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[Intervention Review]

Interleukin-2 as an adjunct to antiretroviral therapy for HIV-positive adults

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ABSTRACT

Background

Human immunodeficiency virus (HIV) continues to be a leading cause of morbidity and mortality, particularly in sub-Saharan Africa. Although antiretroviral drugs have helped to improve the quality of life and life expectancy of HIV-positive individuals, there is still a need to explore other interventions that will help to further reduce the disease burden. One potential strategy is the use of interleukin-2 (IL-2) in combination with antiretroviral therapy (ART). IL-2 is a cytokine that regulates the proliferation and differentiation of lymphocytes and may help to boost the immune system.

Objectives

To assess the effects of interleukin-2 (IL-2) as an adjunct to antiretroviral therapy for HIV-positive adults.

Search methods

We searched the following sources up to 26 May 2016: the Cochrane Central Register of Controlled Trials (CENTRAL), published in the Cochrane Library; MEDLINE; Embase; the Web of Science; LILACS; the World Health Organization (WHO) International Clinical Trial Registry Platform (ICTRP); and ClinicalTrials.gov. We also checked conference abstracts, contacted experts and relevant organizations in the field, and checked the reference list of all studies identified by the above methods for any other potentially eligible studies.

Selection criteria

Randomized controlled trials (RCTs) that evaluated the effects of IL-2 as an adjunct to ART in reducing the morbidity and mortality in HIV-positive adults.

Data collection and analysis

Two review authors independently screened records and selected trials that met the inclusion criteria, extracted data, and assessed the risk of bias in the included trials. Where possible, we compared the effects of interventions using risk ratios (RR), and presented them with 95% confidence intervals (CI). We assessed the overall certainty of the evidence using the GRADE approach.



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Main results

Following a comprehensive literature search up to 26 May 2016, we identified 25 eligible trials. The interventions involved the use of IL-2 in combination with ART compared with ART alone. There was no difference in mortality apparent between the IL-2 group and the ART alone group (RR 0.97, 95% CI 0.80 to 1.17; 6 trials, 6565 participants, *high certainty evidence*). Seventeen of 21 trials reported an increase in the CD4 cell count with the use of IL-2 compared to control using different measures (21 trials, 7600 participants). Overall, there was little or no difference in the proportion of participants with a viral load of less than 50 cells/mL or less than 500 cells/mL by the end of the trials (RR 0.97, 95% CI 0.81 to 1.15; 5 trials, 805 participants, *high certainty evidence*) and (RR 0.96, 95% CI 0.82 to 1.12; 4 trials, 5929 participants, *high certainty evidence*) and (RR 0.96, 95% CI 0.82 to 1.12; 4 trials, 5929 participants, *high certainty evidence*) and (RR 0.96, 95% CI 0.82 to 1.12; 4 trials, 5929 participants, *high certainty evidence*) and (RR 0.96, 95% CI 0.82 to 1.12; 4 trials, 5929 participants, *high certainty evidence*) and (RR 0.96, 95% CI 0.82 to 1.12; 4 trials, 5929 participants, *high certainty evidence*). There was probably an increase in grade 3 or 4 adverse events (RR 1.47, 95% CI 1.10 to 1.96; 6 trials, 6291 participants, *moderate certainty evidence*). None of the included trials reported adherence.

Authors' conclusions

There is high certainty evidence that IL-2 in combination with ART increases the CD4 cell count in HIV-positive adults. However, IL-2 does not confer any significant benefit in mortality, there is probably no difference in the incidence of opportunistic infections, and there is probably an increase in grade 3 or 4 adverse effects. Our findings do not support the use of IL-2 as an adjunct to ART in HIV-positive adults. Based on our findings, further trials are not justified.

23 April 2019

No update planned

Other

This is not a current research question.

PLAIN LANGUAGE SUMMARY

Interleukin-2 as an adjunct to antiretroviral therapy for HIV-positive adults

Why did we do this review?

HIV is still a major cause of death worldwide, particularly in Africa. HIV multiplies in the blood and damages the immune system. Therefore if HIV-positive, one is more vulnerable to contract infections. The current drug treatment, antiretroviral therapy (ART), stops the virus from multiplying thereby allowing the body's immune system to recover. Interleukin- 2 (IL-2) is a protein in the body which helps the process of multiplication of white blood cells which are the cells that fight infections. Although IL-2 increases the amount of white cells we do not know if by increasing these we can add additional benefits to the use of ART alone. The aim of this Cochrane Review was to find out if using an extra treatment with antiretroviral therapy (ART), namely IL-2, compared to using ART alone can reduce illness and death in HIV-positive adults.

Key messages

We found that IL-2 causes an increase in the CD4 immune cells (*high certainty evidence*). However, there is no difference in important effects such as death and other infections (*high certainty evidence*). There is probably an increase in side-effects for those people using IL-2 (*moderate certainty evidence*). Our findings do not support further use of IL-2 as an add-on treatment to ART in HIV-positive adults.

Main results

After conducting a comprehensive search on 26 May 2016, we included 25 eligible trials conducted in six countries. There was no difference in the number of deaths between the IL-2 group and those that got ART alone (6 trials, 665 participants, *high certainty evidence*). Seventeen of 21 trials reported an increase in the CD4 cell count with the use of IL-2 compared to ART alone using different measures. Overall, there was no difference in the proportion of participants with a suppressed viral load of less than 50 cells/mL (5 trials, 805 participants, *high certainty evidence*) or less than 500 cells/mL by the end of the trials (4 trials, 5029 participants, *high certainty evidence*). Overall there may be little or no difference in the incidence of opportunistic infections (7 trials, 6141 participants, *low certainty evidence*). There was probably an increase in grade 3 or 4 adverse events (6 trials, 6291 participants, *moderate certainty evidence*). None of the included trials reported on adherence.