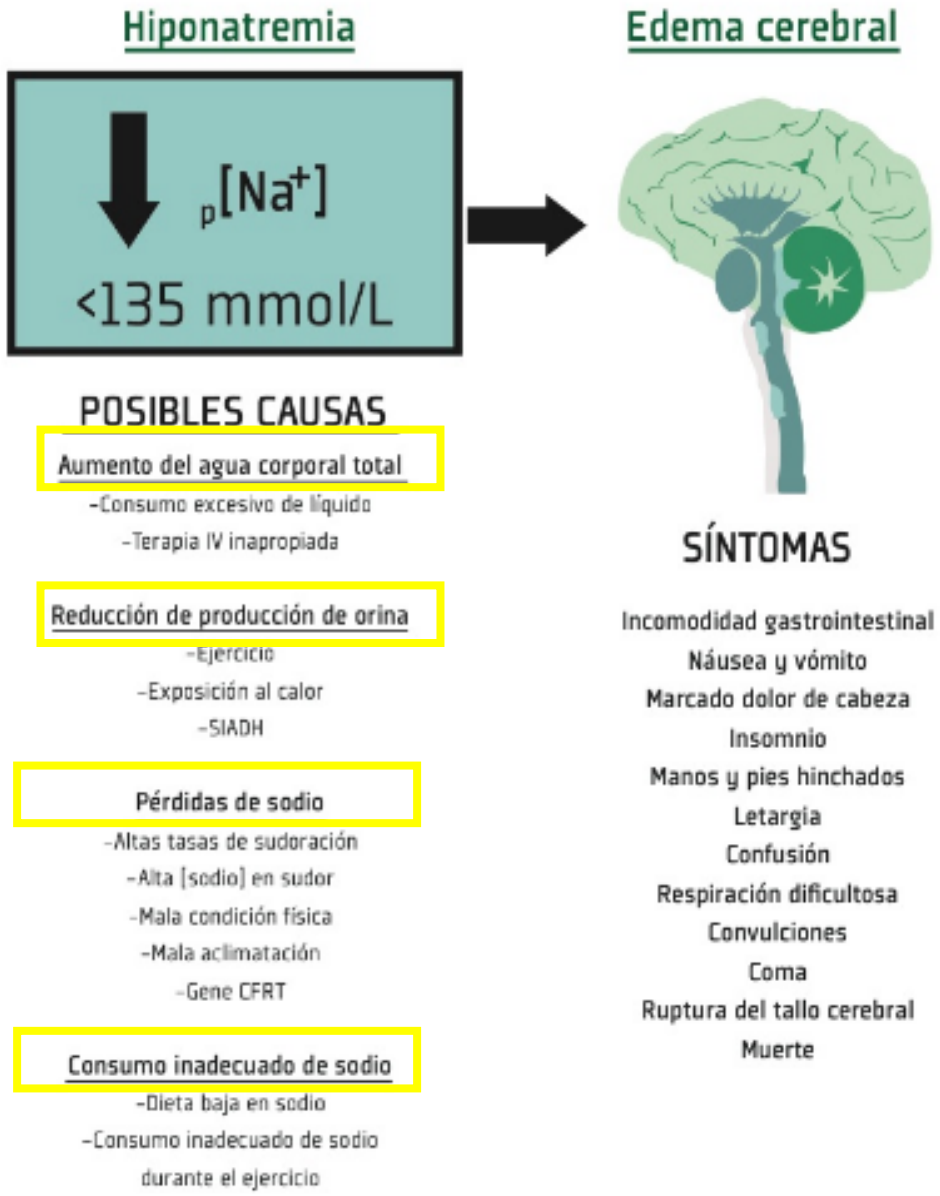
CONCLUSION: The available evidence suggests that use of ACE inhibitors and angiotensin 2 receptor antagonists or thiazide diuretics have the potential to reduce zinc levels in hypertensive patients. Additional research using larger participant numbers and accounting for dietary zinc intakes are required.

HIPONATREMIA

- **Síntomas**
  - Aparato gastrointestinal: náuseas, vómitos.
  - Sistema Nervioso Periférico: calambres musculares, alteraciones visuales.
  - Sistema Nervioso Central: cefalea, letargia, convulsiones, coma.

Tabla 1. Síntomas de la hiponatremia en función de las concentraciones plasmáticas de sodio (Na).

[Na]plasmático (mmol/l)	Gravedad	Síntomas
130-135	Leve	Asintomática
125-130	Moderada	Náuseas y malestar general
<125	Grave	Cefalea, letargia y desorientación



FÁRMACOS QUE PRODUCEN HIPONATREMIA

- **Diuréticos**: particularmente diuréticos tiazídicos, incluyendo combinaciones con IECA y ARA.
- **Antidepresivos**: antidepresivos tricíclicos (amitriptilina, desipramina, imipramina), ISRS (fluoxetina, citalopram), IMAO (fenelcina, tranilcipromina), venlafaxina.
- **Antipsicóticos**: fenotiazinas (flufenacina, tioridacina), haloperidol.
- Antiepilépticos: carbamazepina, oxcarbazepina, ác. valproico, lamotrigina.
- **Antibióticos**: ciprofloxacino, trimetoprim-sulfametoxazol, rifabutina. Antiarrítmicos: amiodarona.
- **Antihipertensivos**: IECA, ARA, amlodipino.
- **Antineoplásicos**: vincristina,vinblastina, cisplatino,carboplatino, agentes alquilantes, metotrexato
- **Otros**: Inhibidores de la bomba de protones, AINES, oxitocina, análogos de ADH.

HIPONATREMIA DILUCIONAL

LA INFORMACIÓN
Jueves, 25 Febrero 2016, 00:53

Un triatleta fallece en el Ironman de Frankfurt por hidratarse solo con agua

Al sudar a los largo de las 19 horas de competición, el cuerpo perdió todo el sodio y no tomó sales para recuperarlo. Las condiciones eran extremadamente duras especialmente en el tramo final de la prueba y el termómetro marcaba más de 35 grados.

Lunes, 27 junio 2016

UN ESTUDIO EN EL IRONMAN DE FRANKFURT CON 1.100 COMPETIDORES DEMUESTRA QUE ES UN PROBLEMA MÁS EXTENDIDO DE LO QUE SE PENSABA

La hiponatremia afecta a más de un 10% de los finisher ironman

DDT Jueves, 9 julio 2015

LEO LATASCH, DIRECTOR DE LOS SERVICIOS DE EMERGENCIA DE FRANKFURT, CONFIRMA QUE LA FALTA DE SODIO POR LA SUDORACIÓN FUE LA CAUSA DE LA MUERTE

El triatleta falleció por beber demasiada agua para hidratarse y no tomar sales

Un triatleta británico de 30 años (no un australiano de 40 años como dijo en primera instancia las fuentes de ironman) falleció ayer al no superar un edema cerebral que se produjo en el Ironman de Frankfurt debido a las altas temperaturas y a un déficit de sales según confirmaron fuentes médicas. El deportista británico se derrumbó nada más cruzar la

COMPOSICIÓN BEBIDAS DE HIDRATACIÓN ISOTÓNICAS

- **Aporte energético**: 80-350 kcal
- **Aporte de CHO**: 4-8 % CHO (75 % IG elevado)
- **Sodio:** 460-1150 mg/L (20-50 mOsml/L)
- **Potasio**: 120-225 mg/L
- **Osmolaridad**: 200-330 mOsm/L

LAXANTES

TIPO	FÁRMACO
ESTIMULANTES	BISACODILO, ALOE (ALOINA), SENNA
AGENTES OSMOTICOS	LACTULOSA, SORBITOL, MANITOL, HIDRÓXIDO DE MAGNESIO
LUBRICANTES	ACEITES MINERALES **BETACAROTENO, RETINOL,VIT D,E, K…**
STOOL SOFTENERS	DOCUSATE SODIUM AND CALCIUM
FORMADORES DE MASA	PSYLLIUM HUSK

MINERALES, VITAMINES, AA, ÁCIDOS GRASOS…

SUPLEMENTOS DE FIBRA

Fibra soluble: glucomanan, *Plantago* spp., *Althea*, *Linum unsitatisimum*

Separar 2h antes o 2h después de las comidas

DEPLECCIÓN MAGNESIO

Medications that reduce magnesium levels:

(i) *H2 blockers*: for example, cimetidine and nizatidine

(ii) *Proton pump inhibitors*: for example, esomeprazole, omeprazole, and pantoprazole (*FDA WARNING*: supplementing magnesium will not correct deficiency; you must stop the drug)

(iii) *Antacids*: aluminum and magnesium hydroxide and sodium bicarbonate

(iv) *Antibiotics*: for example, amoxicillin, azithromycin, doxycycline, minocycline, levofloxacin, ciprofloxacin, cephalexin, sulfamethoxazole and trimethoprim, and tetracycline

(v) *Antihistamines*: for example, astemizole and terfenadine

(vi) *Antivirals*: for example, delavirdine, lamivudine, and zidovudine

(vii) *Antiepileptic medications*: phenytoin and phenobarbital

(viii) *Blood pressure drugs*: hydralazine and combination of ACE inhibitors with HCTZ (enalapril and HCTZ)

(ix) *Diuretics*: for example, furosemide, ethacrynic acid, chlorothiazide, chlorthalidone, metolazone, and indapamide

(x) *Cardiac glycoside*: digoxin

(xi) *Cardiac drugs*: sotalol, amiodarone, bretylium, and quinidine

(xii) *CNS stimulants*: methylphenidate

(xiii) *Cholesterol agents*: cholestyramine and colestipol

(xiv) *Corticosteroids*: betamethasone, dexamethasone, hydrocortisone, prednisone, and triamcinolone

(xv) *Inhaled corticosteroids*: fluticasone, flunisolide, and triamcinolone

(xvi) *Estrogens*: DES, estradiol, estring, and estrogen-containing drugs: HRT and BCP

(xvii) *Immunosuppressants*: cyclosporine and tacrolimus

(xviii) *Nonsteroidal aromatase inhibitors for breast cancer*: anastrozole

(xix) *Osteoporosis*: raloxifene

(a) On the other hand, magnesium decreases bisphosphonate absorption

(xx) *SERMs (selective estrogen receptor modulators)*: raloxifene, tamoxifen, and toremifene

(xxi) *Sulfonamides*: antibiotics and some diabetic medications

(xxii) *Nutraceuticals*: for example, high-dose calcium, high-dose vitamin D, and caffeine

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Gracias ;)