Impact of adverse drug reactions on treatment interruption in TB patients with and without HIV co-infection

It has been reported that HIV/tuberculosis (TB) co-infected patients experience a higher rate of adverse drug reactions to treatment than those without HIV, although few data exist for co-infected patients since highly active retroviral therapy (HAART) has become widely available. This study tested whether the presence of HIV co-infection had an impact on the frequency of serious adverse events, especially those causing treatment interruption, even if HAART is co-administered.

Methods
Retrospectively, consecutive unselected adult HIV-infected individuals treated for TB between February 1997 and November 2003 (n=156) were identified and compared with a control group of HIV-uninfected patients (n=156) treated for TB during the same period. The occurrence of serious (grade III/IV) adverse drug reactions and episodes of treatment interruption were identified. HAART was defined as use of ≥3 antiretroviral drugs in combination.

Results
Serious adverse events occurred in 40% of TB+HIV+ individuals and 26% of TB+HIV- individuals (p=0.008). The most frequent adverse event in TB+HIV+ individuals was peripheral neuropathy, which occurred in 22 (14%) compared with three (2%) of those without HIV co-infection (p<0.0001). Of these 22 co-infected individuals, 17 were receiving concomitant HAART and 11 used regimens containing the nucleoside reverse transcriptase inhibitors stavudine (d4T) and/or didanosine (ddI). However, excluding those who received ddI and/or d4T in whom the only adverse event was peripheral neuropathy, the overall frequency of adverse events was little changed at 38%.

In both populations, hepatotoxicity developed in 13%. Rash occurred with a similar incidence in both groups. Persistent vomiting was significantly more common among TB+HIV+ individuals (p=0.006), and a greater number of TB+HIV+ patients had more than one serious adverse event (p=0.02). Interruption of anti-TB treatment occurred in 13% of TB+HIV+ and 15% of TB+HIV- individuals (p=0.74). HAART was discontinued in 11 out of 111 TB+HIV+ individuals (10%) while they were receiving anti-TB treatment. Five HAART regimens were prescribed, but no differences were seen in the frequency of adverse events with different regimens.

Conclusion
A similar frequency of discontinuation of anti-TB treatment occurred in HIV-infected and uninfected individuals, despite a greater rate of serious adverse events in those who were HIV infected.

Editorial comment
Since a retrospective collection of data was performed in the study, some adverse events may not have been recorded. However, rates of underreporting should have been similar in TB+HIV+ and TB+HIV- patients. Adherence to treatment was satisfactory, as reflected by the high rates of treatment completion, low rates of relapse of TB and the good virological response to HAART.

There are some limitations of the study, such as potential bias due to ethnic mix, difficulties in assessing the extent of TB, alcohol and other drug abuse, etc. However, the presented data suggest that, despite a higher frequency of serious adverse events during anti-TB treatment in TB+HIV+ patients, treatment interruption occurs in these individuals no more frequently than in HIV-uninfected patients with TB.

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