Janusmed

Driftstatus Nyheter i Janusmed

Så här söker du

Sök på läkemedelsprodukt och/eller substans

klopidogrel × citalopram × omeprazol × repaglinid × hydroxizin × atorvastatin × levotyroxin × Kalcipos-D (Tuggtablett) × metformin × alendronsyra ×

Namn på produkter eller substanser

Rensa sökning

Inkludera utgångna/ej tillgängliga läkemedelsprodukter

Interaktioner D3 | Riskprofil III | Njurfunktion X | Fosterpåverkan 2 | Amning 3 | Kön och genus C

Interaktioner

Startsida interaktioner Aktuellt Användarhandledning E-utbildning CYP3A4-hämmare/inducerare FAQ Skriv ut

Tjänsten ger generell information utifrån substansens egenskaper och administreringssätt och tar inte hänsyn till patientens ålder, kön eller aktuell dosering.

11 interaktioner mellan valda läkemedel

Lägg till Annat än läkemedel (allt) Annat än läkemedel som har interaktioner med valda preparat

Rensa tillval

Läkemedelsprodukt / substans	Interaktioner
alendronsyra (Enteral peroral) 10	C3
atorvastatin (Enteral och parenteral) 141	B4
citalopram (Enteral och parenteral) 193	C3 C0 C0
hydroxizin (Enteral och parenteral) 49	C0
+ Kalcipos-D (Tuggtablett)	C3 C3 B3
klopidogrel (Enteral och parenteral) 145	D3 C3 C0 B4
levotyroxin (Enteral peroral) 57	C3 C3 B4
metformin (Enteral peroral) 51	B4
+ omeprazol 122	C3 C3 C3 B3
repaglinid (Enteral och parenteral) 50	D3

+ Expandera

D3 klopidogrel - repaglinid

Visa all info Skriv ut Kontakta oss

klopidogrel Enteral och parenteral

repaglinid Enteral och parenteral

Medicinsk konsekvens

Exponeringen för repaglinid ökar upp till 4-faldigt vid samtidig behandling med klopidogrel. Risken för hypoglykemi är förhöjd.

Rekommendation

Kombinationen bör undvikas. Överväg behandling med annat antidiabetikum än repaglinid.

Mechanism

Inhibition of CYP2C8 by clopidogrel´s acyl-β-D-glucuronide-metabolite.

Background

In a phase I study in 9 healthy volunteers given repaglinide (0.25 mg), the subjects received concomitant clopidogrel for 3 days (300 mg on day 1, followed by 75 mg daily) or placebo in a crossover manner (1). It was found that the geometric mean AUC of repaglinide was increased 5.1- and 3.9-fold on days 1 and 3, respectively, when compared with the placebo phase (1). The blood sugar levels were significantly lower in clopidogrel phase compared with the control (1). A physiologically based pharmacokinetic model indicated that inactivation of CYP2C8 by clopidogrel acyl-β-D-glucuronide leads to uninterrupted 60-85% inhibition of CYP2C8 during daily clopidogrel treatment, suggesting that clopidogrel is a strong CYP2C8 inhibitor (1).

24 healthy male volunteers were divided into three groups in an open-label, parallel study with two phases, with a washout period of at least 1 week between phases. Each participant in each group received a single small-dose cassette of pitavastatin, pioglitazone and repaglinide. In the drug-drug interaction phase, 600 mg rifampicin, 200 mg trimethoprim or 300 mg clopidogrel was administered with a small-dose cassette for each group, respectively. The pharmacokinetics of repaglinide co-administered with clopidogrel was compared with its pharmacokinetics in the absence of co-administered drug. The AUC of repaglinide was 3.1 fold higher than that of the control when administered with clopidogrel (2).

In a case-control study concomitant use of clopidogrel was associated with increased risk of hypoglycemia among patients taking repaglinide; adjusted odds ratio 2.42 (95% CI: 1.75-3.35) (3). In a retrospective cohort study 15 patients already taking clopidogrel (75 mg daily) and started on repaglinide (1.5 mg daily) were matched (for age and gender) with a control group of 15 patients who were not taking clopidogrel but started on the same dose repaglinide. Hypoglycemia (<3,9 mmol/L) was present in significantly more patients in the clopidogrel and repaglinide group (6/15) compared to the repaglinide group (0/15). (4)

› Visa inte hela bakgrundstexten

Referenser › Dölj referenser

1. Tornio A, Filppula AM, Kailari O, Neuvonen M, Nyrönen TH, Tapaninen T et al. Glucuronidation Converts Clopidogrel to a Strong Time-Dependent Inhibitor of CYP2C8: A Phase II Metabolite as a Perpetrator of Drug-Drug Interactions. Clin Pharmacol Ther. 2014;96:498-507.
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C3 kalcium - alendronsyra

Visa all info Skriv ut Kontakta oss

kalcium Enteral (peroral)

Kalcipos-D (Tuggtablett)

alendronsyra Enteral (peroral)

Medicinsk konsekvens

Interaktionen kan leda till minskad absorption av bisfosfonater, med risk för utebliven effekt.

Rekommendation

Administering av bisfosfonater på morgonen och kalcium eller läkemedel innehållande metalliska katjoner på kvällen rekommenderas för att undvika interaktion. Vid multipla dagliga doser bör man vänta åtminstone 30 minuter innan intag av kalcium/aluminium/magnesium.

Mechanism

Metallic cations chelate biphosphonates, which can result in reduced absorption and impaired therapeutic response to biphosphonates.

› Visa inte hela mekanismtexten

Background

Biphosphonates can form complexes with a number of divalent metallic ions which may lead to impaired absorption of biphosphonates (1,2,3). According to data on file (Sanofi Winthrop 1996) the tiludronic acid exposure in terms of AUC was halved when tiludronic acid was administered simultaneously with aluminum/magnesium hydroxide combination (Maalox) in a phase I study with 12 healthy volunteers. However, bioavailability was only minimally affected when Maalox was given 2 hours after tiludronic acid (4).

In 126 subjects the rate of absorption of risedronate was significantly increased when oral risedronate 30 mg was given 0.5, 1 or 4 hours prior to a meal compared with 2 hours after dinner (5). In another studies the optimal time for risedronate (6) and clodronate (7) to be administered was 0.5 hours before breakfast.

In 15 healthy women the oral bioavailability of alnedronate was estimated to 0.76% after overnight fast. There was a 2 hour wait before any food or beverage. Breakfast (egg, toast, marmelade, bacon, orange juice) with and without calcium supplement (1 gram) was taken 30 minutes, 1 hour and 2 hours after oral administration of 20 mg alendronate. The bioavailability of alendronate was decreased by approximately 40% if breakfast was eaten 30 minutes or 1 hour after aledronate administration compared to the 2 hour wait. The alendronate absorption was not decreased more when calcium supplementation was added to breakfast suggesting that the meal itself more than calcium affects the alendronate absorption (8).

› Visa inte hela bakgrundstexten

Referenser › Dölj referenser

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C3 kalcium - levotyroxin

Visa all info | Skriv ut | Kontakta oss

kalcium Enteral (peroral)

Kalcipos-D (Tuggtablett)

levotyroxin Enteral (peroral)

Medicinsk konsekvens

Kalciumkarbonat kan förhindra absorptionen av levotyroxin (liotyronin) och effekten av levotyroxin kan därmed minska något.

Rekommendation

Interaktionen kan undvikas genom att intaget av levotyroxin/liotyronin och kalcium separeras med ett tidsintervall på åtminstone 4 timmar. Noggrann kontroll av sköldkörtelfunktionen rekommenderas.

Mechanism

In vitro studies indicate that levothyroxine is adsorbed onto the calcium carbonate when the pH is low (particularly as in the stomach), which would reduce the amount of levothyroxine for absorption.

› Visa inte hela mekanismtexten

Background

In a controlled study, twenty patients (age range, 27-78 years; n=11 men) with hypothyreoidism who were treated with levothyroxine (a stable long-term regimen) alone, to which was then added 1200 mg calcium carbonate daily for 3 months, were followed (1). While taking calcium carbonate their mean free T4 level was significantly reduced from 17 pmol/L at baseline to 15 pmol/L, and rose again to 18 pmol/L when calcium carbonate was discontinued. The mean thyrotropin level was significantly increased from 1.6 mU/L to 2.7 mU/L during calcium carbonate treatment, and then decreased to 1.4 mU/L after calcium was stopped.

Hypothyroidism of a 64-year-old woman was well controlled with 88 microg/d of (TSH 2 mIU/L) when she had been diagnosed with osteopenia and oral calcium carbonate was added to the regimen. The patient took the calcium carbonate at the same time as L-T4 and 3 months later thyroid function test results showed an increase in TSH serum level (9.8 mIU/L) and a decrease in serum free thyroxine (FT4) level (0.2 ng/dL). The L-T4 dose was increased to 112 microg/d, which improved the patient's symptoms during the following months (TSH level 6.4 mIU/L) and later to 125 microg/d (when TSH 2.7 mIU/L). The patient stopped taking calcium carbonate during the following months, without medical advice, and her TSH level decreased (to 0.1 mIU/L). L-T4 dose was decreased to 88 microg/d. (6)

A woman with thyroid cancer given levothyroxine 125 micrograms daily to suppress serum TSH levels showed a reduced response (fatigue, weight gain) when she took calcium carbonate for prevention of osteoporosis together with levothyroxine. Over a 5-month period her serym TSH levels were increased from 0.08 mU/L to 13.3 mU/L. Her THS levels had fallen to 0.68 mU/L within 3 weeks of discontinuation of calcium carbonate (2).

Other case reports have described 5 patients with elevation in TSH levels while co-administered calcium carbonate with levothyroxine. TSH levels were reversed to normal when administration was separated with 2 to 4 hours interval (2,3,4,5,7). › Visa inte hela bakgrundstexten

Referenser › Dölj referenser

1. Singh N, Singh PN, Hershman JM. Effect of calcium carbonate on the absorption of levothyroxine. JAMA. 2000;283:2822-5.
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C3 levotyroxin - omeprazol

Visa all info | Skriv ut | Kontakta oss

levotyroxin Enteral (peroral)

omeprazol Enteral och parenteral

Medicinsk konsekvens

Vid långtidsbehandling kan protonpumpshämmare minska absorptionen av levotyroxin.

Rekommendation

Sedvanlig monitorering av TSH räcker. Byte till levotyroxin i mjuka gelatinkapslar eller lösning (om tillgängligt) kan förbättra absorptionen av levotyroxin.

Mechanism

The absorption of levothyroxine is decreased due to gastric pH alteration by long-term PPI. › Visa inte hela mekanismtexten

Background

TSH levels of 92 patients (37 in study group and 55 controls) on stable levothyroxine for at least 6 months were measured. Patients in study group received also lansoprazole and TSH concentrations were measured before and at least 2 months after start of the PPI use. In the study group the mean change in the TSH level from before to after initiation of lansoprazol was 0.69 ± 1.9 micro IU/mL (P = 0.035). In the control group the mean change in the TSH level during the study period was 0.11 ± 1.06 micro IU/mL (P = 0.45). (1)

Omeprazole 40 mg daily for at least 6 months caused a variable increase in TSH levels (median 1.7 mU/L versus 0.1 mU/L before treatment) in 10 women with multinodular goitre and gastroesophageal reflux disease receiving a stable dose of levothyroxine to suppress thyroid growth. The effect was reversed by an increase in the thyroxine dose by 37 %. (2)

In a randomised, crossover study in 20 healthy subjects pantoprazole 40 mg daily for 1 week had no effect on the AUCs of TSH or thyroxine after a single dose of levothyroxine (4 microg/kg). (3)

A retrospective population-based analysis linking biochemistry and prescription data reported that PPIs increased serum TSH concentration over 5 mU/l in 5.6% patients (4).

An in vitro study studied pH dissolution of levothyroxine in soft gelatin capsules dissolved in glycerin, levothyroxine in tablets, or as generic levothyroxine sodium in tablets. All formulations were sensitive to the pH of the dissolution media, supporting that an increase in pH by PPI may decrease levothyroxine absorption. Levothyroxine in soft gelatin capsules was less sensitive to pH changes than the two other formulations, and may work better in vivo (5).

A woman with Hashimoto's thyroiditis-associated hypothyroidism treated with pantoprazole and a tablet levothyroxine (150 µg/day), taken simultaneously in the morning, experienced high TSH levels until the levothyroxine treatment was switched from tablet to soft gel capsules (125 µg/day). An intestinal absorption test was performed with a dose of 600 µg levothyroxine soft gel capsules versus 600 µg tablet and showed an [AUC]0-4h of 16,240 and 10,960 nmol*h/L, respectively (6).

In a prospective observational cohort study on 24 patients with levothyroxine treatment for replacement or suppressive purposes and levothyroxine absorption problems due to concomitant PPI treatment (omeprazole, pantoprazole, lansoprazole, and esomeprazole), a switch from tablet to soft gel capsules decreased TSH serum concentrations significantly (P< 0.0001) (7).

A systematic review included seven studies with a before-after design to investigate the effects of concomitant PPI use with intake of levothyroxin and confirmed these data: concomitant intake of PPI with levothyroxine capsules resulted in mostly small, yet significant increases in TSH levels (approximately 10-20%, except for (2)) (8). Of note, four of these 7 studies have already been described above (8).

› Visa inte hela bakgrundstexten

Referenser › Dölj referenser

1. Sachmechi I, Reich DM, Aninyei M, Wibowo F, Gupta G, Kim PJ. Effect of proton pump inhibitors on serum thyroid-stimulating hormone level in euthyroid patients treated with levothyroxine for hypothyroidism. Endocr Pract. 2007 Jul-Aug;13:345-9.
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C3 klopidogrel - omeprazol

Visa all info | Skriv ut | Kontakta oss

klopidogrel Enteral och parenteral

omeprazol Enteral och parenteral

Medicinsk konsekvens

Effekten av klopidogrel kan minska. Höga doser av omeprazol/esomeprazol kan troligen öka risken.

Rekommendation

Överväg behandling med en svagare hämmare av CYP2C19, t. ex. pantoprazol, istället för omeprazol.

Mechanism

Inhibition of CYP2C19 catalysed clopidogrel bioactivation by omeprazole.

Background

Clopidogrel is a pro-drug, which in vivo is converted to an active metabolite in a two-step process (1). First, metabolism by CYP1A2, CYP2B6, and CYP2C19 leads to the formation of 2-oxo-clopidogrel (1). In the next step, 2-oxo-clopidogrel is oxidized to the active metabolite by CYP2B6, CYP2C9, CYP2C19 and CYP3A4. CYP2C19 has been described to contribute substantially to both metabolic steps, whereas CYP3A4 plays an important part in the second step (1). The active metabolite binds irreversibly to the platelet adenosine diphosphate (ADP) P2Y12-receptor and thus inhibits platelet aggregation (2). Studies in healthy volunteers have shown omeprazole 80 mg daily to cause up to 45 % decrease in exposure to the active clopidogrel metabolite, measured as AUC (3). Exposure to the active clopidogrel metabolite was also decreased, but to a smaller extent, by esomeprazole and lansoprazole (60 mg daily), omeprazole (20 mg daily), and pantoprazole (80 mg daily; 14 % decrease in AUC) (3).
In some controlled studies on platelet inhibition by clopidogrel in healthy subjects or patients, the effect of clopidogrel was decreased by dexlansoprazole, esomeprazole, lansoprazole, omeprazole, pantoprazole or rabeprazole, but conflicting data exist (3). Some observational studies and meta-analyses have shown an increased risk of cardiovascular events for patients concomitantly treated with clopidogrel and proton pump inhibitors (4, 5, 6, 7), but this association was not seen in studies adjusting for propensity score (3). The association was not unique for omeprazole/esomeprazole and was not seen in randomized studies (3, 7), implying that proton pump inhibitor use in itself is associated with/markers of increased cardiovascular risk. A pharmacokinetic interaction between clopidogrel and PPI may be more likely to be clinically relevant in individuals carrying CYP2C19 loss of function alleles (8). Considering the pharmacokinetic properties and in view of the lack of conclusive clinical evidence, a weaker inhibitor of CYP2C19 than omeprazole, such as pantoprazole, should be considered when used concomitantly with clopidogrel (9). The FDA, MHRA and EMA have also advised against the use of omeprazole or esomeprazole in patients on clopidogrel (3). › Visa inte hela bakgrundstexten

Referenser › Dölj referenser

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C3 citalopram - omeprazol

Visa all info | Skriv ut | Kontakta oss

citalopram Enteral och parenteral

omeprazol Enteral och parenteral

Medicinsk konsekvens

Plasmakoncentrationen av (es)citalopram kan öka med cirka 50-100%. Samtidig behandling ökar risken för biverkningar av (es)citalopram tex risken för kliniskt relevant QT-förlängning och därmed risken för Torsades de Pointes och kan öka risken för plötsligt hjärtstillestånd.

Rekommendation

Överväg sänkning av (es)citalopramdosen eller behandling med pantoprazol i stället för omeprazol/esomeprazol för att undvika interaktionen.

Mechanism

Omeprazole inhibits the metabolism of es/citalopram by inhibiting CYP2C19.

› Visa inte hela mekanismtexten

Background

In one study in 16 healthy subjects, the AUC of escitalopram increased 51% (39-64%) after pretreatment with omeprazole (30 mg/d) for 6 days. The half-life increased from 26.5 to 34.8 h (1).
In another study, including 9 healthy volunteers, the AUC of escitalopram increased by 120% and the AUC of R-citalopram by 25% after concomitant administration of 20 mg racemic citalopram and 20 mg omeprazole (2).

A 6-month, prospective study evaluating QT-interval prolongation as a response marker for S-citalopram dosage during co-administration with omeprazole in geriatric patients (n=152) found that the risk of the QT-interval prolongation (greater than 450 ms) is increased among the patients with co-administration (OR=3.7; 95% C 1.5-9.4) (3). Concomitant use was estimated to increase the S-citalopram levels by 3-fold (3).

A retrospective cohort study evaluating the association between citalopram and omeprazole use and the risk of sudden cardiac arrest (SCA) in an Asian population, showed that the cumulative incidence of SCA was higher in patients with concomitant use than those treated with citalopram or omeprazole alone (4). The hazard ratio of SCA was 1.32 (95% CI 1.17-1.50) for citalopram use alone, 1.08 (95% CI 0.98-1.20) for omeprazole use alone, and 2.23 (95% CI 1.79-2.97) for concomitant use (4).

A case report describes a patient with OCD treated with an off label high dose of 30 mg escitalopram (approved maximal dose is 20 mg). This dose was initially well tolerated, but when esomeprazole treatment was started, she soon experienced symptoms of possible serotonin syndrome (5).

› Visa inte hela bakgrundstexten

Referenser › Dölj referenser

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C0 citalopram - klopidogrel

Visa all info | Skriv ut | Kontakta oss

citalopram
Enteral och parenteral

klopidogrel
Enteral och parenteral

Medicinsk konsekvens

Risken för blödningar ökar.

Rekommendation

Försiktighet rekommenderas när patienter behandlas med både klopidogrel och serotoninåterupptagshämmare p.g.a. den ökade risken för blödningar. Om kombinationen inte kan undvikas överväg tillägg av pantoprazol, H2-blockare (ej cimetidin) eller misoprostol för gastroprotektion.

Mechanism

Synergistic inhibitory effect on platelet aggregation.

Background

In a retrospective cohort study including in total 27 058 patients, the risk for bleeding after discharge after myocardial infarction was investigated. Use of an SSRI and ASA or clopidogrel or both was associated with an increased risk of bleeding among patients following acute myocardial infarction, beyond the risk associated with the antiplatelet therapy alone. The HR for bleeding was 2.35 (95%CI 1.61-3.42) in patients using SSRI, ASA and clopidogrel compared to patients using only ASA. Among patient treated with low dose acetylsalicylic acid + SSRI the HR was 1.42 (95% CI 1.08-1.87). Compared with ASA + clopidogrel alone, the HR was 1.57 (95% CI 1.07-2.32) for patients taking ASA + clopidogrel + SSRI (1).

A randomized, double-blind, crossover trial in 15 healthy volunteers found that fluvoxamine attenuated the laboratory response to clopidogrel, possibly through inhibition of CYP2C19, whereas citalopram did not affect this response (2). All subjects had a good laboratory response to clopidogrel, with a mean aggregation of 23.5 ± 3.2% and a mean platelet reactivity index of 47.7 ± 3.9% (p<0.001 compared with baseline for both methods) (22). Laboratory response to clopidogrel was significantly attenuated in the presence of fluvoxamine compared with the response in the presence of citalopram as tested both by aggregometry (32.3 ± 4.2% vs 23.4 ± 3%, p=0.04) and by vasodilator-stimulated phosphoprotein phosphorylation (52.7 ± 5.1% vs 35.9 ± 4.2%, p=0.02) (2). Both fluvoxamine and citalopram tended to reduce adenosine diphosphate-induced aggregation: 80.8 ± 3.4% at baseline, 67.3 ± 6.3% while receiving citalopram, and 65.8 ± 6.4% while receiving fluvoxamine (2).

› Visa inte hela bakgrundstexten

Referenser › Dölj referenser

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C0 hydroxizin - citalopram

Visa all info | Skriv ut | Kontakta oss

hydroxizin
Enteral och parenteral

citalopram
Enteral och parenteral

Medicinsk konsekvens

Båda läkemedlen kan öka QTc-intervallet och det finns risk för Torsade de Pointes, särskilt hos patienter med riskfaktorer för Torsade de Pointes.

Rekommendation

Om läkemedlen kombineras hos patienter med riskfaktorer för Torsade de Pointes bör lägsta effektiva dos användas, elektrolyter monitoreras och vid behov korrigeras. EKG bör kontrolleras före samt efter insättning av kombinationen. Kombinationen bör undvikas om QTc-intervallet före insättning är 480 ms eller längre. Samtidig behandling bör avslutas om QTc ökat med 60 ms eller mer efter insättning eller om QTc är 500 ms eller längre. Risken för Torsade de Pointes varierar mellan individer och viktiga riskfaktorer är långt QT-syndrom, strukturell hjärtsjukdom, bradykardi, sepsis, elektrolytrubbningar (hypokalemi, hypokalcemi och hypomagnesemi) och nedsatt läkemedelselimination. Behandling med diuretika eller diarrésjukdom kan orsaka hypokalemi. Kvinnligt kön och ålder över 65 år är också associerat med en ökad risk.

Mechanism

Additive prolongative effect on QT-time.

Background

Hydroxyzine has been associated with prolonged QT-time and cases of Torsades de Pointes (1,2,3,4,5). European Medicines Agengy's Pharmacovigilance Risk Assessment Committee (PRAC) states that hydroxyzine use must be avoided in patients who already are taking other medicines that increase the risk of QT prolongation (3). › Visa inte hela bakgrundstexten

Referenser › Dölj referenser

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B4 atorvastatin - klopidogrel

Visa all info | Skriv ut | Kontakta oss

atorvastatin Enteral och parenteral

klopidogrel Enteral och parenteral

Medicinsk konsekvens

Atorvastatin kan minska aktiveringen av klopidogrel något.

Rekommendation

Ingen dosjustering nödvändig.

Mechanism

Clopidogrel is a prodrug which needs to be activated by the CYP3A4 enzyme. Atorvastatin is a also a substrate of this enzyme. Atorvastatin may have minor effect on metabolic activation of clopidogrel. › Visa inte hela mekanismtexten

Background

Platelet aggregation was measured in 19 atorvastatin, 9 pravastatin and 16 not statin treated patients receiving clopidogrel. Atorvastatin but not pravastatin attenuated the antiplatelet activity of clopidogrel. (2)

Flow cytometry measurement of ADP-stimulated expression of P-selectin on platelets was used as a marker for the antiplatelet effect of clopidogrel in 47 clopidogrel treated PTCA/stenting patients. Atorvastatin and simvastatin reduced the inhibitory effect of clopidogrel. In three patients there were almost no effect. (1)

In an epidemiological database study it has been concluded that the benefits of clopidogrel can also occur in patients receiving atorvastatin. No differences were found in the clinical outcomes of patients (883 received atorvastatin + clopidogrel, 693 receiving atorvastatin) with acute coronary syndromes. Atorvastatin-clopidogrel combination was associated with decrease in mortality and stroke. (3)

Atorvastatin (20 mg), fluvastatin (20 mg), lovastatin (20 mg), pravastatin (20 mg), simvastatin (20 mg), or carivastatin (0.3 mg) did not influence inhibitiooof platelet aggregation of high dose (600 mg) clopidogrel in a placebo controlled study in 77 patients. (4)

Atorvastatin or simvastatin for at least 4 weeks did not impair the inhibition of ADP-induced platelet aggregation in patients receiving 600 mg (high loading dose) clopidogrel. (5)

Atorvastatin or pravastatin did not influence the clopidogrel-induced inhibition of platelet activation in acute coronary syndrome patients (atorvastatin 10 mg n=21, pravastatin 40 mg n=24: clopidogrel n= 30, controls without clopidogrel n=15). (6)

Statins in general and atorvastatin in particular did not affect the ability of clopidogrel to inhibit platelet flunction in patients undergoing coronary setting. (7)

Atorvastatin 20 mg for 5 weeks did not influence the clopidogrel induced platelet aggregation inhibition or reduction of the membrane expression of P-selectinand CD40L induced by ADP in 51 clopidogrel treated (375 mg loading dose followed by 75 mg/d for at least 3 months) acute coronary syndrome patients. (8)

Concomitant statin treatment has been shown to even improve platelet inhibition compared to clopidogrel given alone. (9)

Platelet function was tested in 21 healthy volunteers receiving clopidogrel 75 mg/d for 10 weeks. Simvastatin (20 mg/day for 1 week) and fluvastatin (80 mg/d for 1 week) reduced the efficacy of clopidogrel whereas pravastatin (40 mg/d for 1 week), rosuvastatin (10 mg/d for 1 week), and atorvastatin (20 mg/d for 1 week) had no effect. (10)

A clinical trial in 4162 patients with an acute coronary syndrome randomly assigned in a 1:1 fashion to pravastatin 40 mg or atorvastatin 80 mg daily found no evidence of interaction in the clopidogrel/no clopidogrel subgroup for the primary end point (interaction P = .65) (primary end points: death from any cause, myocardial infarction, documented unstable angina requiring rehospitalization, revascularization with either percutaneous coronary intervention or coronary artery bypass grafting, or stroke). At 30 days, there was a trend for less occurrence of the primary end point in patients randomized to atorvastatin compared with pravastatin, irrespective of whether they were taking clopidogrel. This becomes significant at 2-year follow-up in clopidogrel-treated patients (21.66 % vs 26.18% P = .0091). (11)

In a subanalysis of the TRITON-TIMI 38 study there was no influence of concomitant use of statins (or calcium-channel blocker) on clinical outcome in patients treated with either clopidogrel or prasugrel (12).

A small prospective, randomized, nonblind, controlled trial evaluated the effects of clopidogrel on platelet function upon coadministration with atorvastatin and could not find differences in platelet function and the levels of platelet activation markers, ischemic events in subsequent 6 months or bleeding events between the active and control groups (13). › Visa inte hela bakgrundstexten

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B4 levotyroxin - metformin

Visa all info | Skriv ut | Kontakta oss

levotyroxin Enteral (peroral)

metformin Enteral (peroral)

Medicinsk konsekvens

Serumnivåerna av TSH kan minska och blodglukosnivårerna öka.

Rekommendation

Interaktionens kliniska betydelse är inte fastställd. Monitorera tyroideafunktionen och blodglukosnivåerna vid inledning och avslutande av samtidig behandling.

Mechanism

Unknown.

Background

In a 1 year retrospective study metformin treatment (1747 ± 611.2 mg/day) resulted in a significant decrease in serum TSH levels by 38% (from 1.45 ± 0.53 to 1.01 ± 1.12 mU/l) in 71 diabetic patients recieving L-thyroxine (L-T4) at substitution doses (88.7 ± 15.4 µg/day) independently of their basal TSH value. In 203 diabetic patients who started metformin treatment (1735 ± 659.8 mg/day) at recruitment but no L-T4 substitution the decrease in TSH was significant only in those patients with a basal-high-normal serum TSH. No change in TSH levels was observed in the control group (n=119) who did not recieve either metformin or L-T4 (1).

Initiation of metformin treatment in 4 patients with chronic hypothyroidism on fixed doses of L-T4 for several years caused suppression of TSH to subnormal levels without clinical symptoms of hyper thyroidism in any patients. There was no change in free T4 or free T3 in one patient (2).

Eight obese, postmenopausal women with type 2 diabetes and primary hypothyroidism on stable doses of thyroxine replacement treatment were treated with metformin 1,700 mg daily for 3 months. Basal TSH significantly decreased from 3.11 ± 0.50 to 1.18 ± 0.36 µUI/ml. In two of the patients TSH was suppressed below normal.Three months after metformin withdrawal mean TSH was significantly higher than after metformin (2.21 ± 0.37 µUI/ml), but not different from basal TSH. The mean free T4 increased from 1.23 ± 0.06 to 1.32 ± 0.04 ng/dl (not significant) during metformin administration and decreased after metformen withdrawal (3).

In 29 diabetic, euthyroid patients on L-T4 substitution a significant TSH decrease (from 2.37 ± 1.17 to 1.41 ± 1.21 mIU/l) was observed after 1 year on metformin treatment. Also in the group with untreated hypothyroidism (n=18) TSH was significantly decreased after 1 year on metformin. No significant change in free T4 was observed in either group (4).

The producer of levothyroxine informs that levothyroxine may reduce the effect of drugs that decrease blood glucose levels. Blood sugar levels are raised and dosage of anti-diabetic agents may require adjustment (5).

However, in 13 patients recieving metformin 1000 mg twice daily for six months, but no levothyroxine suppression, metformin did not suppress thyrotropin levels (6). › Visa inte hela bakgrundstexten

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B3 kalcium - omeprazol

Visa all info | Skriv ut | Kontakta oss

kalcium Enteral (peroral)

Kalcipos-D (Tuggtablett)

omeprazol Enteral (peroral)

Medicinsk konsekvens

Absorbtionen av kalcium kan minska vid samtidig behandling. Vid långtidsbehandling, framförallt när höga doser protonpumpshämmare används under flera år, ökar risken för frakturer.

Rekommendation

Interaktionens kliniska betydelse är ännu ej fastställd. Överväg att dubblera den dagliga kalciumdosen (utan att öka D-vitamindosen) vid samtidig behandling.

Mechanism

The change in pH dependent disintegration and dissolution of calcium carbonate by increased gastric pH related to PPI treatment.

› Visa inte hela mekanismtexten

Background

A randomised, douple-blind, cross-over study in 18 elderly women found that omeprazole decreased the absorption of substituted calcium (carbonate; total dose of 500 mg/day) by about 40-60% (1). The mechanism of this interaction was thought to be the change in pH dependent disintegration and dissolution of calcium carbonate by increased gastric pH related to omeprazole treatment (1).

A study found that use of a proton pump inhibitor omeprazole is associated with low bone mineral density in maintenance haemodialysis patients (7).

In coherence with the above described studies, several epidemiologic studies have observed an association between a long-term proton pump inhibitor therapy (particularly a high-dose regimen of PPI) and an increase in fracture risk (2,3,4,5,6). The overall fracture risk has been found to be increased (odds ratio OR, 1.18) as well as the risk for hip fractures (OR, 1.44-1.45), and the risk for spine fractures (OR 1.60) (2,3). The risk of (hip) fracture was significantly increased among patients prescribed long-term high-dose PPIs (Adjusted OR, 2.65) (3). In addition, the strength of the association increased with increasing duration of PPI therapy (Adjusted OR for 1 year, 1.22; for 2 years, 1.41; for 3 years, 1.54; and for 4 years, 1.59) (3). Intriguingly, in the study by Targownik and colleagues (4), a relation between the use of proton pump inhibitors and hip fractures was only observed after 5 years of therapy. They found that that use of proton pump inhibitors was associated with increased risk of an osteoporosis-related fracture (vertebral, wrist or hip fracture) (odds ratio OR, 1.92). In particular, there was a significant increase in the risk of hip fracture after 7 years of exposure to proton pump inhibitors (OR, 4.55) (4). More-over, use of PPIs is associated with an increased risk of fracture when taken alone or in combination with bisphosphonates (9,10).

In conclusion there are 7 large, well-designed studies which have consistently reported an association between the use of proton pump inhibitors and fractures and that this association appears to be both dose-and duration-dependent. One mechanism of the phenomena may be a decrease in calcium absorption in patient with concomitant PPI. However, some authors have regarded the clinical risk of fracture as limited, and whether these associations represent a genuine risk to patients have been argued (8). › Visa inte hela bakgrundstexten

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