Effect of combined B-vitamin supplementation on bone mineral density in adults: a 2-year randomised controlled trial

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Introduction
➢ Osteoporosis, a musculoskeletal condition characterised by low bone mineral density (BMD) and deterioration of bone microarchitecture, affects over 200 million people worldwide, with significant adverse health and economic impacts.1
➢ Large cohort studies report strong positive associations between homocysteine (Hcy) concentrations and risk of osteoporotic fracture and/or low BMD,2,3, with an estimated 4% increased risk of fracture for every 1µmol/L increase in Hcy. Likewise, a higher risk of hip fracture was reported in Norwegian women with lower (< 2.9 nmol/L) compared to higher (> 6.6 nmol/L) serum folate concentrations.2
➢ Other evidence links low vitamin B12 status with poorer bone health, with data from the Framingham Osteoporosis Study showing that plasma B12 concentrations < 148pmol/L were associated with significantly lower BMD.4
➢ There is also some, albeit limited, observational evidence showing associations of dietary intakes or status of vitamin B6 and riboflavin with BMD. Therefore B-vitamin supplementation may be beneficial in maintaining BMD, but to date no previous randomised trial has investigated the effect of all four vitamins in this context.

Aim
➢ To investigate the effect of low-dose B-vitamin supplementation for 2 years on BMD in adults

Methods
Ulster University (n=120) University College Dublin (n=120)

Participant recruitment (n=240)
Inclusion criteria: Community-dwelling adults ≥50 years, not using B-vitamin supplements, low fortified food intake (≤4 portion(s)/week), no gastrointestinal diseases

Baseline (pre-intervention) & 24-months (post-intervention)
Anthropometrics, blood pressure measurements, hand grip strength, DXA bone scan, health & lifestyle questionnaire, dietary assessment (FFQ and 4-day food diary), blood sample (B-vitamin biomarker analysis) and cognitive assessments (MMSE, FAB, RBANS)

Randomisation

Active Placebo
Vitamin D 10µg

B-vitamin Treatment
Folic Acid 200µg, B12 10µg, B6 10mg, riboflavin 5mg, vitamin D 10µg

Data & biochemical analysis
Data analysis and B-vitamin biomarker analysis

Figure 1. OptiAge RCT Study Design

Results Summary
➢ B-vitamin supplementation for 2 years had no overall effect on BMD (Table 1), which declined in both groups by approximately 1% (ranging from ~0.7% to ~1.4%).
➢ In participants with lower baseline vitamin B12 status, B-vitamin supplementation decreased the extent of decline in BMD at the total hip (Figure 2a) and femoral neck (Figure 2b) over the 2-year period vs placebo.

Results

Table 1. BMD response to B-vitamins for 2 years

<table>
<thead>
<tr>
<th></th>
<th>Active Placebo (n=102)</th>
<th>B-vitamin Treatment (n=103)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>General</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>70.6 (69.1, 72.0)</td>
<td>68.7 (67.3, 70.1)</td>
<td>0.085</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>28.6 (27.6, 29.6)</td>
<td>28.2 (27.3, 29.1)</td>
<td>0.619</td>
</tr>
<tr>
<td>Sex, n (% male)</td>
<td>42 (41)</td>
<td>39 (38)</td>
<td>0.732</td>
</tr>
<tr>
<td><strong>BMD (g/cm²)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total hip</td>
<td>0.970 (0.941, 1.000)</td>
<td>0.968 (0.940, 0.996)</td>
<td></td>
</tr>
<tr>
<td>Post</td>
<td>0.962 (0.933, 0.991)</td>
<td>0.957 (0.928, 0.985)</td>
<td></td>
</tr>
<tr>
<td>Change</td>
<td>-0.009 (-0.013, -0.004)</td>
<td>-0.012 (-0.016, -0.007)</td>
<td>0.353</td>
</tr>
<tr>
<td>Femoral neck</td>
<td>0.891 (0.866, 0.917)</td>
<td>0.903 (0.878, 0.928)</td>
<td></td>
</tr>
<tr>
<td>Post</td>
<td>0.884 (0.859, 0.909)</td>
<td>0.895 (0.870, 0.921)</td>
<td></td>
</tr>
<tr>
<td>Change</td>
<td>-0.008 (-0.013, -0.003)</td>
<td>-0.007 (-0.012, -0.002)</td>
<td>0.938</td>
</tr>
<tr>
<td>Lumbar spine</td>
<td>1.120 (1.084, 1.156)</td>
<td>1.132 (1.093, 1.171)</td>
<td></td>
</tr>
<tr>
<td>Post</td>
<td>1.111 (1.076, 1.146)</td>
<td>1.117 (1.157, 1.110)</td>
<td></td>
</tr>
<tr>
<td>Change</td>
<td>-0.010 (-0.017, -0.003)</td>
<td>-0.014 (-0.020, -0.007)</td>
<td>0.170</td>
</tr>
</tbody>
</table>

Data shown as mean (95% CI) or %; Change shown as adjusted mean; Analyzed on an intention-to-treat basis.

Table 1. BMD response to B-vitamins for 2 years

Conclusions
➢ Low-dose B-vitamin supplementation for 2 years resulted in significant responses in B-vitamin biomarkers, but there was no overall corresponding effect on BMD within the total cohort.
➢ Improving B-vitamin status appears to have benefits in maintaining bone health specifically in adults with lower vitamin B12 status. Further studies are warranted to confirm this finding.

References

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