

Evidence Assessment: Summary of a Systematic Review

Who is this summary for?

For Doctors and Health Personal, administrators and managers of health facilities and stakeholders involved in tuberculosis prevention.

Isoniazid for preventing tuberculosis in HIV-infected children

Key findings

- In HIV-positive children not taking ART, isoniazid medication reduces the number of children developing active TB by 69%, and death by 54% ;
- The number of children with adverse effects were similar in children receiving isoniazid medication as the control group in both children on ART and not on ART;
- No benefit or harm has been identified with the use of isoniazid in HIV-positive children taking ART.

Background

Tuberculosis (TB) is a common cause of severe lung disease and death in HIV-positive children. Childhood TB is common in poor countries, especially those with a coexisting burden of HIV/AIDS disease. HIV-positive children have a higher risk of developing TB than HIV-negative children. Isoniazid prevents TB in HIV-positive adults and is currently used in children who are at high risk of developing TB disease after exposure to someone with TB. However, there is limited information on the effect of isoniazid medication in reducing active TB or death if given to HIV-positive children without known TB contact.

Question

What are the effects of TB preventive treatment versus placebo in HIV-positive children with no known TB contact on active TB, death, and reported adverse events?

Isoniazid for preventing tuberculosis in HIV-infected children in Cameroon

The HIV/AIDS prevalence rate among adults aged 15-49 years is 4.3% in 2011. The number of new cases of tuberculosis rose from 11 655 to 16 477 between 2004 and 2014, and almost half of TB patients are infected with HIV. Isoniazid is already used for patients with HIV in Cameroon. This intervention might reduce the mortality burden of disease in children.

Table 1: Summary of the systematic review

	What the review authors searched for	What the review authors found
Studies	Randomized controlled trials (RCTs).	Three randomized controlled trials met the inclusion criteria.
Participants	HIV-positive children, below 13 years, without TB disease currently (irrespective of prior history of TB treatment, infection or prophylaxis). We included children on antiretroviral therapy (ART).	In one study HIV-positive children were older (median age 24.7 to 38 months) another (median age 3.2 months). Two included children who had a previous history of TB treatment or prophylaxis, 16% and 12%, respectively, compared to another study that excluded all children who had a history of TB or known exposure to a microbiologically confirmed case of TB.
Interventions	Any TB drug or drug combination.	The included studies randomly assigned children to isoniazid prophylaxis or placebo group. The dose of isoniazid prophylaxis (10 mg/ kg with a variability of 8 mg/kg to 12 mg/kg) and frequency of treatment (either daily or three times weekly) varied. Children assigned to the control groups received placebo with identical appearance to isoniazid prophylaxis tablets, and administered in a similar way to isoniazid prophylaxis in the respective studies.
Controls	Inactive placebo.	Inactive placebo.
Outcomes	<p>Primary outcomes</p> <ul style="list-style-type: none"> • Active TB <p>Secondary outcomes</p> <ul style="list-style-type: none"> • Death • Grade 3 or higher clinical adverse events • Grade 3 or higher laboratory adverse events 	<p>Primary outcomes</p> <ul style="list-style-type: none"> • Active TB; • Death; • Clinical adverse events; • Laboratory adverse events.
Date of the most recent search: 17 February 2017		
Limitations: This is a moderate quality systematic review, AMSTAR =11/11		
Citation: Zunza M, Gray DM, Young T, Cotton M, Zar HJ. Isoniazid for preventing tuberculosis in HIV-infected children. Cochrane Database of Systematic Reviews 2017, Issue 8. Art. No.: CD006418. DOI: 10.1002/14651858.CD006418.pub3.		

Table 2: Summary of findings

Isoniazid prophylaxis compared to placebo for HIV-positive children not on antiretroviral therapy (ART)			
Patient or population: HIV-positive children not taking ART			
Settings: any setting			
Intervention: isoniazid prophylaxis daily or three times weekly			
Comparison: placebo			
Outcomes	Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
Active TB	0.31 [0.11-0.87]	240 (1)	Low
Death	0.46 [0.22-0.99]	240 (1)	Low

Applicability

The trials were conducted in Africa, two in South Africa and one in Ethiopia. These interventions are not resource intensive and may be applied in other low resources settings such as Cameroon.

Conclusions

Isoniazid prophylaxis given to all children diagnosed with HIV may reduce the risk of active TB and death in HIV-positive children.

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