Multivitamin Supplements for delaying HIV Disease Progression and Mortality

CITATION

RESEARCH QUESTION
Does multivitamin supplements delay the progression of HIV disease and mortality?

THE STUDY DESIGN
Randomized double blind placebo controlled trial

STUDY SETTING
Dar es Salaam, Tanzania
April 1995 – August 2003

PARTICIPANTS
Included: HIV-infected pregnant women
Excluded: No mention of it was made

INTERVENTIONS & OUTCOMES

Supplementary Appendix available at www.nejm.org

Interventions
All women received standard doses of antenatal folic acid and iron.
**Multivitamins:**
20 mg of vitamin B1, 20 mg of vitamin B2, 25 mg of vitamin B6, 100 mg of niacin, 50 µg of vitamin B12, 500 mg of vitamin C, 30 mg of vitamin E, and 0.8 mg of folic acid.

**Vitamin A:**
30 mg of beta-carotene plus 5000 IU of preformed vitamin A

**Multivitamins & vitamin A:**
Same doses listed above

**Control:**
Placebo

Received a daily oral dose of one of the four regimens for the duration of the follow-up

**Outcomes**
Clinical disease progression, HIV-related complications, CD4+ cell counts, Viral load

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**RISK OF BIAS**
(Risk Scale: Low – Moderate – High)

**SELECTION BIAS:** Low – Moderate
HIV-infected pregnant women were randomly assigned in blocks of 20. Allocation concealment not reported.

**PERFORMANCE BIAS:** Low
(I.e what else happened that may have affected the result?)
All women received standard doses of antenatal folic acid and iron. Placebo controlled trial. All clinical and follow-up staff were unaware of the women’s treatment assignments.

**DETECTION BIAS:** Moderate
All clinical and follow-up staff were unaware of the women’s treatment assignments.

Defined Diarrhea and Dysentery. Stage of HIV/AIDS – WHO criteria.

Blood specimen (baseline and every six months) for the measurement of CD4+. A sample of 300 women was randomly selected for the measurement of viral load.

Cause of death was approximated by using verbal-autopsy techniques by conducting standardized interviews with relatives, reviewing medical records, or both.

Cause of death was ascertained in a blinded fashion.

**ATTRITION BIAS:** Low
The authors do not state the number of people that were lost to follow-up.

All analyses were conducted according to the intention to treat.

**STUDY FINDINGS**

<table>
<thead>
<tr>
<th></th>
<th>Placebo n = 267</th>
<th>Multivitamins n = 271</th>
<th>Multivitamins &amp; vitamin A n = 268</th>
<th>Vitamin A n = 272</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of events</td>
<td>No. of events RR (95%CI)</td>
<td>No. of events RR (95%CI)</td>
<td>No. of events RR (95%CI)</td>
</tr>
<tr>
<td>Progression to stage 4 or death from AIDS-related causes</td>
<td>83</td>
<td>67 0.71 (0.51-0.98)</td>
<td>70 0.80 (0.58-1.10)</td>
<td>79 0.88 (0.64-1.19)</td>
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<tr>
<td>Death from AIDS-related causes</td>
<td>66</td>
<td>52 0.73 (0.51-1.04)</td>
<td>60 0.91 (0.64-1.28)</td>
<td>65 0.93 (0.66-1.32)</td>
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<tr>
<td>Progression to stage 4</td>
<td>31</td>
<td>18 0.50 (0.28-0.90)</td>
<td>22 0.67 (0.39-1.15)</td>
<td>23 0.68 (0.40-1.17)</td>
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<tr>
<td>Progression to ≥stage 3</td>
<td>166</td>
<td>163 0.72 (0.58-0.90)</td>
<td>163 0.79 (0.64-0.98)</td>
<td>165 0.81 (0.65-1.00)</td>
</tr>
<tr>
<td>≥2-stage increase</td>
<td>145</td>
<td>131 0.66 (0.52-0.84)</td>
<td>133 0.74 (0.59-0.94)</td>
<td>134 0.74 (0.58-0.93)</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Placebo n = 267</td>
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<tr>
<td></td>
<td>Mean value</td>
<td>Mean difference (95%CI)</td>
<td>Mean difference (95%CI)</td>
<td>Mean difference (95%CI)</td>
</tr>
<tr>
<td>CD4+ cell count</td>
<td>449± 255</td>
<td>48 (10 to 85)</td>
<td>41 (4 to 77)</td>
<td>-15 (-45 to 14)</td>
</tr>
<tr>
<td>Viral load</td>
<td>4.67±0.86</td>
<td>-0.18 (-0.32 to -0.03)</td>
<td>-0.07 (-0.21 to 0.09)</td>
<td>-0.03 (-0.17 to 0.11)</td>
</tr>
</tbody>
</table>

**COMMENTS**
Multivitamins delayed the onset of disease progression. Adding vitamin A to the multivitamin supplement reduced the benefit of the latter regimen.

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