

Is use of medication associated with blood levels of micronutrients?

A cross-sectional study of a geriatric population of hospital Gelderse Vallei

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Introduction

Vitamin B12 and vitamin D deficiency are common in elderly people. Estimates for different populations suggest prevalences of about 25% and 50-80% respectively.

Micronutrient deficiencies may result in serious health problems which can be treated or prevented if recognized in time. A well known example is metformin-induced neuropathy, caused by vitamin B12 deficiency, which can be mistaken for the irreversible diabetic neuropathy.

Causes of deficiencies are several. Also medication might be a contributing factor, but knowledge about drug-nutrient associations is far from complete.



Objective

Main objective of this cross-sectional study is to investigate associations between use of medication and micronutrient blood levels in a geriatric outpatient population of the Dutch hospital Gelderse Vallei in Ede.

We focus on vitamin B12 and vitamin D blood levels. Medications of interest are metformin next to the four most frequently used drugs in the study population: proton pump inhibitors, beta blockers, statins and ACE inhibitors. Furthermore, we will give an overview of prevalences of the micronutrients vitamin B12, vitamin D, vitamin B1, vitamin B6, folic acid, sodium, potassium and calcium.

Methods

Literature search

Subject: associations between use of drugs and micronutrient blood levels

Database: PubMed

Cross-sectional study

Study population: 512 geriatric outpatients of the hospital Gelderse Vallei in Ede

Data: electronic patient records

Time period: January 1st - November 15th 2011

Statistical software: SPSS 15.0

Method of data analysis: ANCOVA

Effect measure: difference between adjusted means

P-value: 2-sided

Results

90% Of the patients of our study population takes one or more medications. Mean number of drugs used per geriatric outpatient is 5.6. Some details of micronutrient prevalences are illustrated in table 1.

The mean differences in micronutrient blood levels between users and nonusers of a specific drug plus corresponding p-values are illustrated in table 2 and 3.

A. Medication

Table 1. Use of medication in 512 outclinic geriatric patients of hospital Gelderse Vallei in the time period January 3 – November 15, 2011

| Ranking | Medication | % Users (N=512) | |
|---------|------------------------|-----------------|-------------------------------|
| | | all | Supplement users ² |
| 1 | proton pump inhibitors | 36.3% | |
| 2 | beta blockers | 32.2% | |
| 3 | statins | 27.9% | |
| 4 | ACE inhibitors | 21.1% | |
| 11 | metformin | 11.7% | |

C1. Use of medication and vitamin B12 levels

Table 3. Exposure to medication and vitamin B12 status in 512 geriatric outclinic patients of the Dutch hospital Gelderse Vallei: analysis of covariance of log transformed vitamin B12 blood levels

| Medication (yes, no) | Vitamin B12 blood level (nmol/l) | |
|----------------------|---------------------------------------|-----------|
| | mean difference (exposed – unexposed) | p - value |
| Metformin | - 51 | 0.002 |
| PPI's ¹ | - 33 | 0.096 |
| Beta blockers | - 29 | 0.070 |
| Statins | + 22 | 0.246 |
| ACE inhibitors | - 28 | 0.083 |

¹ Proton pump inhibitors
² Time period electronic patient records: August 1 – October 25, 2011
³ Time period electronic patient records: August 1 – November 15, 2011

B. Use of supplements and prevalences of vitamin B12, D and B6

Table 2. Prevalences of micronutrient categories in geriatric outclinic patients of the Dutch hospital Gelderse Vallei (January 3 – November 15, 2011)

| Micronutrient | Category ¹ | Cut-off level | Geriatric outpatients (%) | | |
|---------------------------------|-----------------------|---------------|---------------------------|------|------|
| | | | all | no | yes |
| Vitamin B12 (N=490) | 1 | <150 pmol/l | 4.3 | 5.8 | 1.2 |
| | 2 | 150-500 | 79.2 | 80.4 | 76.7 |
| | 3 | >500 | 16.5 | 13.8 | 22.1 |
| Vitamin D (N=190) | 1 | <35 nmol/l | 48.8 | 55.5 | 34.8 |
| | 1.5 | 50-75 | 33.7 | 32.8 | 35.8 |
| | 2 | >75-250 | 17.4 | 11.8 | 30.2 |
| 3 | >250 | 0 | 0 | 0 | |
| Vitamin B6 ² (N=112) | 1 | <35 nmol/l | 0 | 0 | 0 |
| | 2 | 35-110 | 46.8 | 48.6 | 43.6 |
| | 3 | >110 | 53.2 | 51.4 | 56.4 |

¹ Micronutrient blood levels category 1: deficient, category 2: normal, category 3: increased
² ATC-coded supplements
³ Not routinely measured in study population

C2. Use of medication and vitamin D 25(OH) levels

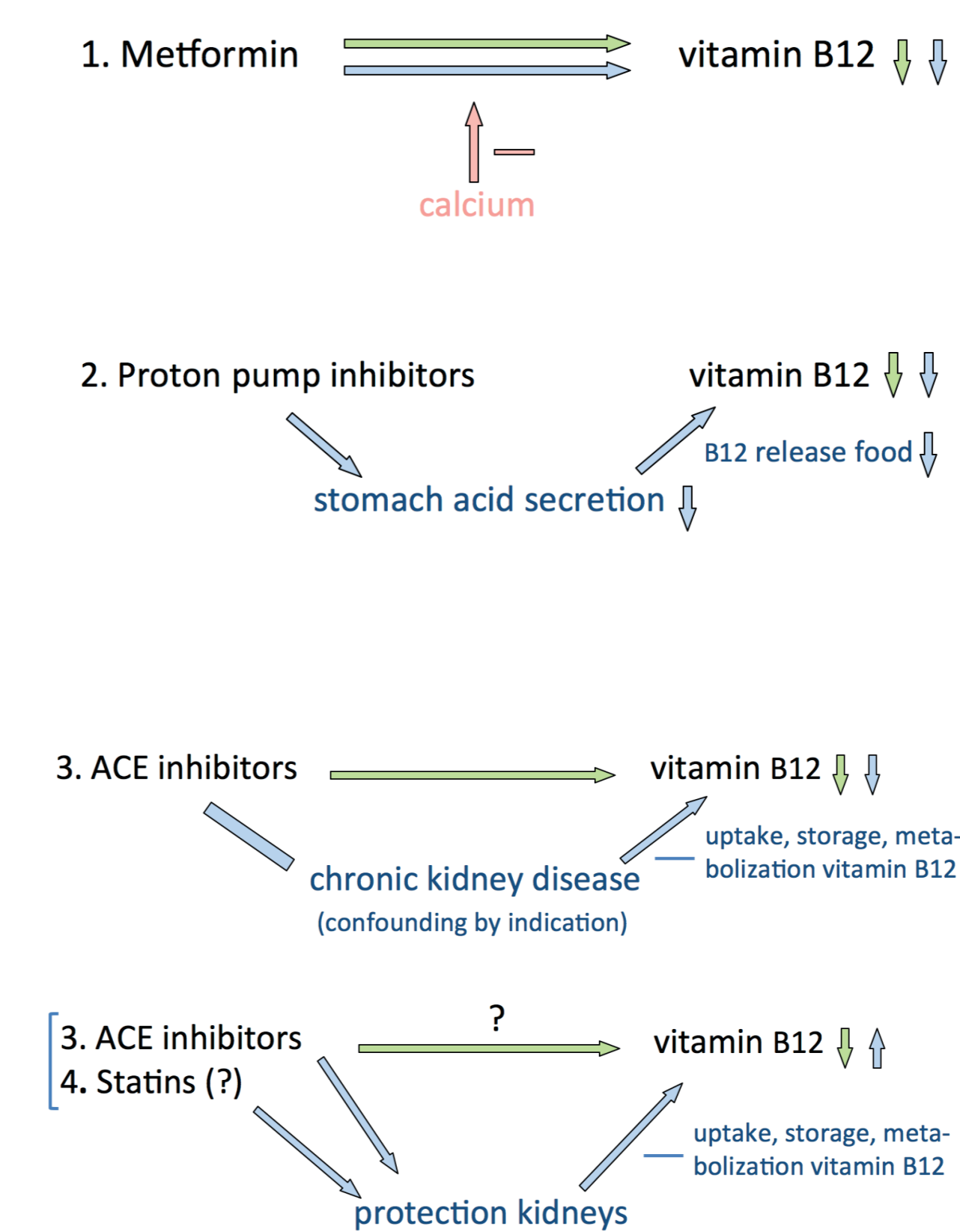
Table 4. Exposure to medication and vitamin D 25(OH) status in geriatric outclinic patients of the Dutch hospital Gelderse Vallei: analysis of covariance of square root transformed vitamin D 25(OH) blood levels

| Medication (yes, no) | Sub-population | Vitamin D 25(OH) blood level (nmol/l) | |
|----------------------|--------------------|---------------------------------------|-----------|
| | | mean difference (exposed – unexposed) | p - value |
| Metformin | N=154 ² | - 23.1 | 0.031 |
| PPI's ¹ | N=154 | + 11.3 | 0.053 |
| Beta blockers | N=154 | + 9.7 | 0.109 |
| Statins | N=154 | + 11.8 | 0.108 |
| ACE inhibitors | N=190 ³ | + 5.9 | 0.036 |

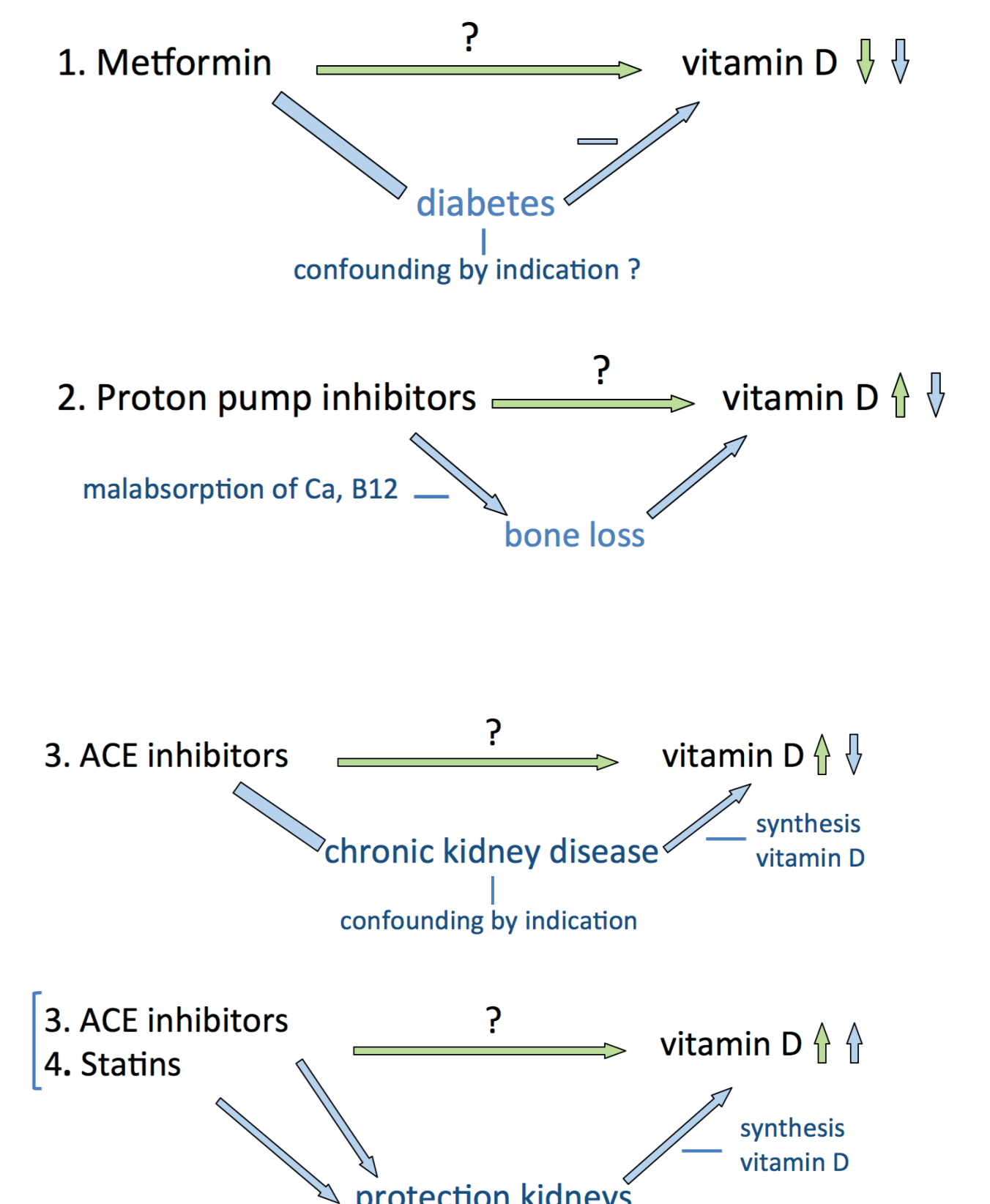
¹ Proton pump inhibitors
² Time period electronic patient records: August 1 – October 25, 2011
³ Time period electronic patient records: August 1 – November 15, 2011

Discussion

Use of medication and vitamin B12 blood levels



Use of medication and vitamin D 25(OH) blood levels



Green coloured: results cross-sectional study; blue coloured: results literature search

Table 5. Strengths and limitations of a cross-sectional study about the association between use of medication and micronutrient blood levels in a Dutch geriatric hospital population

| Limitations | Strengths |
|--|---|
| Entanglement of medication with its indication (disease) | Systematic approach |
| Cross-sectional design | Literature search |
| Registration of supplement use | Use of supplements as a covariate in ANCOVA |
| Vitamin D subpopulations ¹ | |

¹ Vitamin D 25(OH) was routinely measured in study population after July 2011, while vitamin B12 was routinely measured during the whole study period, from January 3 until November 15, 2011

Conclusion

High prevalence of vitamin D deficiency in study population

Clinical relevance of vitamin D and B12 deficiency

Possible associations between medication use and vitamin B12 and vitamin D blood levels

Polypharmacy in elderly

Reasons to continue research

