Online Available at www.thepharmaresearch.info

THE PHARMA RESEARCH, A JOURNAL

The Pharma Research (T. Ph. Res.), (2010), 3; 10-16.
Published on- 15 June 2010

ISSN 0975-8216

Case Study

A PROSPECTIVE, OBSERVATIONAL COHORT STUDY TO ELICIT ADVERSE EFFECTS OF ANTI-TUBERCULOSIS DRUGS AMONG PATIENT TREATED FOR ACTIVE TUBERCULOSIS

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ABSTRACT

Tuberculosis is one of the foremost public health problems causing an enormous problem of suffering and death. Chemotherapy is the basic approach to clinical tuberculosis control. Essential anti-tuberculosis drugs are Isoniazid (INH), Rifampicin (RMP), Pyrazinamide (PZA), Ethambutol (E) and Streptomycin(S). The study was conducted on the tuberculosis patients of Mathura Hospital (U.P) during March 2009 to February 2010. Total 212 newly diagnosed pulmonary and extra pulmonary tuberculosis patients were included in the present study. Patients were kept under observation during whole treatment period. Clinical biochemical monitoring from the basis of diagnosing side effect due to anti-tuberculosis therapy. Among the 212 cases studied, 66.04% were male and 33.96% were female. The symptom based common minor side effects of anti-tuberculosis drugs were nausea, vomiting, anorexia, diarrhoea (41.98%, 10.36%, 12.74%, and 2.36% respectively). Of the 212 patients treated for tuberculosis, 43 patients (20.28%) had major side effects. Among them, 15 patients (7.08%) experienced jaundice, 21 patients (9.90%) experienced flu syndrome and seven patients (3.30%) experienced skin rash. In this study showed that male with above 35 years of age of the patients are more prone to major adverse effect.

Keywords: Tuberculosis, Adverse Effect, Side Effect, Anti-Tuberculosis Drug

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1.0 INTRODUCTION

Tuberculosis causes a great deal of ill health in the populations of most low-income countries; it is the single most common cause of death in individuals aged fifteen to forty-nine years.

The world adopts DOTS strategy for TB control thought the national TB control programs in different countries and is making good progress. A major adverse reaction to one of the first-line antituberculosis drugs, which results in discontinuation of that drug has several implications. There may be considerable morbidity, even mortality, particularly with drug-induced hepatitis [1–4]. These events may incur substantial additional costs because of added outpatient visits, tests, and in more serious instances hospitalizations [3, 4]. Alternative agents may have greater problems with toxicity, and are often less effective, so that treatment must be prolonged.

The occurrence, risk factors, morbidity, and mortality of adverse events from isoniazid (INH), particularly hepatotoxicity, have been well defined [1, 2, 5]. Adverse to rifampicin (RMP) and ethambutol (E) have been well documented [6–8,] although causality of these drugs may be less certain because they are seldom using alone. Authoritative treatment guidelines [9] have state that "there does not appear to be a significant increase in hepatotoxicity when PZA is added to INH and RIF, based on results from large scale randomisation trial" [10-12].

The currently recommended anti-tuberculosis regimens are usually well tolerated. However some patients may experience problems, usually due to the bulk of the drugs, a single day's dose consisting of 6-7 tablets. Drug related side effects might be minor or major. In general, a patient who has minor side effects should be encouraged to continue the treatment with symptomatic measures such as antacids, antihistamines, antiemetics, or analgesic. If major side effects occur, the regimen, or the offending drug, if identified, must be stopped. Further management depends on the nature of side effects and may have to be done in a hospital.

It has been very important to draw attentions of all health workers towards side effects of anti-tuberculosis drugs since side effects can be harmful to the patients. Pharmacists have an ethical obligation to notify the appropriate bodies whenever side effects are suspected. The decision to report such cases should not dependent on whether the potential side effects are already well known. Instead, pharmacists are encouraged to report any suspected side effects. Side effects of anti-tuberculosis drugs is already well known, further report on the occurrence will be helpful in minimizing if not avoiding this undesirable effect. Hence, it has been attempted to find the occurrence of anti-tuberculosis drug-induced side effects in Mathura Hospital.

2.0 PATIENTS AND METHOD

Study site: The study was conducted on the patients of Mathura Hospital (U.P).

Patients: From March 2009 to February 2010, a prospective cohort evaluation of anti-tuberculosis drugs-induced side effects. A total 212 newly diagnosed tuberculosis patients, attending at this hospital.

The study comprises 155 patients with new pulmonary tuberculosis and 67 patients with extra-pulmonary tuberculosis. Among 67, 31 had tuberculosis pleural effusion and 36 with tuberculosis lymphadenopathy.

Sample Collection: Written informed consent was taken from each patient enrolled in this study. After taking the consent of the patient, Patient Information Form was filled.

Patients with active TB were seen at least monthly by the nurse case manager and treating physician. At the time of these visits, patients were questioned specifically regarding occurrence of common side effects to TB drugs. Liver trans-aminases were checked routinely in all patients after 1 month of therapy, and thereafter if symptoms arose. Patients were encouraged to return at any time if new symptoms or problems arose during therapy. If drug-induced hepatitis was suspected or observed then INH, RIF, and PZA were stopped, and if a rash or drug fever occurred then all anti-TB agents were stopped. Once the side effect improved, drugs were restarted, one by one. When the responsible drug was not known, the timing and order of rechallenge were at the discretion of the treating physician.

From patients' medical and nursing records, information was abstracted regarding age, sex, greater problems with toxicity, and are often less effective, symptoms, alcohol and intravenous drug use, co-morbid conditions, other medications, whether women were pregnant or postpartum, method of detection, site of disease, potential risk factors for active TB, results of acid-fast bacillus smear, cultures, drug sensitivity results, dose plus duration of all anti-TB drugs prescribed, and patients' weight. Adverse reactions disease was considered active if the diagnosis was made as a result Records of patients who developed side effects were reviewed in detail for risk factors for side effects, specific investigations such as hepatitis serology or ultrasonic examinations, as well as consequences including hospitalizations, additional visits to clinic by patients, or at patients' homes by nurses.

3.0 RESULT

A total 212 patients were included in the study. Among the study the variables are summarised in table 1 and symptoms based approach to side effects (minor, major and other) of Anti-tuberculosis are summarised in table 2, figure 1&2.

Table 1: Profile of tuberculosis patients enrolling in this present study

Variables		Frequency	Percent
Sex	Male	140	66.04%
	Female	72	33.96%
Age	15 to 35	156	73.58%
	36 and above	56	26.42%
Disease extent	Sputum positive	170	80.19%
	Sputum Negative	42	19.81%
Alcoholic		112	52.83%
Non alcoholic		100	47.17%

Table 2: Symptom- based Approach to Side Effects of Anti-tuberculosis Drugs Minor side effect:

Sl No.	Side effects	Frequency	Percent
1	Nausea	89	41.98%
2	Vomiting	22	10.38%
3	Anorexia	27	12.74%
4	Abdominal pain	19	8.96%
5	Itching, No rash	54	25.47%
6	Joint pains	48	22.64%
7	Burning sensation in feet	33	15.57%

Major side effect:

Sl No.	Side effects	Frequency	Percent
1	Jaundice	15	7.08%
2	Skin rash	07	3.30%
3	Flu syndrome	21	9.90%

Other side effect:

Sl No.	Side effects	Frequency	Percent
1	Bitter taste	04	1.89%
2	Angina	02	0.94%
3	Diarrhoea	05	2.36%
4	Constipation	03	1.42%
5	Sweating	11	5.19%
6	Imsomnia	09	4.25%
7	Body pain	07	3.30%

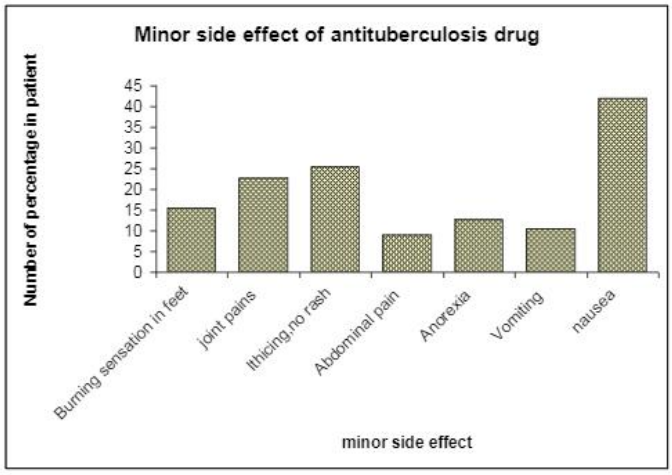

Fig1: Symtoms based approach to minor side effect of antituberculosis drug.

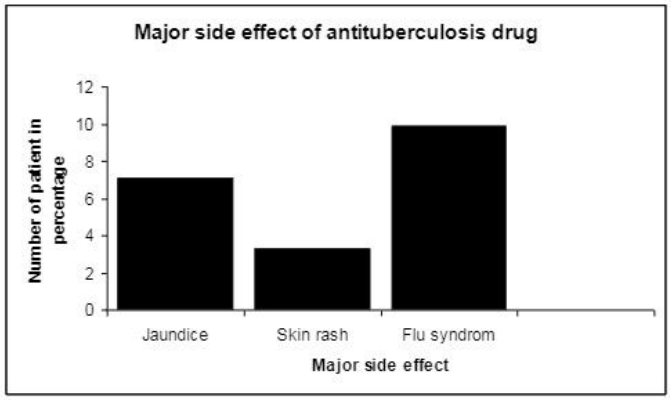

Fig2: Symtoms based approach to major side effect of antituberculosis drug

Table 4 and fig 3, 4 demonstrated that influence of age, gender, disease extent, alcohol intake in patients experiencing major side effect (jaundice, skin rash, flu syndrome)

Table 4: Age, gender, disease extent, alcohol intake in patients experiencing major side effects.

Major side effect		Frequency	Percent
Total		29	13.68%
Sex	Male	21	15%
	Female	08	11.11%
Age	15 to 35	20	12.82%
	36 and above	09	16.07%
Disease extent	Sputum positive	22	12.94%
	Sputum Negative	07	16.67%
	Alcoholic	16	14.29%
	Non alcoholic	13	13%

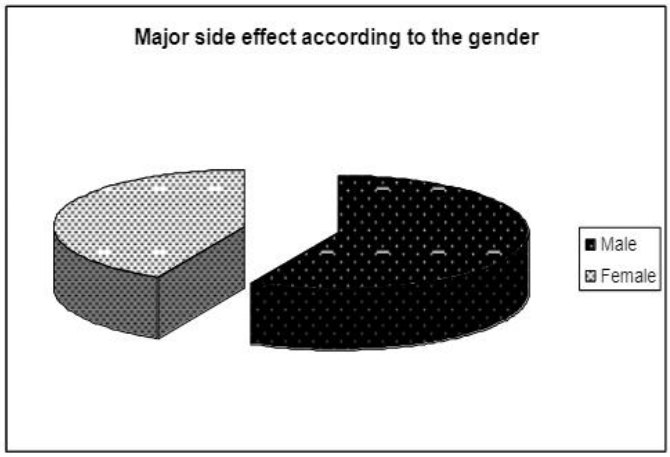

Fig 3: Comparison of major side effects in male and female gender.

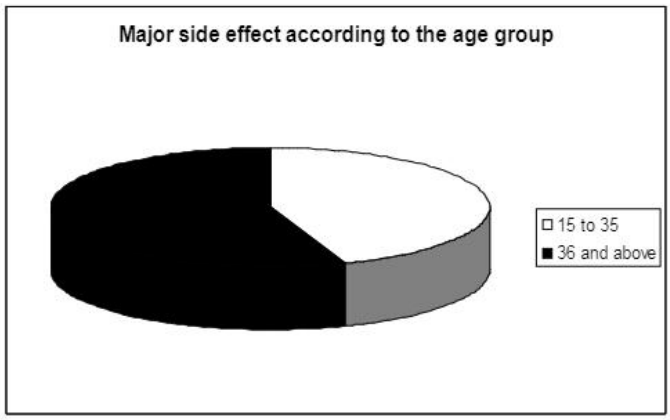

Fig 4: Comparison of major side effects in different age groups.

4.0 Discussion

In the study, 212 cases of tuberculosis, males (66.04%) were found higher in number than females (33.96%).

Symptom Based Approach to Side Effects of **Anti-Tuberculosis Drugs**[13]:

Minor side effects: In this study, 89 patients (41.98%) experienced nausea. Similarly, 22 patients (10.38%) experienced vomiting, 5 patients (2.36%) diarrhoea and 27 patients (12.74%) experienced anorexia. The drugs, which are responsible for these side effects, may be Pyrazinamide and Rifampicin.

Abdominal pain was experienced by 19 patients (8.96%). The drugs, which are responsible for this side effect, may be Pyrazinamide, Rifampicin and Isoniazid.

Itching without rash was experienced by 54 patients (25.47%). The drugs, which are responsible for this side effect, may be Pyrazinamide, Rifampicin and Isoniazid.

Forty-eight patients (22.64%) experienced joint pain (arthralgia). The drug, which is responsible for this side effect, may be Pyrazinamide.

Thirty-three patients (15.57%) experienced burning sensation in feet. Isoniazid may be the responsible drug for this side effect.

Major side effects: Of the 212 patients treated for tuberculosis, 43 patients (20.28%) had major side effects. Among them, 15 patients (7.08%) experienced jaundice. The drugs that are responsible for this side effect may be Pyrazinamide, Rifampicin and Isoniazid [7].

Seven patients (3.30%) experienced skin rash. The drugs, which are responsible for this side effect, may be Pyrazinamide, Rifampicin and Isoniazid.

In addition, 21 patients (9.90%) experienced flu syndrome. The drug, which is responsible for this side effect, may be Rifampicin.

In this study fig-3&4 shows that male (15%) and 35 above age (16.07%) of patients are more prone to major adverse effect than female (11.11%) and 35 under age (12.82%) of patients.

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