A Review of Isoniazid Preventive Therapy (IPT): benefits and challenges

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Tuberculosis Global Epidemiology

• In 2013:
  – 9 million cases
  – 1.4 million deaths
    • 430,000 deaths among HIV+,
  – 500,000 cases in children < 15 years

• Second only to HIV/AIDS as second killer worldwide
Swaziland, WHO TB 2014

• In 2013
  – Case notifications: 7,078
    • 10% < age 15
  – TB Incidence: 1,382 per 100,000
  – HIV+ TB patients: 4,747 (74%)
  – HIV+ screened for TB: 100,138
  – HIV+ given INH: 429
  – 5,000 deaths in TB/HIV pts
Latent Tuberculosis Infection (LTBI)

- *M. tb* contained by the immune system
- Results in a dormant or latent stage of TB
- From this latent stage, the bacteria can reactivate to cause TB disease at any time
- Treatment of latent TB infection (LTBI) can decrease the risk of reactivation
Isoniazid Preventive Therapy (IPT)

- INH is the mainstay for latent TB treatment
- Effectiveness is 60-90%
  - Due to variable adherence, actual effectiveness is 25-90%
- Trial comparing IPT for 12, 24, 52 weeks
  - 24 weeks decreased TB by 65%
  - Less hepatitis than with 52 weeks

IPT preventing TB in HIV+ Children

• Frigati et al. 2011, South Africa
  – Double blind, placebo controlled trial in HIV+ children on ART
  – DSMB terminated placebo arm at 4 months due to demonstrated benefit of INH on mortality
  – Children receiving placebo were switched to INH
  – Concluded: IPT reduces the risk of TB in HIV+ children on ART by 0.23 (95% CI 0.05-1)

IPT preventing TB in HIV+ Children

• Further evidence...
• Grey et al. 2014, South Africa
  – RCT to assess the efficacy, tolerability and safety of IPT in HIV+ children on ART
    • 85 received INH, 82 received placebo
  – 4 cases of TB in INH group, 7 in placebo group, all susceptible to INH
  – Conclude: IPT is safe and well tolerated in HIV+ children on ART

IPT in HIV+ Children on ART

• Ayieko et al. Meta-analysis, 2014
  – Included 8 RCTs of IPT in children
  – confirmed that INH is more efficacious in preventing TB
  – Concluded: IPT reduces the risk of developing TB by 59% among children aged 15 years and younger excluding infants (95% CI 0.31-0.55)

A Trial of Mass Isoniazid Preventive Therapy for Tuberculosis Control

- 78,744 miners enrolled, randomized into 15 clusters
  - Intervention group: TB screening & IPT x 9 mos
  - Primary outcome: TB incidence during 12 mos after intervention ended
IPT in high risk populations

• Among 63,174 miners with outcomes:
  – 887 TB cases in the intervention clusters
  – 856 in the control clusters
  – TB incidence: 3.02 & 2.95 cases/100 person-years

• Conclude: Mass screening & treatment for LTBI had no significant effect on TB in South African gold miners

• BUT... IPT was successful in preventing TB during treatment

• Mistake to conclude IPT not beneficial, suggests longer duration indicated while remain at high risk
G Churchyard: “IPT as an Umbrella”
Current IPT Delivery is Inadequate

• Among eligible
  – Children: only 8% to 20% receive IPT
  – HIV+ patients: Far below global target of 50%
Why current IPT delivery is inadequate?

- Focus historically on TB disease treatment not prevention
- Difficulty excluding TB disease
- Long duration of IPT
- Overestimation of the complications of INH
  - Concerns about toxicity and generation of INH resistant TB are unsubstantiated
- Inability to ensure IPT adherence:
  - LTBI is asymptomatic, therefore testing is provider-initiated
  - Because patients are asymptomatic, less motivated to take long treatment
Additional References


4. UpToDate 2014: Treatment of Latent TB in HIV negative patient, CR Horsburg

5. Targeted tuberculin testing and treatment of latent tuberculosis infection. American journal of respiratory and critical care medicine 2000;161:S221-4
