

PRESCRIPTION PATTERN OF SECOND LINE ANTITUBERCULAR DRUGS PRESCRIBED BY PRIVATE PRACTITIONERS: AN OBSERVATIONAL STUDY



Medical Science

KEYWORDS : Prescription pattern, Second line anti-tubercular drugs, Private practitioners.

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ABSTRACT

Tuberculosis (TB) is a chronic infectious disease caused by Mycobacterium Tuberculosis. One third of the global TB cases occur in India annually. In the event of resistance to first line anti TB drugs, second line drugs like Kanamycin, levofloxacin, Ethionamide, Cycloserine, Amikacin, Prothiomamide and PAS etc. are prescribed. All PPs are not well aware about the treatment of TB guidelines; they at times irrationally prescribe the TB regimen. A total number of 82 patients were enrolled. Second line ATT was started concomitantly with 1st line ATT in 51 (62.20%) patients. Out of all patients, 57 (69.51%) did not fall in criterion set for starting 2nd Line ATT. Only 15 (18.29%) patients were done any of the investigation for deciding 2nd Line ATT. Irrespective of combination used Levofloxacin was the most commonly used 2nd Line ATT drug. Only 2.44% (n=2) prescriptions were found to be rational while rest 77.56% (n=80) prescriptions were irrational.

INTRODUCTION

Tuberculosis (TB) is a chronic infectious disease caused by Mycobacterium Tuberculosis. The disease primarily affects lungs and causes pulmonary tuberculosis (PTB). It also affects intestine, meninges, bones, and joints, lymph glands, skin and other tissue of body.^[1] There were 8.6 million new TB cases in 2012 and 1.3 million TB deaths.^[2] One third of the global TB cases occur in India annually. In 2012, out of the estimated global annual incidence of 8.6 million TB cases, 2.3 million were estimated to have occurred in India.^[3]

Pulmonary tuberculosis is treated by first line anti TB drugs like Isoniazid, Rifampicin, Pyrazinamide, Ethambutol, and Streptomycin. In the event of resistance to first line anti TB drugs, second line drugs like Kanamycin, levofloxacin, Ethionamide, Cycloserine, Amikacin, Prothiomamide and PAS etc. are prescribed. There after sputum, acid fast bacilli culture and drug susceptibility testing are certain guidelines to prescribe second line anti-TB drugs. In 1999, WHO and its partners launched the Directly Observed Treatment Short course Chemotherapy- Plus (DOTS-Plus) for MDR-TB and to enable access to second-line drugs under rational use and cost-effectiveness of using second line drugs for managing MDR-TB.^[4]

In 2002 India's Revised National Tuberculosis Control Programme (RNTCP) introduced guidelines for involvement of PPs through an initiative called "Public Private Mix" (PPM) which encompasses training activities and formal collaboration with the RNTCP.^[5] As PPs are dealing with the major bulk of the patients they are the backbone of health care system. Almost half of patients with TB in India initially seek help from the private healthcare sectors, where diagnosis, treatment and reporting practices often do not meet national or international standards for TB.^[6-8]

All PPs are not well aware about the treatment of TB guidelines; they at times irrationally prescribe the TB regimen. It is common observation that to ensure extra coverage one or more second line drug is added without adhering to principals made for prescribing them.

MATERIALS AND METHOD

It was a cross sectional, observational study was in the Department of Pharmacology and Department of Pulmonary and Sleep Medicine, NSCB medical college, Jabalpur, from October 2014 to September 2015 with an aim to evaluate prescription pattern of private practitioners for second line

anti-tubercular drugs as compared to standard guidelines.

All patients attending the Department of Pulmonary and Sleep Medicine OPD and admitted in the ward, who were found to have been treated with one or more second line anti tubercular drugs by Qualified, Registered private medical practitioner of Mahakaushal area, was included in the study after informed written consent. Patients who did not give informed, not able to communicate properly, treated by non qualified, general practitioner of indigenous system of medicine and consultants of department of pulmonary and sleep medicine, NSCB medical college, and who were prescribed 2nd line ATT drugs less than one week were excluded.

Detailed history of the patient was taken and data was collected by receiving previous prescription of private practitioner in second line anti tubercular drugs. Data was compare with standard guideline (RNTCP).

OBSERVATIONS AND RESULTS

A total number of 82 patients were enrolled. Most of the patients were young adults in the age group of 21-40 years (48.78%, n=40) with mean age 37.13 years (n=82), while 65.85% (n=54) were males and 35.15% (n=28) were females.

Second line ATT was started concomitantly with 1st line ATT in 51 (62.20%) patients. Nine (10.98%) patients were started 2nd line ATT within six months while rest 26.83% were started after six months of starting 1st line ATT.

Out of all patients, 57 (69.51%) did not fall in criterion set for starting 2nd Line ATT. Indication for starting 2nd Line ATT in 11 (13.41%) patients was being Defaulters, while 10 (12.20%) and 4 (4.88%) patients were Relapse and failure cases respectively.

Only 15 (18.29%) patients were done any of the investigation for deciding 2nd Line ATT. Culture drug sensitivity (CDS) was done in 6 (7.32%) patients, Gene Expert in 5 (6.10%), while PCR and LPA were in 2 (2.44%) patients each.

A single 2nd Line drug was used in 89.02% (n=73) patients. Combination of 2nd Line ATT drugs used in rest 10.98% (n=9) patients, while a combination of four drugs (Levofloxacin + Kanamycin + Cycloserine + Ethionamide) was used in only 3.66% (n=3) patients (**Table 1**).

Table-1
Showing profile of 2nd line ATT in patients

S. No.	Profile	Drugs	Number of patient	Percent (%)
1	Single	Levofloxacin	49	59.76
		Moxifloxacin	12	14.63
		Ofloxacin	9	10.98
		Kanamycin	3	3.66
2	Two	Levofloxacin + Kanamycin	5	6.10
		Levofloxacin + Ofloxacin	1	1.22
3	Four	Levofloxacin +Kanamycin +Cycloserine +Etionamide	3	3.66
Total			82	100

Irrespective of combination used Levofloxacin was the most commonly used 2nd Line ATT drug followed by Moxifloxacin, Kanamycin (injectable), Cycloserine and Ethionamide(Graph-1).

Most number of patients (70.49%, n=66) were in 1-2 month of 2nd Line ATT, only 1.22% (n=1) patient were there within 1st month, 3.66% (n=3) within 2-3 month, 6.10% (n=5) within 3-4 month, 1.22% (n=1) within 4-5 month, 3.66% (n=3) patients within 5-6 month and more than six months of therapy. Only 2.44% (n=2) prescriptions were found to be rational while rest 77.56% (n=80) prescriptions were irrational.

Figure - 1
Showing frequency of 2nd line drugs choice

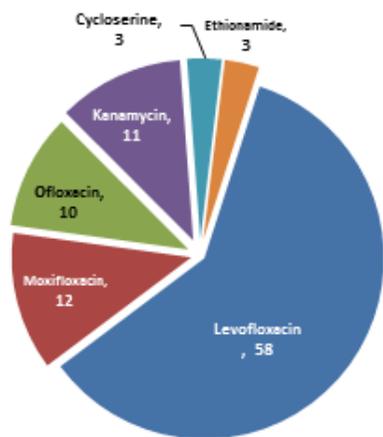


Table-2
Showing physician profile who prescribed 2nd line ATT

S. No.	Qualification	Number of Patient	Percent (%)
1	MBBS	6	7.32
2	MD Medicine	56	68.29

3	MD Chest	10	12.20
4	MD Paediatrics	3	3.66
	Other*	7	8.54
6	Avush/Quacks	0	0.00
Total		82	100.00

*Other=MD/MS/DM/MCH Qualification

Out of all 82 patients 36.39% (n=30) patients prescribed an adequate drug dose. Rest of the 63.41% (n=52) patients were prescribed inappropriate dose.

Physician’s profile for 2nd Line ATT prescriptions as shown in Table 3, most number (68.29%, n=56) of prescriptions were by MD Medicine physicians while only 12.20% (n=10) by any chest physician.

DISCUSSION

The 2nd Line ATT is mainstay to treat failure and MDR-TB suspect cases, should consist of at least four second-line anti-TB drugs include at least a fluoroquinolone, an injectable anti-TB drug, ethionamide (or prothionamide) and either cycloserine or PAS (paraaminosalicylic acid) if cycloserine cannot be used.^[9]

Time lapse between starting of 2nd Line ATT and starting point of 1st Line ATT is important to decide rationality of such prescriptions on temporal basis. Out of all patients (N=82), 51 (62.20%) patients were started 2nd Line ATT concomitantly with 1st Line ATT and 9 (10.98%) within 6 month of starting of 1st Line ATT, and can be accounted irrational on temporal basis according RNTCP guidelines except in case diagnosed MDR. Rest 26.83% (n=22) patients were started 2nd Line ATT after six months.

According to primary criteria to define MDR suspects is as in RNTCP, all failures of new TB cases, smear +ve previously treated cases who remain smear +ve at 4th month onwards and all pulmonary TB cases who are contact of known MDR-TB cases. All smear -ve previously treated pulmonary TB cases at diagnosis and HIV-TB co-infected cases at diagnosis, serve as additional criterion.^[10] For starting 2nd Line ATT 69.51% patients did not fall neither in relapse, defaulter or failure, still only 18.29% were exposed to proper diagnostic test for drug sensitivity which should have been done in all cases. Indication for starting 2nd Line ATT in 13.41% (n=11) patients was being Defaulters, 12.20% (n=10) patients were Relapse case while 4.88% (n=4) patients were treatment failure cases. CDS was done in 6 (7.32%) patients, Gene Expert in 5 (6.10%), while PCR and LPA were in 2 (2.44%) patients each. Dholakia *et al* (2012) reported in a study that 89% physicians used the drug susceptibility test (DST) for diagnosis.^[11]

Combination of four drugs (Levofloxacin+Kanamycin+Cycloserine+Ethionamide) was used in only 3.66% (n=3) patients while a four drug combination is the only rational for 2nd Line therapy should be use unless indicated otherwise (WHO Guideline). Dhingra *et al* (2008) reported 16 patients had taken more than 12 months of ATT and more than five drugs.^[12] Udwadia *et al* (2010) reported tendency to over treat, only 3 of the 106 respondents could write an appropriate prescription for treatment of MDR-TB.^[13] The resistance is low for individual drugs and even lower for two and three drugs. Therefore, use of combination chemotherapy with three or more drugs results in cure.^[14] Factors for emergence of drug resistant TB include suboptimal dosing, split dosing, inadequate number of anti tubercular drugs and prescription of second line anti TB drugs to non DR-TB patients.^[15]

Irrespective of combination used Levofloxacin was the most commonly used 2nd Line ATT drug. The currently best fluoroquinolone, moxifloxacin has potent activity against *Mycobacterium tuberculosis* and has been recommended by the guidelines for the treatment of pulmonary tuberculosis. A meta-analysis by **Chen et al (2015)** suggests that there is a trend for the addition of moxifloxacin to standard first-line therapy for non-drug resistant TB resulted in better outcome.^[16,17]

Rationality of prescription of 2nd Line ATT was decided on the basis of proper indication, prior drug sensitivity workup, rationality of combination of drugs used and adequacy of dose in present study. In present study overall only 2.44% (n=2) prescription were rational while rest 77.56% (n=80) prescriptions were irrational. As far as Adequacy of drug dose concern 36.39% (n=30) patients were prescribed an adequate drug dose. In 80 faulty prescription percentage of adequate dose prescription was only 36.59% (n=30). **Jain et al (1998)** reported that only 29.70% (n=30) were correct for doses as per the body weight of the patient.^[18] which is comparable to present study. A higher incidence of irrational prescription was found in 9.52% prescriptions by PPs were correct as reported **Mishra et al (2013)** in a recent study. They also reported that factors for drug resistance were present in 67.62 % and overdosing was present in 53.33%.^[19] **Rizvi and Hussain (2001)** reported that 39% doctors resorting to four drug regimen, only 7.3% could write the correct dosages^[20] which is far better than our study. Similar findings could be quoted from studies done in Maharashtra India, where results of one study gave 71% wrong prescriptions amongst postgraduates^[21] and another indicated 79 different prescriptions among 122 practitioners.^[22] **Behera and Balamugesh (2006)** found that weight of was recorded in less than half of the patients. Giving higher dosages will cause increased incidence of side effects and thereby decreasing the compliance with therapy. Similarly, lower dosages will cause emergence of bacterial resistance and then treatment failure.^[23]

CONCLUSION

We conclude that most of the PPs need to be trained for making proper diagnosis of MDR TB for which second line drugs are main stay. There is also need of better drug testing facilities and training for rational use of second line anti TB drugs. It will help in improving quality of second line ATT prescription and will improve MDR TB scenario.

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