Early initiation of antiretroviral therapy for individuals with HIV infection: A systematic review

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Background

The 2010 World Health Organization (WHO) guidelines recommend initiating antiretroviral therapy (ART) at a CD4 count of ≤350 cells/μL. Several countries use a threshold of ≤500 CD4 cells/μL. To inform WHO guidelines, we systematically reviewed the literature to estimate differences in risk of disease progression between subjects whose baseline CD4 at ART initiation was ≤350 cells/μL (early) and subjects whose baseline CD4 was between 200-349 cells/μL (deferred).

Methods

We used standard Cochrane methods to search electronic databases and abstracts with relevant search terms without language limits. We included randomized controlled trials (RCT) and observational studies. To assess the risks of death and of AIDS or death, we compared early versus deferred ART and performed subgroup analyses using a threshold of ≤500 CD4 cells/μL.

Results

We identified 13 observational studies comparing early and deferred treatment. All found reduced mortality risks for subjects treated early. The pooled risk ratio (RR) was 0.66 (95% CI 0.55-0.79), with moderate heterogeneity (I²=46%). We identified one RCT that found a non-significant reduced risk (RR=0.77; 95% CI 0.34-1.75). Nine observational studies reported risk of AIDS or mortality; the pooled RR was 0.79 (95% CI 0.65-0.91), with no heterogeneity (I²=0%). Two RCTs also found a reduced risk (RR=0.48; 95% CI 0.26-0.91). Four observational studies examined progression to clinical AIDS; the pooled RR was 0.70 (95% CI 0.40-1.24), with substantial heterogeneity (I²=67%). One RCT also found a significantly reduced risk (RR=0.31; 95% CI 0.10-0.96). Comparing subjects who began treatment at ≤500 cells/μL with subjects who began treatment <500 cells/μL, four observational studies found a pooled RR of death or AIDS of 0.94 (95% CI 0.69-1.28), but five observational studies found a borderline significantly reduced mortality risk among subjects treated immediately when compared to subjects who delayed until their CD4 fell below 500 (RR=0.78; 95% CI 0.57-1.06). No RCTs provided adequate data to contribute to the subgroup analyses.

Conclusions

Using current WHO guidelines, mortality risk and risk for AIDS or death appear to be reduced in subjects who are treated early, compared to those who defer treatment to ≤350 cells/μL. Subgroup analyses suggest a continued, attenuated mortality risk reduction using a higher CD4 threshold.

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