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**No reductions in vitamin concentrations or nutritional indices in early Alzheimers's disease without vascular disturbance.**

Thomas Bøhmer MD, PhD.

Ingun Ulstein MD, PhD.

Oslo University Hospital, Oslo, Norway.

# Importance of vitamins

- A,E, C- antioxidant defence
- B<sub>1</sub>- acute dementia, eg. Wernicke, reversible
  - cofactor
  - transcriptional regulator of enzymes
- B<sub>6</sub>, B<sub>12</sub>, Folate and C
  - C1- metabolism, conversion of methionin to homocystein
- B<sub>6</sub> and B<sub>12</sub> - neuronal function
  - production of neurotransmitters and nucleic acids

**Ascorbic acid, PLP (B6), $\alpha$ -tocopherol and thiamine-PP in controls (MMSE 27) and in Alzheimer patients (MMSE 17) (Mean, SD.)**

	<b>Controls</b>	<b>Alzheimer</b>	<b>P</b>
<b>Ascorbic acid (45-92 umole/l)</b>	<b>80 (28)</b>	<b>44 (25)</b>	<b>0.01</b>
<b>S-PLP (15-160 nmol/l)</b>	<b>90.2 (14)</b>	<b>24.8 (3.3)</b>	<b>0.060</b>
<b><math>\alpha</math>-tocopherol (16-36 umol/l)</b>	<b>37.6 (9.6)</b>	<b>25.2 (11.5)</b>	<b>0.005</b>
<b>Thiamine-PP (55-125 nmol/l)</b>	<b>86.0 (12.5)</b>	<b>65.8 (27.5)</b>	<b>0.014</b>

# Vitamins deficiency causing Alzheimer disease ?

- **present early in diseased patients or prior to disease**
- **before weight loss**
- **without other diseases**
  - **vascular,**
  - **neurological,**
  - **psychiatric**

## Background characteristics (table 1A)

Mean (SD)	Controls N=63	MCI N=25	AD N=48	p -value
Age years	73 (6.2)	69 (7.0)	72( 7.9)	0.06
BMI (weight/h <sup>2</sup> )	25.9 (3.5)	24.3	23.6 (3.4)	0.04
Diastolic BP	82.6 (12.2)	77.0 (9.0)	87.0 (29)	0.04
Vascular score (0-16)	1.02 (1.2)	0.74 (0.96)	0.67 (1.0)	0.17
Alcohol units/week	5.3 (3.5)	4.3 (4.9)	2.3 (3.6)	0.002

## Background characteristics (table 1B)

Mean (SD)	Controls N=63	MCI N=25	AD N=48	p- value
Hgb (11.7-15.3 g/100 ml)	13.8 (1.2)	14.0(1.0)	14.0 (1.2)	0.47
CRP micro (0-4 mg/l)	3.2 (3.1)	1.5 (1.2)	1.7 (2.3)	0.28
Homocystein (5-15 umol/l)	12.1 (4.2)	11.0 (2.3)	12.8 (4.4)	0.08
Thyroxine (8-21pmol/l)	16.4 (3.0)	17.1 (3.2)	16.5 (2.0)	0.58
Cholesterol. (3.9-7.8 mmol/l)	5.6 (1.2)	5.7 (1.0)	6.0 (1.2)	0.33

## Cognitive testing results, mean (SD), in healthy controls, MCI, and demented patients

	Controls N=63	MCI N=25	AD N=48	p-value
MMSE	29.1 (1.0)	27.4 (1.8)	24.3 (3.3)	<0.001
Clock-drawing test	4.7 (0.6)	4.2 (1.0)	3.7 (1.2)	<0.001
CERAD-immediate memory	20.7 (3.9)	17.7 (4.9)	12.8 (5.1)	<0.001
CERAD-delayed recall	6.9 (1.8)	3.9 (2.8)	1.6 (1.8)	<0.001
TMTA	50 (23)	53 (31)	66 (33)	0.018
TMTB	137 (92)	136 (64)	162 (83)	0.33

## Vitamin concentrations, mean (SD) in healthy controls, MCI, and demented patients (AD)

Vitamin name Normal values	Control N=63	MCI N=25	AD N=48	p-value
Vit B1, TPP (95-200 nmol/l)	157 (29)	161 (35)	161 (32)	0.72
Vit B6, P6-P (15-160 nmol/l)	57 (63)	51 (27)	58 (43)	0.94
Folate (>10 nmol/l)	22.7 (9.4)	25.7 (10)	22.9 (11.1)	0.44
Vit- B12 (150-650 pmol/l)	407 (159)	427 (116)	397 (204)	0.053
Vit –C (45-100 umol/l)	63 (18)	61 (16)	63 (29)	0.90
Vit A (retinol 1.2-3.6 umol/l)	2.3 (0.58)	2.2 (0.5)	2.3 (0.5)	0.43
Vit E ( $\alpha$ -tocopherol 17-45 mol/l)	36 (6.3)	36 (6.9)	36 (8.2)	0.89
25- OHvit.D (37-131 nmol/l)	73 (18)	61 (19)	65 (20)	0.68



## Intake of vitamins and supplements the last month, N (%)

	All N=132	Controls N=63	MCI N=25	AD N=48
Multivitamins	33 (24)	19 (30)	6 (24)	8 (17)
Vit B1 and B6	13 (9.4)	7 (11)	2 (8)	4 (8)
TrioBe	9 (6.5)	2 (4)	4 (16)	6 (12)
Vit C	19 (13.8)	9 (14)	1 (4)	9 (18)
Vit D	13 (9.4)	3 (5)	4 (16)	6 (12)
Omega 3 or fishoil	62 (45)	30 (48)	15 (60)	17 (35)
Any vitamins	84 (61)	39 (62)	20 (80)	25 (51)

# Conclusions

1. There was no vitamin deficiencies in our patients with MCI or early AD.
2. Vitamin substitution generally seems therefore not to be a promising treatment modality.
3. Reductions in vitamin concentrations seem not to be useful as biomarker .
4. The vitamin reductions we ascribed earlier might have been caused by CRF increases.

# Percentage changes in micronutrients with increasing increments of CRP. Error bars represent the upper and lower quartiles.

Zinc

Copper

Vitamin E

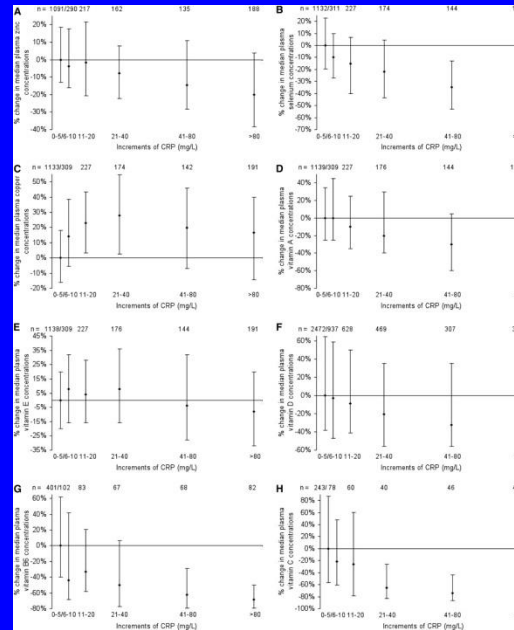
Vitamin B-6

Selen

Vitamin A

Vitamin D

Vitamin C



CRP 21-40



Andrew Duncan et al. Am J Clin Nutr 2012;95:64-71

# Discussion

1. Normal vitamin concentrations in early AD was also found by Marcel GM. J Alzh Dis. 2014.
2. They found however, reductions in n-3- and n-6 polyunsaturated fatty acids which might be caused by patients with more advanced disease (MMSE-range 20 -30)
3. Some MCI subgroups may benefit from substitution therapy eg.B-vitamins and w-3 fatty acids as recently suggested (Jerneren F. Am J Clin Nutr doi:10.3945 ajcn.114.103283)

## Factors indicating vascular disease (score 0-16).

- **Significant hypertension**
- **Coronary heart disease**
- **Myocardial infarction**
- **Atrial fibrillation**
- **Valvular heart disease**
- **Pre-cerebral arterial stenosis > 75 %**
- **Cerebral infarction/bleeding**
- **Stroke, later strokes**
- **Unilateral infarction /bleeding**
- **Unilateral hyperreflexia/spasticity**
- **Aphasia/dysphasia**
- **Dysarthria**
- **Dysphagia**
- **Epilepsy**
- **Diabetes mellitus**

# Biomarkers

Clifford J Lancet Neurology 2013: Update of hypothetical model of Alzheimer's disease biomarkers:

Ab- amyloid deposition, PGD PET  
Increased CSF levels of total tau and phosphorylated tau

Mousavi M et al. Dementia Geriatr Cogn Disor Extra 2014 Serum metabolomic biomarkers of dementia:

3-4,hydroxybutanoic acid,  
docosapentanoic acid,  
Uric acid