EFFECT OF SELENIUM SUPPLEMENTATION ON CD4 T-CELL RECOVERY AND MORBIDITY AMONG HIV-POSITIVE INDIVIDUALS IN RWANDA: A RANDOMIZED CONTROLLED TRIAL

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Background

- HIV infection compromises the nutritional status of infected individuals and poor nutritional status can accelerate progression of the disease.
- Selenium deficiencies, indicated by low plasma selenium concentrations, have been documented among HIV-positive individuals, particularly in areas of the world with low selenium levels in the soil as in much of Sub-Saharan Africa. However, evidence of the effect of selenium supplementation on viral load and CD4 counts from randomized clinical trials is limited.
- Three RCTs documenting the effect of daily selenium supplementation have produced mixed results. Additional evidence from other settings and populations is required to more accurately determine the effect of selenium supplementation on HIV progression in HIV-infected individuals.

Our RCT aimed to examine the effect of selenium supplementation on CD4 T-cell counts, viral suppression and quality of life among ART-naive individuals in Rwanda.

Methods

- We conducted a patient and provider blinded, randomized placebo-controlled clinical trial among 300 ART-naive individuals in Rwanda.
- Participants were recruited from three health facilities and eligibility criteria included:
  - HIV-infected adults (21 years of age or older);
  - Not being pregnant;
  - Being able to provide informed consent.
- Participants were randomized using a simple randomized block design to receive either 200 µg selenium or an identical placebo taken daily for 24 months (Figure 1).
- The study ran for 24 months and the primary outcome measure was change in CD4 T-cell count at 6, 12, 18 and 24 months.
- For analyses of the primary outcome, patients were censored after ART initiation.

Methods (continued)

- Secondary outcomes included:
  - Time to viral suppression; a composite of CD4 T-cell depletion to 350 cells/mm3 as confirmed by 2 consecutive measures, or start of ART, or the emergence of a documented CDC-defined AIDS-defining illness; mortality; and adverse events.
  - Baseline demographic and clinical characteristics were tabulated and compared using Fisher’s Exact test for dichotomous outcomes and Wilcoxon’s rank sum test for continuous outcomes.
  - All analyses were based on the intention-to-treat (ITT) approach using the randomized treatment assignment.
  - For the primary outcome, we used linear regression with generalized estimating equations (GEE) for the repeated measures.
  - Both time-to-event analyses (Cox proportional hazards regression and Kaplan-Meier curves) and simpler contingency table analyses were used to determine whether selenium supplementation could delay the initiation of ART.
- As self-reported adherence was measured over time, we used it as a time-varying covariate.

Results

- Three-hundred participants, randomized (151 to the selenium arm and 149 to placebo) had an average CD4 T-cell count of 555 cells/mm3.
- Seventeen participants were lost to follow-up, one non-AIDS death occurred among the 23 participants in the selenium arm and 8 (in placebo) women were time censored due to pregnancy and resulting ART initiation.
- Table 1 summarizes baseline characteristics of both treatment arms.
- Results of the GEE linear regression are summarized in Table 2.
- The rate of CD4 depletion was reduced by 43.8% among patients receiving selenium supplementation (95% Confidence Interval [95% CI] 74–87.9%).
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- The differences in CD4 depletion rates are shown in Figure 2A.

Methods (continued)

- Overall, we found no treatment effect for the composite outcome (hazard ratio: 1.00, 95% CI: 0.66-1.54) or viral suppression (Hodds Ratio [OR]: 1.38, 95% CI: 0.71-5.84), but the trial was underpowered for the composite outcome.
- No significant differences between treatment and placebo arms were noted across all adverse events.

Conclusion

- Among ART-naive HIV-positive adults in Rwanda, 24-month selenium supplementation was safe and significantly decreased the rate of CD4 T-cell depletion (as measured by rate of CD4 T-cell depletion).
- Evidence of a beneficial effect of ART initiation was more limited and may warrant more research.