

ORIGINAL RESEARCH

Assessment of fluoroquinolone resistance among pulmonary tuberculosis patients

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ABSTRACT

Background: Tuberculosis is most commonly found among people living in poor conditions and in deprived areas, especially in elderly people and those with unstable social or psychiatric backgrounds, such as hostel dwellers, street dwellers, alcoholics, and drug misusers, as well as in immunocompromised patients. The present study was conducted to assess fluoroquinolone resistance among pulmonary tuberculosis patients.

Materials & Methods: 58 pulmonary TB patients of both genders were included. All patients were subjected to DST for first-line drugs (FLDs) and second-line drugs. FQs DST was also performed using automated Mycobacterial Growth Indicator Tube-960 liquid culture technique. The immunochromatographic assay was performed to distinguish Mycobacterium tuberculosis complex (MTBC) from non-MTBC

Results: Out of 58, males were 38 and females were 20. One drug resistance such as Ofloxacin was seen in 28, levofloxacin in 3 cases, moxifloxacin in 1 and Kanamycin in 1 case. Two drug resistance such as Kanamycin+ Ofloxacin in 2 and Levofloxacin+ Ofloxacin in 1 case. Three drug resistance such as Ofloxacin+ Levofloxacin+ Moxifloxacin in 1 and Ofloxacin+ Levofloxacin+ Kanamycin in 1 case and all sensitive isolates was seen in Ofloxacin+ Levofloxacin+ Kanamycin+ Moxifloxacin in 20 cases. The difference was significant ($P < 0.05$).

Conclusion: Fluoroquinolone resistance among drug sensitive and multidrug resistance tuberculosis isolates was high.

Key words: Fluoroquinolone, Pulmonary Tuberculosis, Ofloxacin

INTRODUCTION

Tuberculosis is most commonly found among people living in poor conditions and in deprived areas, especially in elderly people and those with unstable social or psychiatric backgrounds, such as hostel dwellers, street dwellers, alcoholics, and drug misusers, as well as in immunocompromised patients.^{1,2} In developing countries, tuberculosis is most common among very poor people, especially those who are severely malnourished or HIV positive.³ Awareness, in both primary and secondary care, of these epidemiological facts increases the chances of prompt diagnosis of tuberculosis.^{4,5} Whereas post-viral cough, asthma, reflux oesophagitis, postnasal drip, or lung cancer are more likely explanations in developed countries, cough that persists for more than three weeks despite treatment with a broad-spectrum antibiotic should, in developing countries of Africa, Asia, and Europe, lead to examination of at least two specimens of sputum for tubercle bacilli, one of which should be an early morning specimen.⁶

Fluoroquinolones (FQs) are a group of bactericidal antibiotics acting on DNA gyrase and have a high activity against *Mycobacterium tuberculosis* (Mtb).⁷ These are classified as group A drugs by the World Health Organization (WHO) and form the backbone of multidrug/extensively drug-resistant TB (M/XDR-TB) treatment due to their good oral bioavailability, affordable cost and excellent safety profile.⁸ The emergence of resistance to FQs also accelerates the progression of disease among multidrug-resistant (MDR) patients and is a risk factor for the development of XDR-TB.⁹ The present study was conducted to assess fluoroquinolone resistance among pulmonary tuberculosis patients.

MATERIALS & METHODS

The present study comprised of 58 pulmonary TB patients of both genders. The consent was obtained from all enrolled patients.

Data such as name, age, gender etc. was recorded. Two slides for acid-fast bacilli were made directly from each sample collected from spot and morning sputum specimens and stained by Ziehl-Nielsen method. All patients were subjected to DST for first-line drugs (FLDs) and second-line drugs. FQs DST was also performed using automated *Mycobacterium Growth Indicator Tube-960* liquid culture technique. The immunochromatographic assay was performed to distinguish *Mycobacterium tuberculosis* complex (MTBC) from non-MTBC. Data thus obtained were subjected to statistical analysis. P value < 0.05 was considered significant.

RESULTS

Table I Distribution of patients

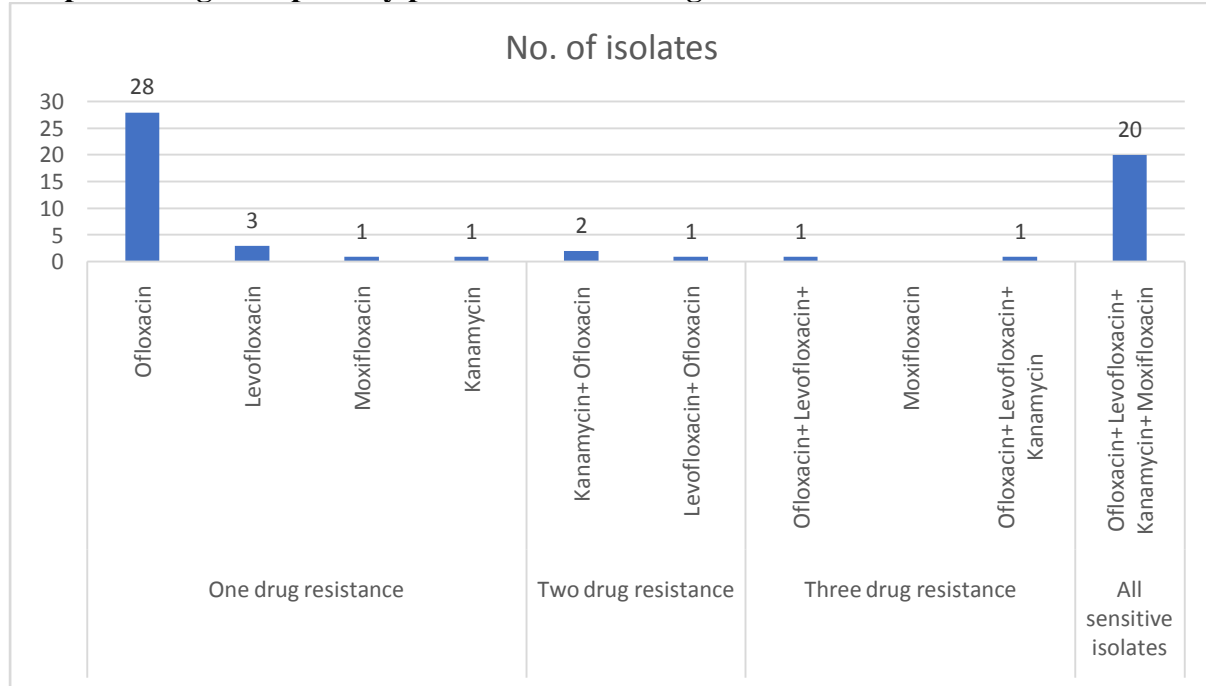
Total- 58		
Gender	Males	Females
Number	38	20

Table I shows that out of 58, males were 38 and females were 20.

Table II Drug susceptibility patterns in multidrug-resistant *M. tuberculosis* isolates

Drug resistance pattern	Drugs	No. of isolates	P value
One drug resistance	Ofloxacin	28	0.01
	Levofloxacin	3	
	Moxifloxacin	1	
	Kanamycin	1	
Two drug resistance	Kanamycin+ Ofloxacin	2	0.05
	Levofloxacin+ Ofloxacin	1	
Three drug resistance	Ofloxacin+ Levofloxacin+ Moxifloxacin	1	1
	Ofloxacin+ Levofloxacin+ Kanamycin	1	
All sensitive isolates	Ofloxacin+ Levofloxacin+ Kanamycin+ Moxifloxacin	20	-

Table II, graph I shows that one drug resistance such as Ofloxacin was seen in 28, levofloxacin in 3 cases, moxifloxacin in 1 and Kanamycin in 1 case. Two drug resistance such as Kanamycin+ Ofloxacin in 2 and Levofloxacin+ Ofloxacin in 1 case. Three drug resistance such as Ofloxacin+ Levofloxacin+ Moxifloxacin in 1 and Ofloxacin+ Levofloxacin+ Kanamycin in 1 case and all sensitive isolates was seen in Ofloxacin+ Levofloxacin+ Kanamycin+ Moxifloxacin in 20 cases. The difference was significant (P < 0.05).

Graph II Drug susceptibility patterns in multidrug-resistant *M. tuberculosis* isolates

DISCUSSION

Most tuberculosis programmes use direct smear examination of sputum but, if resources permit, culture is desirable.¹⁰ Reliable susceptibility testing is a luxury few developing countries can afford, although it is especially desirable for purposes of re-treatment.¹¹ Rapid methods of culture and susceptibility testing are widely available in the wealthier nations.^{12,13} Molecular techniques have provided quick, sensitive, and specific tests for *Mycobacterium tuberculosis*—such as polymerase chain reaction, DNA and RNA probes, and γ interferon tests—but these are expensive and technically demanding.¹⁴ They are most useful in diagnosing multi-drug resistant organisms quickly and in differentiating *M. tuberculosis* from other, non-infectious mycobacterial species.^{15,16} The present study was conducted to assess fluoroquinolone resistance among pulmonary tuberculosis patients.

We found that out of 58, males were 38 and females were 20. Sharma et al¹⁷ determined the FQs resistance among drug sensitive and drug-resistant pulmonary TB patients in a tertiary care centre in north India. A total of 1619 sputum/smear-positive specimens of pulmonary TB patients were subjected to DST for first-line drugs (FLDs) and second-line drugs. In addition, FQs DST was also performed using automated *Mycobacterium Growth Indicator Tube-960* liquid culture technique. The immunochromatographic assay was performed to distinguish *Mycobacterium tuberculosis* complex (MTBC) from non-MTBC. *Mycobacterium tuberculosis* (Mtb) was isolated in 1499 sputum specimens; 1099 culture specimens were sensitive to FLDs, 249 grew as multidrug-resistant (MDR) Mtb and the remaining 151 isolates revealed any drug resistance to FLDs. While FQs monoresistance among the FLD sensitive isolates was 3.1 per cent (35/1099), 27.3 per cent (68/249) among MDR Mtb isolates had additional FQs resistance.

We found that one drug resistance such as Ofloxacin was seen in 28, levofloxacin in 3 cases, moxifloxacin in 1 and Kanamycin in 1 case. Two drug resistance such as Kanamycin+ Ofloxacin in 2 and Levofloxacin+ Ofloxacin in 1 case. Three drug resistance such as Ofloxacin+ Levofloxacin+Moxifloxacin in 1 and Ofloxacin+ Levofloxacin+ Kanamycin in 1 case and all sensitive isolates was seen in Ofloxacin+ Levofloxacin+ Kanamycin+ Moxifloxacin in 20 cases. In a study by Rosha et al¹⁸, the clinical profile of 28 cases of

multidrug resistant pulmonary tuberculosis was studied. All cases were sputum culture proved, with individual patterns of drug resistance. All patients were from the lower income groups. Though only 6 (21.4%) were smokers, chronic bronchitis and obstructive lung disease was found in 13 patients (46.4%). All denied history of alcohol and substance abuse, 3 (10.7%) gave history of drug reactions requiring modification of 1st line ATT. Four (14.2%) patients had non-insulin dependent diabetes mellitus (NIDDM). Only 5 cases (17.8%) had detailed records of previous ATT. The length of first-line ATT at time of diagnosis of MDR ranged from 1 to 8 years with 20 (71.4%) having taken ATT for 1 or 2 years. The reasons for development of MDR were probed. Fourteen (50.0%) patients admitted to noncompliance, 8 (28.5%) cases had relapse, 5 had treatment failure (17.8%), and 1 had primary drug resistance (3.6%). Among the non-complaint group 6 (21.4%) patients modified drug therapy on their own, 3 (10.7%) frequently changed doctors, 3 (10.7%) had drug reactions and took prolonged monotherapy whereas 2 (7.2%) took treatment from District Tuberculosis Centre (DTC) where there was frequent change in drug therapy. The radiographic patterns seen were cavities in 11 (39.2%), soft lesions in 5 (17.8%), destroyed lobe in 3 (10.7%) destroyed lung in 8 (28.5%) and hydropneumothorax in 1 (3.6%). Among the patients with destroyed lung it was found that 7 had left-sided lung destruction. No correlation between length of ATT and destroyed lung could be established. All patients were HIV negative. Fourteen (50%) patients had two-drug resistance, 7 (25%) had three-drug resistance, 5 (17.8%) were resistant to 4 drugs, while 2 (7.2%) were resistant to 5 or more drugs.

CONCLUSION

Authors found that Fluoroquinolone resistance among drug sensitive and multidrug resistance tuberculosis isolates was high.

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