Research Paper Medical Science

Att Induced Adverse Drug Reactions in Patients Suffering From Pulmonary Tuberculosis.

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ABSTRACT

Tuberculosis is a communicable infectious disease caused by Mycobacterium tuberculosis, recently become second leading infectious diseases that cause death after HIV-AIDS. Adverse drug reactions related to anti-tuberculosis also become important as longer use of these drugs. This study aimed to explore and to observe adverse reactions occurrence of anti-tuberculosis drugs among tuberculosis patients and its management. An observational retrospective study was used in this study. A total of 224 tuberculosis patients were included to this study after inclusion and exclusion criteria. Out of 224 patients, 56 (25%) patients had an experience on adverse drug reactions. The majority case of adverse drug reactions is hepatotoxicity in 38 (16.9%) patients followed by gastrointestinal reactions in 31(13.8%) patients. Skin reaction happened in 21 (9.3%) patients and hyperuricemia in 11 (4.9%) patients. There are some risk factor that may affect on adverse drug reactions occurrence. Isoniazid accounted for 44.6% of the ADRs. Occurrence of ADRs from antitubercular drugs was high in the population and hence further studies encompassing a wider population and covering different regions are needed.

KEYWORDS Anti-tubercular agents, Drug related side effects, Isoniazid, Hepatotoxicity.

Introduction: Tuberculosis an infectious disease caused by Mycobacterium tuberculosis, now become the second leading infectious cause of death in the world (1). Active pulmonary TB incidence estimated around 8 million new cases per year worldwide and approximately cause death 2 million per year (2). Tuberculosis treatment mostly need more than one drug combination to eradicate tuberculosis bacteria. First line anti-tuberculosis drugs recommended by WHO are combination between isoniazid, rifampicin, pyrazinamide, ethambutol and streptomycin (3). The necessity use of multidrug regimens has been associated with increased incidence of adverse drug reactions of anti-tuberculosis drugs. This adverse drug reactions may be mild as well as fatal (2). Antituberculosis agent that commonly use such as, isoniazid, rifampicin and pirazinamide are highly effective but also can cause hepatotoxicity (4). Treatment on people with tuberculosis require treatment for at least six months, it may find difficulty to complete. In view of the high prevalence of TB and widespread use of antitubercular drugs, it has become the need of the hour to monitor for ADRs and increase awareness of ADRs. Hence, the present study was carried out with the objectives, to study the ADR pattern due to first line anti-tubercular drugs and also to study the predisposing factors and to carry out the causality and severity assessment of the reported ADRs

Methodology: The study was done in CMCH, Bhopal. The target population was Tuberculosis infected patients undergoing antitubercular treatment (ATT) with first line drugs. Any patient undergoing treatment at the time of study was included. Patients who were lost to follow up within one month, uncooperative or unwilling to be enrolled, or appeared unreliable were excluded. The various study tools used were the Patient profile form which recorded all the information, such as name, age, sex, location, literacy, ethnic group, socioeconomic status, life style factors and dietary factors, any concurrent diseases and medications other than antitubercular agents that the patients might be taking. ADR Reporting Form recorded all the essential information regarding the adverse effects: the onset and severity of the ADR experienced, the impact of ADR on the treatment and work capacity of the patient, the drug(s) involved, the date of starting the suspected drugs and the date of reporting of the ADR. Information on any past or current occurrence of adverse effects due to the ATT drugs being administered to them was collected from the patients. The data was statistically analyzed to determine the association between the ADRs and the different population parameters.

Result: A total of 224 patients were included in the study among whom 56 (25%) reported experiencing ADRs. The occurrence of ADRs according to age groups is maximum within the age group of 21-40 years (n=21)(37.5%) followed by 0-20 years (n=16)(28.5%), 41-60 years (n=10) (17.8%) and lastly in >60 year age group (n=9) (16%). ADRs was slightly more among female (58.9%) than male (41%) patients. We categorized the literacy of the patients as illiterate (uneducated), literate (able to read and write). 29 (51.7%) illiterate patients and 27 (48.21%) literate patients were reported . Occurrence of ADRs was almost equal in both literates andilliterates. The majority case of adverse drug reactions is hepatotoxicity in 38 (16.9%) patients followed by gastrointestinal reactions in 31(13.8%) patients. Skin reaction happened in 21 (9.3%) patients and hyperuricemia in 11 (4.9%) patients. Isoniazid was considered to be responsible for nearly half of the reported ADRs (48.3%), pyrazinamide for 21.7%, rifampicin for 19.7% streptomycin for 6.3% and ethambutal for 4%. Statistical analysis showed no association between the various life style and dietary factors and the occurrence of ADRs.

Discussion: A total of 224 patients were enrolled in the study, among which 56 (25%) developed ADRs. This result is slightly higher than the result of the study by Mishin et al,(5) where ADRs were found to occur only in 16.9% of cases. In another study carried out in Nepalese population by Koju et al,(6) ADRs were reported by 80% of the population.The difference in results could have resulted due to the genetic, demographic and nutritional status differences among the two populations. In this study, majority of ADRs were reported by the age group 21-40 years. This result is in contrast to the study by Yee et al where age over 60 years was associated with increased incidence of ADRs due to anti TB drugs.14 In another study by Shakya et al, patients of younger ages 18- 20 years were seen to be more prone to anti-TB drug induced hepatotoxicity. (6, 7) Female patients experiencing ADRs were only slightly more in our study than the male patients. Astudy by Yee et al,(7) and Shakya et al(8,9) considered female gender as a risk factor for the occurrence of ADRs due to anti-TB drugs. Generally, females are considered to be more at risk of ADRs due to their smaller body size and body weight compared to males. In this study, occurrence of ADRs was more or less equal in the literate and illiterate populations. This could have been because any patient who could read and write was considered literate. This result also could not be compared

with any other studies as again we were unable to find any study associating literacy with occurrence of ADRs due to anti-TB drugs. Type of ADRs found are hepatotoxicity in 38 (16.9%) patients, gastrointestinal reactions in 31(13.8%) patients, Skin reaction in 21 (9.3%) patients and hyperuricemia in 11 (4.9%) patients. Most common adverse reaction is hepatotoxicity. . Hepatotoxicity adverse reaction due to antituberculosis is already widely noticed and there are many researches about these(4, 10, 11, 12,13). American Thoracic Society (ATS) also issued an official ATS statement about Hepatotoxicity of Antituberculosis Therapy in 200615. Common causes of hepatotoxicity are isoniazid, pyrazinamide and rifampicin, mostly in pyrazinamide use in regimens (14). Gastrointestinal reactions include anorexia, nausea, vomiting and epigastric pain caused by mainly all drugs in ATT. Skin reaction such as itchiness, rashes and any other kind of skin reactions are also common. Common causes of skin reactions due to anti-tuberculosis drugs are isoniazid and rifampicin,rarely in use of pyrazinamide and ethambutol.

Management to ADRs occurrence mostly with add on medication, then followed by withhold the medication regimens, continue without changes and the last is change patient's treatment regimens.

Conclusion: 25% patients had an experience on adverse drug reactions, that's a quite large number and potentially interrupted patient's treatment and medication outcome. Hence further studies encompassing a wider population and covering different regions are needed.

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