

Alternatives to INH Chemoprophylaxis

The letter "Is INH alone enough for prophylaxis" made an interesting reading(1). We agree, that time is ripe for some rethinking. However, giving firm recommendations without clinical trial should be strongly discouraged. We would like to elaborate some aspects in this context.

INH and rifampicin, only for 3 months are being already used as chemoprophylactic agents in some parts of UK(2). In situations where there is large initial INH resistance INH and rifampicin chemoprophylaxis would expose a relatively greater number of contacts to single drug prophylaxis of rifampicin. [Contacts of primary INH resistant source, which is 10-90% according to authors(1)].

Also there is some concern about efficacy of rifampicin as single drug prophylaxis in contacts where the source is proved to be excreting INH resistant bacilli. A case of probable rifampicin failure in such situation is described(3) and hence recommendation for chemoprophylaxis of confirmed INH resistance vary from rifampicin alone or rifampicin with ethambutol; both regimens for 9 months(4). INH and thiacetazone for chemoprophylaxis, cannot be recommended as thiacetazone is a less potent drug and have more side effects and a higher primary resistance in Asians including Indians(5).

Another area of research may be the use of combination of antituberculous

drugs which may shorten the duration of prophylaxis. In experimental models, rifampicin and pyrazinamide for 2 months proved better than INH chemoprophylaxis(6). In fact an editorial accompanying the article(6) discusses the exciting possibility of use of rifampicin and pyrazinamide chemoprophylaxis in intermittent schedule (once or twice weekly doses) for 2 months. Approximately as few as 10 doses of medication may give very effective prophylaxis(7). Such prophylaxis should be effective in populations with high INH resistance. Further clinical trials are needed about efficacy, safety, and cost/benefit assessment before any firm recommendations are made about use of alternate regimes to INH prophylaxis.

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Comments

INH chemoprophylaxis is a beneficial and cost-effective tool for the control of tuberculosis. Lately there has been newer research in western world in this context primarily related to the duration of chemoprophylaxis and its side effects. The prolonged duration of six—nine months chemoprophylaxis makes compliance difficult. Therefore, alternate modalities like directly observed biweekly INH prophylaxis for six—nine months or using drugs like rifampicin alone or along with INH for three—four months are being evaluated. INH induced hepatotoxicity has further put it into defame. This, however, is not common in childhood and therefore, not a limiting factor in high prevalence countries like India where most of the persons requiring prophylaxis are in the younger age group(1).

In India, the rising trend of INH resistance has raised doubts about the

INH prophylaxis. The initial resistance to INH has been reported between 10-12% (not 10 to 90% as mentioned by the authors) in our country(2). Recommending rifampicin with or without ethambutol for prophylactic therapy may not be prudent given the enormity of the problem, cost of the therapy and need to use these drugs for 6-9 months when resistance is suspected. In the situation, where there is confidence that the source case has INH resistant organisms, it appears reasonable to treat with rifampicin with or without ethambutol in standard dosages for nine months.

The childhood contacts of known cases of multidrug resistance (rifampicin and INH) may require diligent observation as no other drug has been evaluated for preventive therapy. However, in contacts at a high risk of tuberculosis (*e.g.*, immunocompromized), preventive therapy may be considered. If the organisms are known to be susceptible and active disease has been excluded, nine months of daily ethambutol and pyrazinamide may be considered. If the organisms are resistant to ethambutol as well, pyrazinamide along with quinolones may be used(3).

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