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# Supplementation With B and D Vitamins Improves Metabolic Bone Markers, Homocysteine and Influences Telomere Length

**Wolfgang Herrmann[1] Susanne H. Kirsch[1] Vera Kruse[1] Rudolf Eckert[2] Stefan Gräber[3] Jürgen Geisel[1] Rima Obeid[1],Irene Pusceddu[1,4], Ulrich Hübner[1], Marion Bodis[1], and Markus Herrmann[4]**

*[1]Departmentsof Clinical Chemistry, Saarland University Hospital, Homburg, Germany*
*[2]Geriatric Center, Marienkrankenhaus, St. Wendel, Germany*
*[3]Medical Biometry, Epidemiology, andInformatics, Saarland University Hospital, Homburg, Germany*
*[4]Department of Clinical Pathology, District Hospital Bolzano, Italy*

**Background:** Vitamin D and vitamin B deficiency are common in elderly subjects and are important risk factors for osteoporosis and age-related diseases. Supplementation with these vitamins is a promising preventative strategy. The objective of this study was to evaluate the effects of vitamins D3 and B supplementation on bone turnover, homocysteine metabolism and telomere length in elderly people.

**Methods:** Healthy subjects (n=93; >54 years) were randomly assigned to receive either daily vitamin D3 (1200 IU), folic acid (0.5 mg), vitamin B12 (0.5 mg), vitamin B6 (50 mg), and calcium carbonate (456 mg) (group A) or only vitamin D3 plus calcium carbonate (group B) in a double blind trial. We measured at baseline and after 6 and 12 months of supplementation vitamins, metabolites, bone turnover markers and telomere length.

**Results:** At baseline mean plasma 25-hydroxy vitamin D [25(OH)D] was low (40 or 30 nmol/L) and parathormone (PTH) was high (63.7 or 77.9 pg/mL). 25(OH)D and PTH correlated inversely. S-Adenosylhomocysteine (SAH) and S-adenosyl methionine (SAM) correlated with bone alkaline phosphatase (BAP), sclerostin, and PTH. One year vitamin D3 or D3 and B supplementation increased plasma 25(OH)D by median 87.6% (group A) and 133.3% (group B). PTH was lowered by median 28.3% (A) and 41.2% (B), BAP decreased by 2.8% (A) and 16.2% (B), osteocalin by 37.5% (A) and 49.4% (B), and tartrate-resistant-acid-phosphatase 5b (TRAP5b) by 6.1% (A) and 36.0% (B). Median total homocysteine (tHcy) was high at baseline (group A: 12.6, group B: 12.3 µmol/L) and decreased by B vitamins supplementation (group A) to 8.9 µmol/L (29.4%). tHcy lowering had no additional effect on bone turnover. At baseline, age- and gender-adjusted relative telomere length (RTLresp.T/S) correlated with total folate and 5-methyl-tetrahydrofolate (5MTHF). Subjects with RTL above the median had higher concentrations of total folate and 5MTHF. At the study end RTL correlated in group A with methylmalonic acid (MMA) and choline and in group B with dimethylglycine (DMG). Subjects in the group A with RTL above the median had lower MMA and higher choline.

Vitamin supplementation increased LINE-1 methylation as a surrogate marker for global DNA methylation in the group A but reduced it in the group B. There was no correlation between RTL and LINE-1 methylation at baseline. Subjects with high tHcy had compared with those having normal tHcy a reduced LINE-1 methylation, in a metabolic picture in agreement with an inhibited transmethylation. Multiple backward regression analysis revealed, that baseline tHcy and 5MTHF are significant predictors of RTL; after vitamin supplementation LINE-1 methylation predicted RTL. LINE-1 methylation after vitamins supplementation was predicted of 5MTHF or Hcy.

**Conclusions:** A) Supplementation with vitamin D normalizes PTH in serum that lowers bone turnover, which is seen as improvement of bone metabolism.B) Furthermore, B vitamins supplementation normalizes high HCY which contributes to an increase in bone stiffness by normalization of bone cross-linking, which may modulate the osteoporotic risk and improves bone health.C) Telomeres are related to cellular aging and osteoporosis. Our findings show that telomere biology is influenced by vitamin B status. D) The effect of folate metabolism on telomere length appears to be complex.E) The results suggest a possible effect of B vitamins for telomere biology in cells. Suboptimal B vitamins status and hyperhomocysteinemia are associated with altered DNA methylation and telomere length.