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Analysis of Drug Resistance of 157 Strains of Multidrug Resistant Mycobacterium Tuberculosis in Jilin Province

Zhang Lifu[1], Zhang Wei Yu[2], Yang Xiujun[1], Liu Xin[3], Ma Yingcong[3], Wang Hui[2, *]

[1]Jilin Province Health Testing and Inspection Center, Changchun, China

[2]Jilin Provincial Center for Disease Control and Prevention (Jilin Provincial Institute of Public Health), Changchun, China

[3]Jilin Provincial Research Institute of Tuberculosis Prevention and Control (Affiliated Hospital), Changchun, China

Email address:

hunyuan163@qq.com (Zhang Lifu), 785505392@qq.com (Wang Hui)

[*]Corresponding author

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Abstract: Objective: Through the analysis of drug resistance of 157 strains of multidrug resistant Mycobacterium tuberculosis in Jilin Province, the drug resistance spectrum of multi drug resistant Mycobacterium tuberculosis in Jilin Province was preliminarily established to provide the basis for the treatment of patients with multi drug resistant tuberculosis in the future. Methods: Anti-tuberculosis streptomycin (SM), ethambutol (EMB), of loxacin (OFX) and kanamycin (KM) were tested by L-J ratio. Results: The SM resistance rate in 157 MDR M. tuberculosis strains was 56.05%, EMB The resistance rate 38.85%, OFX The resistance rate 64.97%, KM The resistance rate 14.65%. The XDR resistance rate was 14.01%. The results of drug resistance analysis in different characteristic populations show that second-line drugs OFX and KM drug resistance rates Female patients Higher than male, and statistically significant ($P < 0.05$), the resistance rate of OFX relapse patients was significantly higher than that in naive patients, and was statistically significant ($P < 0.05$). Conclusion: The resistance rate of tuberculosis patients in Jilin Province to the first-line and second-line anti-tuberculosis drugs is at a relatively high level, and the situation of tuberculosis prevention and control is not optimistic. The management of patients should be strengthened in the prevention and treatment strategies, and the use of anti-tuberculosis drugs should be standardized, At the same time, strengthen the ability of tuberculosis laboratory to detect drug-resistant Mycobacterium tuberculosis is strengthened.

Keywords: Mycobacterium Tuberculosis, Multidrug Resistance, Drug Resistance Rate

1. Introduction

The latest data released by the WHO in 2020 showed that about 10 million people worldwide developed tuberculosis and 1.4 million died in 2019 [1]. With the global pandemic of novel coronavirus (COVID-2019) at the end of 2019, human health, economy and society have been greatly impacted, and people have also deeply realized the huge disaster brought by respiratory infectious diseases to human beings. At present, the increase of MDR-TB has become an important reason for the deterioration of the global TB epidemic, and has also become a major problem to control the spread and spread of TB today [2].

In recent years, despite positive progress in both treatment and prevention, MDR-TB remains one of the major factors affecting human health and the Termination TB Strategy [3] Major challenges faced. In order to understand the drug resistance of tuberculosis in Jilin Province, a total of 157 strains of multi drug resistant Mycobacterium tuberculosis in Jilin Province from 2017 to 2020 were collected. The L-J ratio method was used to carry out the drug sensitivity test of 4 first-line drugs and 2 second-line drugs, and the strain composition and drug resistance were compared and analyzed by statistical methods, so as to preliminarily establish the drug resistance pedigree of tuberculosis in Jilin Province, It has a certain prompt and guiding significance for the formulation of a unified treatment plan for tuberculosis and the development of the prevention and treatment of tuberculosis in our province in the future.

2. Materials and Reagents

2.1. Strain Source

Target strains: 157 strains from 9 cities (prefectures) in Jilin Province from 2017 to 2020 and were resistant to both INH and RFP.

Standard strain ($H37R_V$): Provided by the tuberculosis Reference Laboratory of the Chinese Center for Disease Control and Prevention.

2.2. Reagent

Neutral-modified Roche medium, modified Roche susceptibility medium (isoniazid (INH), rifampin (REF), streptomycin (SM), ethambutol (EMB), kanamycin (KM), ofloxacin (OFX)), Determine Roche medium (p-nitrobenzoic acid (PNB), thiazenene dicarboxylate (TCH))) All purchased from Zhuhai Besso Co., Ltd.

3. Method

3.1. Subgeneration and Culture

Will collect the 157 multidrug-resistant M. tuberculosis strains for secondary subculture, with inoculation ring fully scraping the colony on the slope of medium, after shock grinding, respectively inoculation on 2 modified neutral Roche medium, isolation and culture process refer to the standardized procedure of Mycobacterium tuberculosis drug and quality assurance manual sensitivity test [4].

3.2. Sensitization Test

After obtaining secondary subcultured strains, refer to Standardized Operating Procedures and Quality Assurance Manual [4]. The provisions of theThe proportion method in the method of drug sensitivity test, including INH, RFP, SM, EMB, KM, and OFX. 36±1°C was grown at constant temperature until 4 weeks later and colony growth on the medium was recorded and the percentage of resistance was calculated. The percentage <1% was reported as sensitive and> 1% as resistant.

3.3. Quality Control

Refer to the Standardized Operating Procedures and Quality Assurance Manual for Mycobacterium tuberculosis drug susceptibility test [4] Relevant requirements in, will the standard strain (H37Rv) inoculation into modified Roche susceptibility medium to detect the quality of drug-containing medium, less than 20 colonies on control medium, sterile colonies on drug-containing medium, and the test was repeated.

3.4. Statistical Analysis

Experimental results were statistical and analyzed using Microsoft Excel 2016 and SPSS 23, and the database was built using EpiData3.1 software. 0 put to use χ^2 The test compared the difference in drug resistance between patients with pulmonary tuberculosis with different characteristics, with P <0.05 at the =0.05 two-sided test level.

4. Results

4.1. General Information

A total of 157 multidrug-resistant Mycobacterium tuberculosis strains were selected, including 119 male patients, accounting for 75.80%, 38 female patients, accounting for 24.20%, 58 naive patients, accounting for 36.94%, 99 restored patients, accounting for 63.06%.

4.2. Resistance

4.2.1. Arbitrary Drug Resistance

SM resistance in 157 MDR M. tuberculosis strains The number of strains was 88, and the resistance rate was determined 56.05%, be able to bear or endure EMB The number of strains was 61, and the resistance rate was determined 38.85%, be able to bear or endure OFX The number of strains was 102, and the resistance rate was determined 64.97%, be able to bear or endure KM The number of strains was 23, and the resistance rate was determined 14.65%. The order of primary and compound treatment of drug resistance was basically the same, and the order of drug resistance was OFX from high to low > SM >EMB > KM. See Table 1.

Table 1. *Resistance of MDR-Mycobacterium tuberculosis strains.*

Drug resistance	Number of patients	Resistance rate
Any SM resistant	88	56.05%
Any resistance to ENB	61	38.85%
Any OFX resistant	102	64.97%
Any resistance to KM	23	14.65%
Single-resistant EMB	4	2.55%
Single-resistant SM	14	8.92%
Monotolerance OFX	29	18.47%
EMB+SM	13	8.28%
EMB+OFX	4	2.55%
SM+OFX	21	13.38%
KM +OFX	7	4.46%
EMB+OFX+KM	2	1.27%
EMB+SM+KM	1	0.64%
EMB+SM+OFX	26	16.56%
SM+OFX+KM	2	1.27%
EMB+SM+OFX+KM	11	7.01%

4.2.2. Single Resistance, Resistance to 2 Drugs and 3 Drugs

Of the 157 MDR M. tuberculosis strains, 47 were monoresistant and 4 E M B strains, accounting 2.55%, SM 14 strains, proportion 8.92%, OFX 29 strain, proportion 18.47%; Among them, 18 were treated and 29 were treated, with no significant statistical difference (P> 0.05). Resistance to 2 or more species, except EMB + SM + OFX (16 strains, proportion 16.56%). The resistant combinations showed significant statistical differences in initial and treatment patients (P <0.05), The remaining statistical differences were not significant (P> 0.05) are shown in Table 2.

4.2.3. Extensive Drug Resistance

Of the 157 MDR strains, 22 were widely resistant strains, with a broad resistance rate of 14.01%. Eight XDR-T B in naive patients and 14 XDR-T B in naive patients. Among these, 11 strains were resistant to six anti-TB drugs, representing 7% of the MDR-TB strains and 50% of the XDR-TB strains. See Table 2.

Table 2. *Drug resistance of primary and relapse patients (n).*

		Single resistance				Resistance to 2 kinds of drugs				
		amount to	**EMB**	**SM**	**OFX**	**amount to**	**EMB+SM**	**EMB+OFX**	**SM+OFX**	**KM +OFX**
initial treatment	58	18	1	8	9	16	4	1	9	2
retreatment	99	29	3	6	20	29	9	3	12	5
amount to	157	47	4	14	29	45	13	4	21	7
χ^2		0.053	0.251	2.692	0.533	0.052	0.232	0.251	0.364	0.22
P		0.818	0.616	0.101	0.465	0.819	0.63	0.616	0.546	0.639

Table 2. *Continued.*

		Resistance to 3 kinds of drugs					Resistance to 4 kinds of drugs
		amount to	**EMB+SM+OFX**	**EMB+SM+KM**	**EMB+OFX+KM**	**SM+OFX+KM**	**EMB+SM+OFX+KM**
initial treatment	58	7	5	1	0	1	5
retreatment	99	24	21	0	2	1	6
amount to	157	31	26	1	2	2	11
χ^2		3.42	4.196	1.718	1.187	0.148	0.368
P		0.064	0.041	0.19	0.276	0.7	0.544

4.3. Drug Resistance in Populations with Different Characteristics

4.3.1. Ggender and Resistance

Different gender resistance results showed that the first-line drug EMB and SM resistance rates were not significantly different in sex and were not statistically significant (P > 0.05); Second-line drugs OFX and KM drug resistance ratesFemale patientsHigher than male, and statistically significant (P <0.05). See Table 3.

4.3.2. Relationship Between Different Treatment History and Drug Resistance

The results of primary and relapse patients showed that the resistance rate of OFX relapse patients was significantly higher than that of P <0.05), and the effect was significant (P <0.05) (P >0.05). See Table 3.

Table 3. *Arbitrary drug resistance of different sexes, n (%).*

group	Number of patients	Any resistance				
		amount to	**EMB**	**SM**	**OFX**	**KM**
man	119 (75.80%)	192	44 (36.97%)	63 (52.94%)	72 (60.50%)	13 (10.92%)
woman	38 (24.20%)	82	17 (44.74%)	25 (65.79%)	30 (78.95%)	10 (26.32%)
χ^2			0.73	1.93	4.305	5.457
P			0.393	0.165	0.038	0.019
			38.85%	56.05%	64.97%	14.65%
initial treatment	58 (36.94%)	91	17 (29.31%)	33 (56.90%)	32 (55.17%)	9 (15.52%)
retreatment	99 (63.06%)	183	44 (44.44%)	55 (55.56%)	70 (70.71%)	14 (14.14%)
χ^2			3.526	0.027	3.878	0.055
P			0.06	0.87	0.049	0.814
amount to	157		61 (38.85%)	88 (56.05%)	102 (64.97%)	23 (14.65%)

5. Discussion

The increase of drug-resistant TB patients has become one of the important reasons for the rapid rise in TB incidence nowadays, especially the occurrence of MDR-TB has posed a great threat to the effect of epidemic prevention and control [5]. At present, there are about 20 million active tuberculosis worldwide, nearly 10 million new cases every year, and 50 million people worldwide are infected by MDR-TB [6], MDR-TB has had a significant impact on the progress in global TB prevention and control [7]. It is one of the major challenges facing tuberculosis prevention and control. Timely grasp of the bacterial drug resistance of tuberculosis branch rod will have a positive impact on the monitoring of tuberculosis drug resistance.

This study found that the current high MDR data in Jilin Province were available from the national TB Drug Resistance Baseline survey in 2007-2008 [8], First-line anti-tuberculosis drugsSMThe resistance rateAt 56.05%, the resistance rates were 56.90% and 55.56%, EMB, 38.85%, 29.31% and 44.44%, respectively; the first-line drug SM was higher than EMB; and Zhang Weiyu et al [9]. Study the same. OFX resistance was 64.97%, 55.17% and 70.71% in naive and retreated patients, 14.65% in KM, and 15.52% and 14.14% in naive and retreated patients, respectively. In the second-line drugs, OFX resistance rate was significantly higher than KM, and there were significant differences between quinolones resistance in naive and re-treated patients (P <0.05). The recent use of quinolones in the treatment of pulmonary infectious diseases such as community-acquired pneumonia has been widely used, leading to the generation and spread of quinolone-resistant strains [10]. As in previous studies [11]. Today, resistant lineages have shown complexity and diversity, with up to 19 combinations. Single drug resistance was the highest in OFX resistance, which matched the resistance results of OFX resistance in this study, compared with Zhao et al [12]. The findings varied in single resistance to SM.

The global prevalence of XDR-TB in MDR-TB cases has increased from 6.6% to 23.7% [13]. In this study, 22 XDR strains in 157 MDR M. tuberculosis, accounting for the total number of MDR M. tuberculosis 14.01%. XDRIt is much more therapeutically sleepy than the MDR. Therefore, the prevention and control of XDR is particularly urgent. Early detection and early treatment of XDR is the top priority of tuberculosis prevention and control, and it is particularly important to carry out rapid and accurate drug susceptibility experiments of second-line anti-tuberculosis drugs.

This study showed no significant gender differences in frontline SM and EMB resistance rates (P >0.05); Second-line drugsOFX and KM drug resistance ratesFemale patientsHigher than in men, with a significant difference (P <0.05). take part inLiu Binbin [14]. Men and women are more likely than women to develop drug resistance in China, Yuan Yanli et al [15]. Results OFX, KM resistanceNo difference is also different, This may be caused by the excessive proportion of male patients included in this study.

6. Conclusion

To sum up, the resistance rate of first-line and second-line anti-tuberculosis drugs in Jilin Province is at a relatively high level, and the treatment situation of tuberculosis patients should not be objective. Through the study of tuberculosis drug resistance lineage, we have some understanding of drug-resistant TB drug resistance in Jilin Province, It should be considered in clinical treatment selection to avoid cross-resistance. Due to the single sample source of this research and the small number of strains, there are still some limitations. There is a sampling deviation to understand the drug resistance of TB patients with this study, so the results of this study are more meaningful for the study of drug-resistant TB outbreaks.

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