Role of the Clinical Pharmacist in adherence to the treatment of Multidrug-Resistant and Extensively Drug Resistant Tuberculosis

Muhammad Nasir,[1] Mazhar Ali Khan,[1] Nadia Ashiq,[1] Muhammad Haroon,[2] Lala Rukh,[3] Umar Farooq[4]

[1]Programmatic Management of Drug Resistant TB Unit, Lady Reading hospital Peshawar-Pakistan.

[2]Quaid-e-Azam University Islamabad-Pakistan.

[3]Hayatabad Medical Complex Hayatabad-Pakistan.

[4]Indus Health Network Peshawar-Pakistan.

Address for correspondence
Mazhar Ali Khan
Programmatic Management of Drug Resistant TB Unit, Lady Reading hospital Peshawar-Pakistan.
Email:
mali_smile2005@yahoo.com

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MN MAK conceived idea, MN MAK NA drafted the study, MN NA collected data, MAK MH LR did statistical analysis & interpretation of data, NA MH LR critical reviewed manuscript, All approved final version to be published

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The Authors declares that there is no conflict of interest.

Abstract

Background: Different strategies have been employed to improve treatment adherence of TB patients. Individual patient care and follow-up, clear lines of communication, compliance aids, educational materials, and incentives have all been shown to improve adherence.

Objective: The objective of this Study is to investigate the role of Clinical Pharmacist in relation to the adherence to treatment of MDR-TB and XDR-TB.

Methodology: The pilot study was conducted in the PMDT Lady Reading hospital Peshawar. Data was collected by using questionnaire which was designed to collect demographic variables as well as knowledge, attitude and adherence to the treatment of MDR-TB. This study includes all patients who enrolled from Jan 2012 to Dec 2013. All data collected were then coded, edited and entered to Statistical Package for the Social Sciences (SPSS), version 16.0 software and analyzed.

Results: Among study cases 58.47% were male and 41.53% were female. Among study cases 23.88% patients need Pharmaceutical care. Most of the patients faced side effects of drugs, of which Gastrointestinal issues.

Conclusion: Patients' adherence to TB treatment improved when a pharmacist provided patient education on medication use and addressed patients' pharmaceutical care issues.

Key words: DR-TB; Drug Side Effects; Pharmacist; Peshawar; Pakistan

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Introduction

Worldwide, Tuberculosis (TB) continues to be the most important cause of death from a single infectious disease.[1] Although, recent decades have witnessed increased efforts in the fight to end TB, fundamental gaps are hampering these efforts, particularly in resource- constrained settings and in settings with a high burden of disease. The World Health Organization (WHO) estimates that close to 54 million TB deaths were averted between 2000 and 2017 because of improved disease prevention and management, and service delivery, nevertheless, up to 10 million people continue to fall ill with TB every year.[2] Multidrug resistance tuberculosis (MDR-TB) defined as bacillary resistance to at least

two most powerful drugs, Isoniazid (INH) and Rifampicin (RMP). Extensively drug resistant (XDR) tuberculosis is multi drug resistance tuberculosis with further bacillary resistance to any fluoroquinolone and at least one of the three drugs (Kanamycin (Km), Amikacin (Am) and Capreomycin (Cm)).[2] Genetic resistances occurred naturally to anti TB-drugs as a result of chromosomal mutation accompanied mycobacterium replication. The MDR-TB has developed because of improper use of anti TB medicines. MDR-TB is a threat for controlling global TB.[3]

Multi drug resistant tuberculosis is an emerging worldwide problem. WHO declared new cases of MDR-TB is 2.9% among weighted portion of global population.4 Pakistan ranked fifth on the list of 22 global high burdened countries in tuberculosis and forth in the list of 27 high burdened MDR-TB countries.[5] The percentage of MDR-TB is [3,4] in the list of new TB cases and 21 in the list of retreated cases.[6] The emergence of drug resistant strains of mycobacterium is due to poverty, malnutrition, population migration, poor health facilities, inadequate housing and sanitation, urbanization, political instability and refugee influx.[3] MDR-TB treatment is possible but may cost 100 times more than TB treatment cost,[7] failure of treatment may prove more cost in future and each patient of MDR-TB without proper therapy will infect 10-15 people each year.[4]

Adherence has been defined as the extent to which patients' behavior coincides with the health advice given.[8] By contrast, non-adherence to drug therapy can be evaluated by the number of drug doses missed, mistimed, or otherwise administered incorrectly.[9] Non-adherence has been viewed as a behavioral disorder that the pharmacist can help to rectify by identifying risk factors and then planning appropriate interventions.[10] Patients who feel personally responsible for their own therapy, and health in general, tend to be more compliant, which is why the concept of concordance is replacing the terminology of compliance.[11] Different strategies have been employed to improve treatment adherence of TB patients. Individual patient care and follow-up, clear lines of communication, compliance aids, educational materials, and incentives have all been shown to improve adherence.[11,12]

According to WHO statistics, it is expected that the DOT strategy will cause the number of TB cases to fall by 53% and mortality to be reduced by 58%.[13] DOT is arguably the most effective method for increasing adherence, but alone it may be inadequate. Researchers suggest supplementing and thereby strengthening a DOT program with other strategies like patient education and incentives as mentioned above.[14,15] Clinical pharmacists providing pharmaceutical care services have been shown to improve adherence to therapy and reduce potential prescribing errors.[16-18] There are three foundational aspects to pharmaceutical care. First, the patient's pharmaceutical care needs should be identified. Following this, an individualized pharmaceutical care plan should be drawn up, taking into account the patient's knowledge, general health beliefs, and motivation.[19] Finally, the outcomes targeted in the care plan should be evaluated.[20]

The objective of this Study is to investigate the role of Clinical Pharmacist in relation to the adherence to treatment of MDR-TB and XDR-TB.

Methodology

The pilot study was conducted in the PMDT Lady Reading hospital Peshawar. Data was collected by using questionnaire which was designed to collect demographic variables as well as Knowledge, attitude and adherence to the treatment of MDR-TB. This study includes all patients who enrolled from Jan 2012 to Dec 2013. All data collected were then coded, edited and entered to Statistical Package for the Social Sciences (SPSS), version 16.0 software and analyzed.

Data collection

Baseline demographic and clinical data were gathered from patient files, medication, and face-to-face interviews during the registration and post registration. At the first interview, patients' health beliefs and knowledge of their current drugs and doses were assessed through an interviewer-assisted questionnaire.

Patient Education

The clinical pharmacist provided standard oral and written patient education. Before the study commenced, the material was checked by expert physicians, pharmacists, and lay people to ensure readability and clarity. The written material was in the form of an illustrated handout and prepared in a question-and-answer format to enhance readability. After the patient education session, appointments were scheduled for follow-up visits on every month in order to monitor progress and assess therapy adherence. The patients were asked to bring all their drugs, including used and unused containers, with them for the next visit; however, they were not told that these containers would be used to count the number of unused medications.

Measurement of adherence

The patient's adherence to treatment was evaluated for the first-time MDR-TB patients by three different criteria: attendance at the scheduled follow-up visits, investigation reports, and medication counting. Medication counting was performed by subtracting the number of tablets remaining from the number of tablets that had been given at previous appointments.

Identification of the major pharmaceutical care needs and issues of MDR-TB patients

Pharmaceutical care needs were defined as suspected drug-related problems reported by the patient. The patient-reported suspected drug-related problems were recorded in pharmacovigilance form of the concerned patient file and, whenever possible, were supported by objective data such as physical examination by the physician. When these complaints were found to be consistent with an established drug adverse effect or an interaction, they were classified as pharmaceutical care issues.[21,22] The clinical pharmacist made interventions for the determined pharmaceutical care needs when possible.

Statistical analysis

Continuous variables were expressed as the mean (± S.D.), and categorical variables were reported as number (percent). Statistical significance was expressed as a $p < 0.05$ using a confidence interval of 95%. All the statistical analyses were performed using SPSS version 16.0 and MS office 2013 version.

Results

Patient characteristics. Number of the patients are provided in (Table 1). The MDR-TB unit at the Lady Reading Hospital Peshawar have 1 ward for both genders male and female patients, so both genders were included in this section of the study.

Adherence: The effect of pharmacist-directed patient education in terms of improving visit attendance and adherence to the treatment. The number of patients who attended all of the scheduled visits was higher in female group as compared to male group (59.1% versus 40.9%, respectively).

Pharmaceutical care needs: The pharmaceutical care needs of the patients as assessed throughout the study are presented in five main categories (Table 2).

Pharmaceutical care issues: The pharmaceutical care issues defined throughout the study were dermatological, gastrointestinal (GI), metabolic, sensory, and central nervous system (CNS) problems (Table 3). The pharmaceutical care needs and issues that were addressed by the clinical pharmacist are presented in (Table 4).

Table 1: Patients demographic characteristics

Treatment Status	Total no of patients (n=354)	% age
No. of Male patients	207	58.47 %
No. of Female patients	147	41.52 %

Table 2: Patient's Pharmaceutical care needs

Pharmaceutical Care Need	Criteria	No of Patients (n=354)
Pain control	Patients reported pain untreated by analgesics or other therapies	22 (6.21 %)
Respiratory control	Patient reported SOB or chronic cough unrelieved by medication.	26 (7.34%)
Nutrients replacement	Hematologic (Hemoglobin of < 12.6 g/dl [male] or 10.3 g/dl [female] parameters that might be suggestive of nutrient replacement needs	8 (2.25%)
Diabetes control	Random blood glucose concentration recorded of > 190 g/dl at more than 2 occasion, supported by a DM treatment	18 (5.08%)
Appropriate prescribing	Represented by an inappropriate dose quantity	11 (3.10%)

Table 3: Pharmaceutical care issues

S.NO	Pharmaceutical care issues	Criteria	No of patients (n=354)
1	Sensory	Patient reported with or without supporting audiometric results	89 (25.14%)
2	Dermatological	Patient reported with or without supporting clinical examination	06 (1.69%)
3	Gastrointestinal	Patient reported vomiting, nausea and loss of appetite	168 (47.5%)
4	CNS	Psychosis, aggression behavior reported by the Psychologist	18 (5.1%)
5	Metabolic	Laboratory parameters such as SGPT, uric acid and TSH level outside the normal reference range	34 (9.6%)

Table 4: Intervention by the Clinical Pharmacist in response to Pharmaceutical Care Needs or Issues

S. No	Pharmaceutical care needs or issues	Intervention	Observed Outcomes
1	Insufficient quantity of medication (n=23)	Medication sample tablets are arranged from pharmaceutical company	Patients received drugs on time and demonstrated no adherence
2	High blood glucose level (n=18)	Blood glucose monitored and refer to specialist diabetic care	Hyperglycemia corrected
3	Symptoms of nausea, vomiting and loss of appetite (n=168)	Discussion with physician to request liver function test (LFT's) and also prescribed Proton Pump Inhibitors (PPI's)	No development of hepatotoxicity seen LFT's and symptoms of GIT resolved
4	Symptoms of psychosis and aggression behavior observed (n=18)	Discussion with physician to refer to Psychiatric ward and drug Cycloserine was withheld for a week.	After consultation with Psychiatrist and different psychological session patient symptoms resolved
5	Some patients' blood profile were above or below the normal level such Hemoglobin (HB), SGPT, TSH, Uric acid. (n=34)	Medication was prescribe for the HB, TSH and Uric acid while for high level of SGPT drug Pyrazinamide 400 mg was withheld for 10 days.	Symptoms were resolved

Discussion

This study reveals the positive effect of clinical pharmacist-directed patient education on the therapy adherence of MDR-TB patients, while identifying the major pharmaceutical care needs and issues of the MDR-TB patients. The hospital where the study was conducted was Tertiary care hospital. Clinical pharmacist should regularly performed the pharmaceutical care practices in the Hospital. The clinical pharmacist should work as the investigator for finding the pharmaceutical care needs and issues and also educate patients regarding their medications.[21,22]

In this study, which provided subjective and objective measures of adherence, a clear difference was recorded in favor of the patients who had received pharmacist-led patient education. Patient education particular on MDR-TB patient adherence pointed out that information, counseling, reminders, self-monitoring, reinforcements, family therapy, additional supervision, and individualized care have been shown to improve adherence in various combinations.

Medication counting measurements depend, to some extent, on the patient recall and carefulness in returning empty bottles. A spot check at patients' homes may have given a more realistic figure of adherence for the tablet count. The results of this study show that pharmacist-led patient education improves adherence.

The most commonly encountered pharmaceutical care need was pain control and respiratory control: 6.21% and 7.34% respectively of MDR-TB patients reported pain, mostly in the joint pain and arthralgia which usually respond to Non-steroidal Anti-Inflammatory drugs[23,24] are likely to be linked to

Pyrazinamide or Ethionamide use.[25,26]

Needs related to respiratory control were the second most-common pharmaceutical care need in MDR-TB patients. Some patients were treated with oxygen but most responded to bronchodilators or inhaled anticholinergic drugs, while antitussives brought some relief in cases of painful, sleep-disturbing cough. The pharmacist can play a role in drug selection and dosage adjustment of these medications.

Several laboratory parameters that might be suggestive of patients' nutritional status were checked and assessed for any requirement for replacement. More than half of the male patients had hemoglobin concentrations less than 12.6 g/dL. These anemia's may be linked to blood loss through hemoptysis, poor nutrition related to appetite loss, or anemia secondary to chronic infection.[27] Low hemoglobin levels may indicate a poor nutritional status. A Clinical Pharmacist aware of the patient's clinical status should be ready to recommend an appropriate replacement therapy in the form of iron (where deficiency is confirmed), vitamin A, zinc replacement, or special oral feeding formulations.[28,29]

The pharmaceutical care issues identified in this study reflect problems arising from the patients' drug therapy; the most frequently encountered drug-related problem was GI-related and included nausea, vomiting, loss of appetite. Most of these complaints should be interpreted as a direct adverse effect of chemotherapy.[21]

However, severe cases of nausea or vomiting may point to a drug-induced hepatotoxicity. The patient should be carefully monitored and liver function tests performed in order to exclude such a conclusion. Para-Aminosalicylic-acid, Ethionamide, and fluoro-quinolones (levofloxacin and moxifloxacin) have potential for causing GI adverse effects.

The other problem in the MDR-TB patients, affecting 25.14% of the patients, was related to sensory functions, particularly hearing loss as determined by audiometric results. This hearing loss should be interpreted as an adverse effect of Aminoglycoside (Amikacin or Capreomycin) therapy, which all of the patients were taking.

Another common pharmaceutical care issue was related to a wide range of CNS-related complaints such as depression, Psychosis and dizziness. Yew ET al,30 reported that 5.1% of MDR-TB patients experienced CNS-related adverse effects. CNS adverse effects of a serious nature such as depression and psychosis were attributed to Cycloserine, while the milder CNS adverse effects such as insomnia and dizziness were considered to be related to quinolone therapy.[30]

Drug-related metabolic issues encountered in this study were hyperuricemia, Hyperthyroidism which is frequently linked to pyrazinamide administration,[21] and elevated transaminase levels, which can be triggered by any of the components of the standard combination.[21,28]

Considering the positive effect of pharmacist-led patient education on adherence to MDR-TB shown in this study, the importance of education should be emphasized and supplied to every susceptible TB patient as well. This will help prevent development of non-adherence-induced multidrug resistance. When writing pharmaceutical care plans and forming strategies to provide pharmaceutical care services for TB patients, it is essential for the pharmacist to be aware of potential care needs and issues. Thus, the pharmacist can be more confident in making significant contributions to improve patients' quality of life.

Conclusion

Patients' adherence to TB treatment improved when a pharmacist provided patient education on medication use and addressed patients' pharmaceutical care issues.

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