World Journal of Pharmaceutical Sciences
ISSN (Print): 2321-3310; ISSN (Online): 2321-3086
Published by Atom and Cell Publishers
Available online at: http://www.wjpsonline.org/
Original Article

Prescribing pattern of anti-tubercular drugs in a tertiary care hospital

S. M. Biradar[a]*, Prudvi C [b]*, Gaurav Joshi [b], Janak V. Patel[b], N. V. Kalyane [a], Prabhath A J [b].

[a] Department of Pharmacy practice, BLDEA's S. S. M. College of Pharmacy, [b]Pharm.D, BLDEA's S.S.M. college of Pharmacy. Vijaypur-586103. Karnataka, India

Received: 09-04-2016 / Revised: 21-04-2016 / Accepted: 25-04-2016 / Published: 28-04-2016

ABSTRACT

The observational and prospective study was undertaken to assess the prescribing pattern of anti-TB drugs. Among the selected 81 patients 63 (77.78%) were males & 18 (22.22) were females. The maximum numbers of patients were in the age group of 26 to 45 yrs. The patients were screened for sputum sensitivity and classified into normal TB and MDR-TB patients. The often risk factor involved in TB was tobacco chewing (54) followed by smoking (37). The TB was Co-morbid with RVD (24) and anaemia (14). The drug regimen followed in the study was traditional anti-TB drugs (73) and DOTs therapy (08). The patients treated with DOTs therapy was successful and shown culture sensitivity test negative and patient's compliance was very high with DOTs therapy. Some of ADRs were seen with the DOTs therapy, such as skin rashes, nausea, vomiting and brick red urine. As the anti-TB drugs more interacting and often ADRs exhibiting agents, a proper supervision of drug administration is needed under the guidance of clinical pharmacist with other health care professionals in order to reduce the incidence of ADRs, proper management of drug-drug interactions, avoidance of drug resistance and improve the patient compliance.

Keywords: Prescribing pattern; anti-TB drugs; clinical Pharmacist intervention.

INTRODUCTION

Tuberculosis (TB) is an infectious disease caused by mycobacterium tuberculae. A vital organ affected in the TB is lungs; it may also affect the other parts of the body too. The disease has become the rare in high income countries, but it is still a public health problem in low and middle income countries. TB is the second to HIV/AIDS as the major cause of death from any infectious diseases. In 2011 there were 8.7 million cases of TB reported and 1.4 million deaths have occurred. It is estimated that almost 50% of the world's cases of Multi-drug resistant TB (MDR-TB) occur in china and India alone [1].

TB is transmitted by infected droplet of coughs or sneezes of a sputum positive untreated patient. If the bacillus succeeds in infecting a person, only about 5 to 10% of such infected persons (primary infection) develop active disease. In the remaining 90 to 95 % of infected persons, initial infection usually goes unnoticed. In the year 2007, there were approximately 1.96 million new cases of TB reported and 3.31 lakhs deaths have occurred, representing more than 21% of all TB cases of worldwide. India has more new tuberculosis cases annually than any other countries of a world, ranking first among the 22 high burden TB countries worldwide. According to the World Health Organization's (WHO's) Global TB report 2009, Tuberculosis is classified into Pulmonary Tuberculosis (PTB) and Extra Pulmonary Tuberculosis (EPTB). According to the result of sputum smear examinations pulmonary tuberculosis is classified as:

-Pulmonary tuberculosis sputum-smear positive.
-Pulmonary tuberculosis sputum-smear negative.

Extra Pulmonary tuberculosis (EPTB): is a type of tuberculosis, which affects organs other than lungs such as pleura lymph nodes, abdomen, genitourinary tract, skin, joints, tubercular meningitis and tuberculoma of brain etc [2]. Treatment would be a more challenging one in the treatment of MDR-TB due to long duration and expense of Anti Tubercular agents (ATT) [3]. Successful treatment of TB is one of the key indicators of a TB Control Program's performance and essential to containing the emergence of anti-

***Corresponding Author Address: (Dr). Prudvi & S M. Biradar. PharmD,** Department of Clinical Pharmacy Practice, BLDEA's S.S.M. College of Pharmacy and Research Centre & Shri. B.M. Patil Medical College Hospital and Research Centre. BLDE University Campus VIJAYPUR-586103. Karnataka, India; E-mail: prudvi.prudvi7@gmail.com. smbiradar@rediffmail.com*

TB drug resistance. MDR-TB treatment requires medicines that are expensive, involve longer treatment regimens, are toxic, and can cause patients to have severe side effects [4].

Non-adherence may be driven by a myriad of factors that can be practical and behavioural. These factors include personal beliefs/environment, co morbidities, patient perception of drug therapy value, issues related to drug regimen complexity and side effect. Community pharmacists are well positioned to help patients overcome barriers to adherence [5].

In India, 50–60% of clients buying TB drugs in a private pharmacy did so on a daily basis, due to lack of money, and private pharmacies have been called 'a neglected link in TB control'. Incomplete treatment does not cure the disease, and causes unnecessary expense to already poor patients. It also carries the risk of developing resistance to the main tuberculostatics. Multidrug-resistant TB (defined as resistance to at least Isoniazid and Rifampicin) is a man-made problem. On the other hand, because TB patients often visit a pharmacy at an early stage of their disease (before being diagnosed), it has been argued that pharmacies could play an important role in the early detection of TB cases [6]. Patient counselling produced significant improvement in patient's knowledge, attitude and practice score regarding the management of tuberculosis and thereby better therapeutic outcome [5].This shows that counselling does very important role in tuberculosis. The clinical pharmacist can play a major role in improving patient's knowledge and adherence by patient education and by developing education materials like patient information leaflets [7].

India is the country with highest Tuberculosis (TB) burden, accounting for one fifth of the global incidence of TB and is adding 1.8 million new TB cases annually. Social and economic burden of TB in India is very high and indirect cost to the society is estimated to be $3 billion. The government has a Revised National Tuberculosis Control Programme (RNTCP) in which the internationally accepted DOTS (Directly Observed Treatment, Short course) strategy is used. DOTS involves free diagnosis of TB & free medications for complete treatment duration (minimum 6 to 8 months or longer) under direct supervision. The patient needs to visit TB clinic, thrice a week in first couple of months of treatment (intensive phase) & then once in a week during continuation phase. Thus in DOTS, it is ensured that patient adheres to the complete duration of treatment. This helps not only in cure but also reduces the chances of development of Drug Resistant to TB. The entire country now has DOTS coverage [8].

Patients understanding of their treatment regimen can influence their adherence behaviour. Therefore, patient education can be awfully effectual response to many of the difficulties in getting patients to adhere to a complete course of TB therapy. Adherence to treatment may be best understood as a set of interrelated behaviours that includes cognitive formulation of a personal understanding of why pharmacotherapy is prescribed; interpersonal skills to communicate effectively with health care providers; and practical skills related to medication taking. The pharmacist should educate patients on the importance of continuing their chemotherapy despite symptomatic improvement. Pharmacists should become a part of multidisciplinary band (with nurses, physicians, social workers) devoted to successful chemotherapy of TB patients and their families. Patients counselled by pharmacists were more likely to be very satisfied within formation provided about adverse effects. As well, patients found the written information provided by pharmacists more meaningful when used in conjunction with the pharmacist's counselling. Considering all the above aspects, a patient information pamphlet was introduced in the Pulmonology department and the study entitled "Effectiveness of Knowledge based approach for the improvement of patient adherence and reducing the severity of Adverse Drug Reaction in Anti Tubercular Therapy" was carried out. Both the physician and clinical pharmacist were equally participated to improve the enhanced therapeutic outcome in TB therapy by aiming the complete patient care. A thorough education by the pharmacist regarding the treatment, drugs and the possible adverse drug reactions were given [9].

Pharmacists interact with large number of people on a daily basis and are therefore in an ideal position to distribute educational material to the public, not only on the treatment of TB but also on preventative measures. The pharmacist should establish a relationship with his/her patients so that he/she can act as the patient's source of information on their disease condition as well as the treatment they have been prescribed. As TB treatment takes months to complete and has to be taken regularly, most patients require encouragement in order to adhere to their medicaments or treatment. Pharmacists are well-placed to assess adherence to their treatment and identify any factors which may predispose the patient to non-adherence [10].

MATERIAL AND METHODS

Study design and settings: Hospital based prospective observational study was carried out for a period of six months and patients treated with DOTs were followed for period of 12 months, in a tertiary care hospital Shri B.M. Patil Medical College Hospital and Research Centre and District Govt. DOTS centre, Vijaypur of south India. All the patients admitted to the TB care unit of a hospital and DOTs of a Govt centre were screened for inclusion and exclusion criteria. The selected 81 patients were enrolled in to the study and evaluated for the study parameters, such as demographic details of patients, age group distribution, sputum sensitivity, types of TB, risk factors involved , co-morbidity encountered, type of therapy recommended, number of drug-drug interactions and ADRs occurred with the TB patients.

Inclusion criteria:

- Inpatients in general medicine wards, TB & chest ward and ICU of either gender.
- All the patients of either gender diagnosed with TB with confirmed laboratory

Findings will be included in the study.

- Patients who are willing to participate.

Exclusion Criteria:

- Out patients.
- Inpatients other than general medicine wards, ICU, TB & chest ward.
- Pregnant women and children are excluded from the study.
- Patients who are not willing to participate.

Study procedure: After obtaining approval and clearance from institutional ethics committee, 81subjects with suspected Tuberculosis were included in the study. The data were collected from the patient case records, patient history, laboratory data, medication history and patient progress report. The collected data were analyzed for the parameters discussed in results.

RESULTS

In the present study, a total number of 81 patients were evaluated during a period of six months. Out of 81 patients, 63 were males and 18 were females, as shown in table 1. The minimum and maximum age group were detected & categorised into different age groups with male and female ratio, depicted in table 2. Among 81 patients 48 (59.2%) were sputum +ve in which 39(48.1%) were males and 9(11.11) were females and 33(40.7%) were sputum –ve, in which 24(29.6%) were males and 9(11.11) were females as shown in table 3. The selected patients were divided into two types of TB, Normal TB (73) & MDR-TB (08), were detected. Out of 81 patients 73 patients were diagnosed as normal TB that constitute 90.1%, among which 57 (70.3%) were male and 16 were female (19.7%) & 8 patients were diagnosed as MDR-TB that constitute 9.9%, among which 6 (7.4%) were male and 2 (2.4%) were female as shown in table 4.

Among 81 patients 28(34.5%) newly diagnosed cases, in which 23 (28.3%) were male and 5(6.17%) were female & 53 (65.4%) were previously diagnosed TB patients in which 40(49.3%) were male and 13(16%) were female, as depicted in table 5. The major risk factors involved in TB were, smoking, tobacco chewing and alcohol consumption were identified in 81 patients. Among 81patients, total 97 risk factors were identified, in which 37 (38.14) were smokers and 45 (46.391) were tobacco chewers and 06 (6.185) were alcoholic occurred in male patients. Tobacco chewing is the only risk factor occurred in female patients (Table 6).

The selected patients were most of the times co-morbid with RVD, anaemia, liver disease, and hypertension. 24 (44.45) were with RVD in which 20 (37.03) were males and 04 (7.4) were females, 18 (33.3) were with anaemic patients among which 12(22.2) were male and 06 (11.1) were females, 06 (11.1) males patients were co-morbid with liver diseases, 06 (11.1) were with hypertensive patients in which 04 (7.4) were males and 02 (3.70) were females as shown in table 7. It is observed that, the medical practitioner followed the two different types of therapeutic approach namely, traditional anti-TB drugs therapy and DOTs therapy. Out of 81 patients, 73(90.1%) were prescribed with general anti TB drugs in which 57 (70.3%) were males and 16(19.7%) were females. 8(9.9%) were given with DOTs therapy among which 6(7.4%) were males and 2(2.5%) were females as shown in table 8.

Out of 81 patients, 73 patients were prescribed with traditional anti-TB drugs, in which 57 (78.08) have taken therapy for less than 10 days in which 49 (67.12) were males and 08 (10.95) were female and 16 (19.3) patients have taken therapy for more than 10 days in which 08 (10.95) were male and 08 (10.95) were females as shown in table 9. Eight patients were started with DOTs therapy, after completion of 6 months therapy the culture sensitivity test was conducted which was found to be negative in all the patients and therapy was continued for the period of 12 months. After completion of 12 months once again culture test was conducted and all the patients were shown negative sensitivity except one female patient, who died with no apparent reason (Table 10).

Patient compliance was evaluated with DOTs therapy after 12 months, among 7 patients one was having moderate compliance 1 (14.28%) and rest of patients, 6 (87.5%) were high/rich in compliance (Table 11). It is known that anti TB drugs are more likely to have drug interaction and adverse drug reactions, among 81 patients 330 drug-drug interactions (Theriotecal interactions) were found, in which 141(42.7%) were major, 169(51.2%) were moderate and 20 (6.3%) were minor (Table 12). The Rifampicin and pyrazinamide were the drugs most often involved in occurrence of drug interactions among the TB patients. The most common drugs involved in drug interactions were depicted in table 13.

The ADRs affected the mainly three biological systems of the body namely skin, gastro intestinal tract and renal system, the detail statistics are given in table 14. Out of (8 MDR-TB subjects) 81 TB subjects, 9 ADRs are observed in which skin, gastrointestinal and renal systems are affected. ADRs of skin (skin rashes) were seen in 3 patients in which 2 (22.22) were males and 1(11.11) was female. GIT reactions such as nausea and vomiting were seen in 3 patients in which 2 (22.22) were males and 1(11.11) was female, in renal system the observed ADR was brick red urine seen in 3 patients in which 2 (22.22) were males and 1(11.11) was female (Table 14).

DISCUSSION

Among the study population the affecting rate of TB was more in males compare to females, reason might be life style, sex, often exposure to susceptible area and bad habits etc, these finding are well supported by previous finding of kasi srinivas et al,[11].

Age play an important role in affecting the TB, even though middle age adults having a good immune power, the affecting rate of TB is very high with middle age group of people only, the reason might be bad habits such as, cigarette smoking, tobacco chewing and alcoholism etc. In the present study it is seen that the more numbers of patients suffering from TB were in the age group of 26-35, 28 (34.56), followed by 36- 45,13 (28.38) and 18-25,0/ 9 (11.11), these statistic are comparable to previous study kasi srinivas et al [11] in which 26-35 Yrs 13 (28.89%) and 36-45 Yrs 12 (26.67%). The most of subjects were sputum positive, among which males were more in number in comparison with than females, and similar finding have occurred with sputum negative patients, which is deviating to a study conducted by Claude Mambo Muvunyi et al [12], it indicates that there might not be correlation between sex and sputum sensitivity.

Normal TB rate is very high as compare to MDR-TB patients, in both the cases affecting rate is more with males in comparison with females, most of subjects were previously (old) diagnosed cases and only few cases were newly diagnosed. Risk factors were identified in all the patients of which most of patients were tobacco chewers, and other risk factors involved were smoking and alcoholism seen in male patients.

Tuberculosis is the condition most of the times encountered with RVD and co-exists with anaemia and followed by liver diseases and hypertension, similar type of findings observed in the present study, where in all the co-morbidities males were the predominant, similar statistics were observed with Deewan et al. [13] and Parvat kumar et al. [14].

Two types of therapy namely DOTs and general anti-TB drugs therapy was practised in the present study, duration of therapy with anti-TB drugs were less medication adherence may be due to low economic status and poor intention towards the health maintenance. In DOTs therapy medication adherence was high and successful and culture sensitivity test was negative which improves the patient compliance.

Many number of drug-drug interactions were found among which, major were in between the rifampicin+pyrazinamide, rifampicin+isoniazid, ciprofloxacin+theophylline, rifampicin+nevirapine. These results indicate the higher interacting characteristic of anti-TB drugs. ADRs such as, rashes, nausea, vomiting, brick red urine and burning micturation were observed in MDR TB patients may be due to prolonged use of anti TB drugs.

CONCLUSION

The proper diagnosis and rational prescribing of anti-TB drug regimen is a basic necessary for a positive therapeutic outcome in TB patients. In the present study a timely sensitivity testing and selection of drug regimen played important role in obtaining the negative cultural sensitivity test and improved the patient compliance. As the anti-TB drugs more interacting and often ADRs exhibiting agents, a proper supervision of drug administration is needed under the guidance of clinical pharmacist with other health care professionals in order to reduce the incidence of ADRs, proper management of drug-drug interactions, prevention of drug resistance and improve the patient compliance.

Conflict of Interest: The authors have no conflicts of interest.

ACKNOWLEDGEMENT

We are thankful to Principal of *BLDEA's S. S. M. College of Pharmacy and Research centre* and Dean and Principal of Shri. *B.M. Patil Medical College Hospital and Research Centre*, Vijaypur-586103, Karnataka, India, for providing necessary facilities and support.

Table 1: Data obtained about patients demographic characters (Gender)

Gender	Number of patients (Percentage %)
Males	63 (77.78%)
Females	18 (22.22%)
Total	81

Table 2: Age group categorization of individuals in TB patients

Age (in yrs)	Male (%)	Female (%)	Total
18- 25	06(7.40)	03(3.70)	9(11.11)
26-35	20 (24.69	08 (9.87)	28 (34.56)
36-45	19 (23.45)	04 (4.93)	23 (28.38)
46- 55	09 (11.11)	01 (1.23)	10 (12.34)
56- 65	09 (11.11)	-	09 (11.11)
≥ 65	02 (2.46)	-	02 (2.46)
Total	65(80.24)	16(19.75)	81 (99.94)

Table 3: Sputum Tests categorization of individuals in TB patients

Type of TB	Male (%)	Female (%)	Total (%)
Sputum +ve	39 (48.1)	09 (11.11)	48 (59.2)
Sputum-ve	24 (29.6)	09 (11.11)	33 (40.7)
Total	63(77.77)	18(22.22)	81

Table 4: Types of TB diagnosed

Type of TB	Male (%)	Female (%)	Total (%)
Normal TB	57 (70.3)	16 (19.7)	73 (90.1)
MDR-TB	06 (7.4)	02 (02.4)	08 (9.9)
Total	63(77.77)	18(22.22)	81

Table 5: Diagnosis

Type of TB	Male (%)	Female (%)	Total (%)
Newly diagnosed TB	23(28.3)	05 (6.17)	28 (34.5)
Known TB cases	40 (49.3)	13(16.0)	53(65.4)
Total	63(77.77)	18(22.22)	81

Table6: Number of risk factors occurred in male and female patients.

Risk factors	Male (%)	Female (%)	Total (%)
Smoking	37 (38.14)	00 (00)	37 (38.144)
Tobacco chewing	45 (46.391)	09 (9.27)	54 (55.67)
Alcohol	06 (6.185)	00 (00)	06 (6.18)
Total	88(90.72)	09(9.27)	97 (99.99%)

Table7: Type of Co-Morbidities with TB patients.

Co-morbidity	Male (%)	Female (%)	Total (%)
RVD	20 (24.69)	04 (4.93)	24 (29.62)
Anaemia	12 (14.81)	02 (2.46)	14 (17.28)
Liver diseases	06 (7.40)	00 (00)	06 (7.40)
Hypertension	03 (3.7)	02 (2.46)	05 (6.17)
TB *per se*	23 (28.39)	09 (11.11)	32 (39.50)
Total	64 (79.01)	17 (20.98)	81

Table 8: Types of therapy given in individual TB patients

Type of therapy	Male (%)	Female (%)	Total (%)
Traditional anti-TB drugs	57 (70.3)	16 (19.7)	73 (90.1)
DOTs therapy	06 (07.4)	02 (02.5)	08 (09.9)
Total	63(77.77)	18(22.22)	81

Table 9: Duration of patient's stay in hospital

Duration	Male (%)	Female (%)	Total (%)
< 10days	49 (67.12)	08 (10.95)	57 (78.08)
>10 days	08 (10.95)	08 (10.95)	16 (21.91)
Total	57(78.08)	16(21.91)	73

Table10: DOTs therapy for 12 months

	Culture sensitivity test		
Months	**0**	**6**	**12**
Male	+ ve (06)	-ve (06)	-ve (06)
Female	+ve (02)	-ve (02)	-ve (01)
Total	08	08	07

Table 11: Patients compliance with DOTs therapy

Compliance in DOT	Male (%)	Female (%)	Total (%)
Poor	00 (00)	00 (00)	00 (00)
Moderate	00 (00)	01 (14.28)	01 (14.28)
High/rich	06 (85.71)	00 (00)	06 (85.71)

Table12: Drug-Drug Interactions found in individual TB patients

Severity	No. of DDIS (Percentage)
Mild	20 (6.3)
Moderate	169 (51.2)
Severe	141(42.7)
Total No Of DDIs	330

Table13: Major Drug-Drug interactions between the following drugs

Drug	Type of Interactions
Rifampicin+Isoniazide	Concomitant use of both cause hepatotoxicity and decreases isoniazid metabolism.
Rifampicin +Nevirapine	Rifampicin decreases the blood levels of the nevirapine.
Rifampicin+Pyrazinamide	Concomitant use cause liver damage.
Ciprofloxacin+Theophylline	Ciprofloxacin increases the effects of theophylline.

Table14: Biological systems affected with ADR

Biological systems involved	TYPE OF ADR	Male (%)	Female (%)	Total
Skin	Rashes,	2 (22.22)	1(11.11)	03
Git	Nausea, Vomiting	2 (22.22)	1(11.11)	03
Renal	Brick red urine, Burning micturation	2 (22.22)	1(11.11)	03
Total	-	6(66.66)	3(33.33)	09

REFERENCES

1. Francis varaine, michael L rich. Tuberculosis: Practical guide for clinicians, nurses, laboratory technicians and medical auxiliaries. Medecins Sans Frontieres Parterns in Health. 2014 edition. P. 3-113.
2. American Thoracic Society Diagnostic Standards and Classification of Tuberculosis in Adults and Children. Am J Respir Crit Care Med. 2000; 161: 1376–95.
3. V K Dhingra, S Rajpal, Anshu Mittal M. Hanif. Outcome of multi-drug resistant tuberculosis cases treated by individualized regimens at a tertiary level. Clinic Ind J Tuberc. 2008; 55: 15-21.
4. Homa bay TB team Guidelines for Conducting Drug Resistant TB Drug Utilization Reviews: Kenya Field Test. MSH 2012; Oct. 30.
5. Michael Taitel, Jenny Jiang, Kristi Rudkin, Susan Ewing, Ian Duncan.The impact of pharmacist face-to-face counseling to improve medication adherence among patients initiating statin therapy. Patient Prefer Adher. 2012; 6: 323–29.

6. M L Lambert, R Delgado, G Michaux, A Vols, N Speybroeck, P Van der Stuyft et al. Collaboration between private pharmacies and national tuberculosis programme in Bolivia. Trop Med Int Health. 2005; 10(3): 246–50.
7. V Ramanarayana reddy, B Venkateswara rao, A Jayarami reddy, A Kshore babu, G Nagarjuna reddy, K Bharathi priya et al. Clinical study on therapeutic management and impact of patient counseling on tuberculosis. Int. J Adv Pharm Sci. 2010; 1(2): 340-46.
8. Mathew T Francis K, chandrasekaran. Effectiveness of Knowledge Based Approach for the Provement of Patient Adherence and Reducing the Severity of Adverse Drug Reaction in Anti Tubercular Therapy. International journal of Pharmacy Teaching and Practice. 2012; 3(3): 313-17.
9. Nimesh Amrith, Jayasuriyas, Laksiri Nanayakkara, Nayanathara Iddamalgoda, Kathy Derore. A case study among the patients screened at Chest Clinic of Medical Research Institute of Colombo, Food Security and Nutrition among the Tuberculosis infected patients, Sri Lanka. VAN Food Security Analysis. P. 15-30.
10. Gail Mkele, The role of the pharmacist in TB management, SA Pharmaceutical Journal. 2010; March: 8-21.
11. Kasi Srinivas, sreedevi. A study on treatment outcome of new sputum smear positive tuberculosis patients among tribal population in kurnool district. Int. J Res Dev Health. 2013; 1(1): 5-10.
12. Claude Mambo Muvunyi, Florence Masaisa1, Claude Bayingana1, Andre Musemakweri, Leon Mutesa, Teresa Carbonell Hernandez et al .Prevalence and diagnostic aspects of sputum smear positive tuberculosis cases at a tertiary care institution in Rwanda. Afr J Microbiol Res. 2010; 4(1): 88-91.
13. P K Dewan, D Gupta, B G Williams, R Thakur, D Bachani, A Khera et al. National estimate of HIV seroprevalence among tuberculosis patients in India . Int J Tuberc Lung Dis. 2010: 14(2): 247–49.
14. Pravat Kumar Thatoi, Sagar Khadanga. Pulmonary Tuberculosis and its hematological correlates Transw Med J. 2013; 1(1): 11-13.