Reduction of clinical tuberculosis in HIV-infected males with isoniazid prophylaxis

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ABSTRACT Isoniazid (INH) chemoprophylaxis has a positive impact on the development of clinical tuberculosis. Due to the increased prevalence of tuberculosis among HIV-infected individuals, we evaluated the effect of INH on the prevention of clinical tuberculosis in HIV-infected patients. We administered 300 mg of INH daily to 246 HIV-infected, tuberculin skin test-positive patients for 12 months. During 3 years of follow-up, 41 participants died and 94 were lost to follow up. Of the 111 patients followed for the 3 years, 12 developed tuberculosis which is lower than might be expected in an untreated group. INH prophylaxis appears to be an effective method to prevent clinical tuberculosis among HIV-infected, tuberculin skin test-positive patients.

Réduction de la tuberculose clinique chez des hommes infectés par le VIH grâce à une prophylaxie par isoniazide

RESUME La chimoprophylaxie par isoniazide a un impact positif sur l'évolution de la tuberculose clinique. Etant donné l'augmentation de la prévalence de la tuberculose chez les individus infectés par le VIH, nous avons évalué l'effet de l'isoniazide sur la prévention de la tuberculose clinique chez des patients séropositifs. Nous avons administré 300 mg d'isoniazide par jour pendant 12 mois à 246 patients séropositifs chez lesquels le test cutané à la tuberculine était positif. Durant les trois années de suivi, 41 participants sont décédés et 94 ont été perdus de vue. Sur les 111 patients suivis pendant trois ans, 12 ont développé une tuberculose qui était moins forte que celle à laquelle on pouvait s'attendre dans un groupe de patients n'ayant pas eu de traitement. La prophylaxie par isoniazide semble être une méthode efficace de prévention de la tuberculose clinique chez des patients séropositifs qui ont une réaction positive au test cutané à la tuberculine.

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Introduction

HIV infection has recently become one of the most important risk factors for the development of *Mycobacterium tuberculosis* infection into active tuberculosis (TB) [1]. The rate of disease progression for HIV-infected patients ranges between 1.6 and 9.7 per 100 person-years (py) in purified protein derivative (PPD)-positive cases [2-5]. Isoniazid (INH) chemotherapy has been highly effective among HIV-negative individuals at curtailung the progression to clinically active TB [6,7]. Also, in HIV-infected cases, INH prophylaxis reduces the rate of disease progression [2,4,8,9]. In a study from Haiti, 12 months of INH preventive chemotherapy (IPT) was significantly protective [10]. We studied the efficacy of 12 months INH prophylaxis in HIV-infected individuals voluntarily attending the HIV/STI care centre in the city of Kermanshah, Islamic Republic of Iran from October 1997 to December 2001.

Methods

In this prospective study, 290 HIV-positive individuals identified in prison were tested with tuberculin skin test (TST) from 1 October 1997 until 1 April 1998. All HIV-positive cases were male and injecting drug users (IDUs). The patients were classified as TST-positive with a PPD reaction > 5 mm and TST-negative with PPD ≤ 5 mm. After excluding active TB patients, all TST-positive cases received INH preventive chemotherapy (300 mg/day) daily for 12 months under observation [recommended regimen of the World Health Organization (WHO)] [11]. During the term in prison and after release, they were followed up in the HIV/STI care centre for more than 3 years. TB incidence was calculated as the number of confirmed TB cases occurring during the follow-up period expressed as cases/100 py. The efficacy of preventive therapy among the TST-positive patients was measured as the relative risk based on TB incidence in patients who took INH prophylaxis.

The chi-squared test was used to calculate statistical significance.

Results

Of 290 HIV-positive males tested with TST, 255 individuals (87.9%) had PPD > 5 mm. The median age was 37 years. Five of these cases had a previous history of clinical TB. Four cases had active TB at the first visit and were treated with a 6-month regimen of INH. There was no evidence of clinically-active TB in 246 cases (84.8%) and all of them received INH preventive chemotherapy for 12 months. During the 3-year follow-up, 41 participants (16.7%) died and 94 cases (38.2%) were lost to follow up. The remaining 111 cases (45.1%) were evaluated completely. Of 115 HIV-infected, TST-positive patients, 4 (3.5%) developed active TB every year for 3 years following the completion of INH preventive chemotherapy. Of these 12 cases, 8 (66.7%) were smear positive and 3 (25.0%) smear negative for pulmonary TB and 1 had extrapulmonary TB (liver). Eight cases occurred in the 20–40-year-old age group and the remainder were older than 40 years (Table 1).

Discussion

*M. tuberculosis* infection in HIV-infected injecting drug users in our study was very high (87.9%). This rate is more than the estimated rate in the general population (12%) and in HIV-infected persons (23%) between the ages of 15 and 49 years in the...
Eastern Mediterranean Region [72]. According to one study, the prevalence of active TB in TST-positive HIV patients was 7.9/100 py without INH prophylaxis [13]. INH chemoprophylaxis in two large randomized, placebo-controlled series afforded 60% to 90% protection [6,7]. In the present study, the incidence of clinically active TB was 3.5/100 py after 12 months INH preventive chemotherapy. In one study from Haiti on 58 HIV-positive cases the incidence was 1.7/100 py [10]. The rate was 1.2/100 py in the multi-site study by Gordin and colleagues [14], and 1.6/100 py in Spain [15].

One reason for the higher rate of development of clinical TB in our study is the high prevalence (87.9%) of M. tuberculosis infection in our HIV patients versus 53.3% in the Haiti study [10]. Without INH preventive chemotherapy, the prevalence of active TB in that study was 10.0/100 py.

In our study after 12 months of INH preventive chemotherapy only 3.5/100 py had active TB. If we consider the estimated rate of active tuberculosis in the absence of INH prophylaxis in the Haitian study (10%), we might have expected far more cases of clinical tuberculosis during the 3-year follow-up period. It would seem therefore that INH prophylaxis is successful in reducing the number of clinical TB cases. In addition, it has been reported that administration of INH preventive chemotherapy to TST-positive, HIV-infected patients both increases life expectancy and reduces medical costs [16,17].

In conclusion INH prophylaxis provides protection against both endogenous reactivation and exogenous reinfection with M. tuberculosis [17]. We recommend further studies evaluating the efficacy of 6 months of INH prophylaxis and two-drug prophylaxis regimens in HIV-infected patients in our country.

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**References**


