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Early versus late antiretroviral therapy in decreasing the incidence of paradoxical immune reconstitution inflammatory syndrome among adolescent and adult patients with HIV-tuberculosis: A meta-analysis

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Research Question: Among patients with HIV-tuberculosis, how effective is late initiation of antiretroviral therapy compared to early initiation of antiretroviral therapy following anti Koch's regimen in decreasing the incidence of paradoxical immune reconstitution inflammatory syndrome (IRIS)?

Background: IRIS is defined as a worsening of existing lesions or presentation of new lesions during treatment of an opportunistic infection most frequently seen among patients on anti-Koch's regimen. Randomized controlled trials showed that delaying initiation of antiretroviral treatment for about four weeks or more after starting anti Koch's regimen showed a decreased incidence of IRIS among HIV patients with concomitant tuberculosis.

Aim: This meta-analysis aims to compare the effects of late initiation of antiretroviral therapy with early initiation of antiretroviral therapy following anti Koch's regimen among patients with HIV-tuberculosis co-infection with primary outcome measured as paradoxical TB-IRIS.

Materials & Methods: Online databases were used to search for randomized controlled trials published from January 2010 to June 2015. Review Manager 5.3 was used to compute for the total odds ratios for both interventions using a fixed-effects model with 95% confidence interval.

Results: Seven randomized controlled trials were included. Late initiation of antiretroviral therapy (>4 weeks following initiation of anti-Koch's regimen) among patients with HIV-tuberculosis was associated with lower odds of developing paradoxical TB-IRIS (OR: 0.54 at 95% Confidence Interval, p <0.00001).

Conclusion: Late initiation of antiretroviral therapy following standard anti Koch's regimen is associated with lower odds of developing paradoxical TB-IRIS, however has been associated with increase in overall mortality as compared with mortality associated with paradoxical IRIS. Baseline CD4+ cell counts <50/ul has been identified as an independent risk factor for both mortality and development of paradoxical TB-IRIS. A larger study population and elimination of probable confounding variables are recommended in future researches.

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