Analysis of risk factors for drug resistance in tuberculosis patients

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Abstract: Tuberculosis is a serious respiratory infectious disease. The occurrence and prevalence of drug-resistant tuberculosis is one of the main reasons for the recovery of tuberculosis epidemic situation since the middle and late 1980s. According to the World Health Organization (WHO), the global situation of MDR-TB is serious. The two countries with the largest number of MDR-TB patients in the world are China and India. The high drug resistance of tuberculosis is easy to lead to tuberculosis difficult to cure and accelerate the death of tuberculosis patients has become a major obstacle to the current clinical work and prevention and treatment of tuberculosis. A cross-sectional study was conducted to collect tuberculosis patients hospitalized from December 2013 to December 2017. Eighteen patients with drug-resistant tuberculosis and 49 patients with non-drug-resistant tuberculosis were selected as subjects. Logistic regression model was used to analyze the risk factors and to explore the risk factors of drug resistance in patients with tuberculosis. Retreatment and cavity in chest CT are the main risk factors for drug resistance in patients with pulmonary tuberculosis. It is of great significance to take effective intervention measures as soon as possible from the source to reduce the occurrence of drug-resistant tuberculosis. Retreatment and cavity in chest CT are the main risk factors of drug resistance in patients with pulmonary tuberculosis.

1. Introduction

Tuberculosis is a chronic infectious disease which seriously endangers human health. Tuberculosis is not only a very serious public health problem, but also a very social problem worthy of attention. One of the most important reasons for the global warming of tuberculosis is the emergence of drug-resistant tuberculosis, which is also a difficult problem in the global tuberculosis control work.

China is one of the 22 countries with high burden of tuberculosis in the world, the incidence rate is second only to India, and the number of drug-resistant tuberculosis cases in China ranks first in the world, and the number of MDR-TB cases ranks second in the world. 1/4 of the world's MDR-TB patients are in China. The fifth national tuberculosis epidemiological sampling survey in 2010 showed that the drug resistance rate, multi-drug resistant rate and extensive drug resistance rate in China were 42.1%, 6.8% and 2.1% respectively. The spread of drug-resistant patients and the ineffectiveness of chemotherapy lead to high treatment costs, high morbidity and high mortality. Drug-resistant pulmonary tuberculosis has become the main limiting factor of tuberculosis control in China in the future and the problem that needs to be paid more attention to.

Although there are many reported risk factors for drug-resistant pulmonary tuberculosis, the risk factors of drug-resistant tuberculosis are not the same in different countries, regions and nationalities due to the influence of local social, economic, cultural and other factors. Therefore, our study on the risk factors of drug-resistant pulmonary tuberculosis is of great significance. To clarify the risk factors of drug-resistant tuberculosis, in order to take targeted measures to control the development of drug-resistant tuberculosis, to shorten the course of treatment of drug-resistant tuberculosis, improve the cure rate of drug-resistant tuberculosis, and reduce the mortality of drug-resistant tuberculosis to provide a reliable basis.

2. Methods

2.1. Sample collection

From December 1, 2013 to December 31, 2017, 67 patients with pulmonary tuberculosis were diagnosed and treated in Qingdao Thoracic Hospital. Sputum culture was positive in all patients, excluding patients with extrathoracic tuberculosis and tuberculous peritonitis. The sputum culture results and drug sensitivity results of the patients were collected. The basic information of the patients came from the information system of the thoracic hospital.

2.2. Related definitions

The diagnosis of PTB (pulmonary tuberculosis) was carried out according to the diagnostic criteria of China Tuberculosis Prevention and Control Program Guide (2008), according to the results of sputum smear, X-ray and other examination, combined with clinical related symptoms.

Patients with DM are diagnosed according to

the diagnostic criteria of the Chinese guidelines for the Prevention and treatment of Type 2 Diabetes (2013 Edition), that is, they have typical diabetic symptoms.

2.3. Research content

The basic information of the patient comes from the information system of the thoracic hospital, which mainly includes:

(1) General demographic characteristics: including sex, age, nationality, marital status, household registration status, educational level, occupational distribution and so on.

(2) Diabetes related conditions (course of diabetes, blood glucose control machine) and immune status of the body.

(3) Lifestyle and behavioural factors: smoking (cumulative smoking of at least 100 cigarettes, And still smoking in the last month), drinking (at least three times a week more than 0.5L of white wine or more than 5L of beer).

(4) Clinical features: sputum smear grade, imaging features (number of lesions involving lung field, cavity, etc.).

2.4. Statistical analysis

EpiData 3.1 software was used to input the questionnaire, and SPSS21.0 statistical software was used to analyze the data. the measurement data were expressed as mean $\pm$ standard deviation, and the counting data were expressed as percentage. Univariate analysis was carried out by binary Logistic regression, multivariate Logistic regression was used to screen the independent influencing factors of drug resistance, and ratio (odds ratio,OR) was used to evaluate the correlation between influencing factors and drug resistance. 95% confidence interval (95%CI) was used to estimate the range of global parameters. P <0.05 as the difference was statistically significant.

3. Results

3.1. General demographic characteristics

In this study, 67 patients with sputum culture positive pulmonary tuberculosis were included. There were 18 patients in the drug resistance group (Group 1) and 49 patients in the non-drug resistance group (Group 2). The average age of the patients was 25 ~ 87 years old, the average age of the drug-resistant group was 53.11 years old, and the average age of the non-drug-resistant group was 51.35 years. there was no significant difference in the age between the two groups. The sex composition of the two groups was basically the same. men accounted for 88.9% in the drug-resistant group and 71.4% in the non-drug-resistant group. Married patients accounted for 77.8% and non-drug-resistant patients accounted for 87.8% in the drug-resistant group, there was no significant difference between the two groups, and the marital status, household registration status and occupational distribution of the two groups were basically the same between the two groups. The details are shown in table 1.

Table 1. Baseline characteristics of PTB participants

	Group 1	Group 2	P-value
No. subjects	18	49	
Mean(±SD) Age (years)	53.11±10.134	51.35±14.521	0.580
No. men (%)	16(88.9)	35(71.4)	0.137
Marital status			0.310
Married	14(77.8)	43(87.8)	
Others[a]	4(22.2)	6(12.2)	
Household registration,Urban	9(52.9)	22(51.2)	0.901
Occupation			0.599
Workng	10(58.8)	31(66.0)	
Unemployed	7(41.2)	16(34.0)	

Unless indicated otherwise, data are given as n (%).
[a]Others including single or widowed or divorced people.

3.2. Univariate Logistic analysis of drug resistance in pulmonary tuberculosis

Univariate logistic regression analysis showed that retreated pulmonary tuberculosis patients were more likely to develop drug-resistant OR=3.929, 95% CI: 1.266-12.190, P=0.018). Smoking was also a high risk factor for drug resistance. The number of smokers in the drug-resistant group was 2.478 times higher than that in the non-drug-resistant group (OR=2.478, 95% CI: 1.371-4.626,P=0.013). Diabetics are nearly four times more likely to

develop drug resistance than non-diabetics (OR=3.562, 95% CI: 1.156-10.979,P=0.027). The comparison of sputum smears between the two groups showed that the risk of drug resistance in patients with 4 + sputum smears was three times higher than that in patients with negative sputum smears (OR=3.000,95% CI:1.319-4.872,P=0.031). Drug resistance (OR=7.200, 95% CI: 2.103-

24.656,P=0.002) is more likely to occur when there is a cavity in the patient's lungs. However, there was no significant difference between the drug-resistant group and the non-drug-resistant group in drinking alcohol, sputum smear grade 1+~3 + and the cumulative number of lung fields more than 3. Details are provided in table 2.

Table 2. Risk factors related to drug resistance by univariate logistic regression analysis

	OR	95% CI	P-value
Re-treatment	3.929	1.266-12.190	0.018
Smoking	2.478	1.371-4.626	0.013
Alcohol drinking	1.087	0.368-3.212	0.880
Sputum smear grade			0.098
0	-	-	-
1+~3+	2.800	0.649-12.073	0.167
4+	3.000	1.319-4.872	0.031
Cavity	7.200	2.103-24.656	0.002
Cumulative lung field number> 3	1.429	0.466-4.376	0.532
Diabetes	3.562	1.156-10.979	0.027

OR, odds ratio; CI, confidence interval.

Table 3. Risk factors related to drug resistance by multivariate logistic regression analysis

	β	SE	Walds	p	OR	95% CI
Age (years)	-0.027	0.032	0.706	0.401	0.974	0.915-1.036
Re-treatment	1.437	0.763	3.544	0.040	2.490	1.995-4.271
Smoking	1.502	0.769	3.814	0.051	4.490	0.995-20.271
Cavity	2.057	0.791	6.764	0.009	3.824	1.660-6.875
Diabetes	1.024	0.783	1.710	0.191	2.784	0.600-12.912

OR, odds ratio; CI, confidence interval.

3.3. Multivariate Logistic analysis of drug resistance in pulmonary tuberculosis

In multivariate Logistic analysis, the risk factors selected from univariate analysis (diabetes mellitus, initial treatment, smoking, cavity and sputum smear results) were taken as independent variables, and stepwise forward method was used. After adjusting the age difference, the variables that finally entered the regression model were: retreatment (OR=2.490, 95% CI: 1.995-4.271, P=0.040); OR=3.824, 95% CI: 1.660-6.875,P=0.009. See Table 3 for details.

4. Discussion

The treatment of drug-resistant pulmonary tuberculosis is difficult, the infection period is long, the transmission risk is high[1], is one of the main reasons for the high prevalence and mortality of drug-resistant pulmonary tuberculosis[2], so curbing the prevalence of drug-resistant pulmonary tuberculosis is the most important work of global tuberculosis prevention and control.

According to the characteristics of drug resistance in this area, it is of great significance to

select the appropriate combination of anti-tuberculosis drugs to treat drug-resistant tuberculosis[3], which is of great significance to cure drug-resistant tuberculosis patients[4], reduce the source of infection of drug-resistant tuberculosis, and control drug-resistant tuberculosis. The results of this study can truly reflect the drug resistance in this area, and can be used as a reference to guide clinical drug use[5]. Retreated pulmonary tuberculosis patients with cavity in chest CT are easy to resist drugs, which is consistent with the results reported in the relevant literature in China, so corresponding measures should be taken to control the prevalence of drug-resistant tuberculosis.

This study showed that tuberculosis patients had a history of anti-tuberculosis treatment, that is, the risk of drug resistance in retreated tuberculosis patients with previous tuberculosis was 2.490 times higher than that in newly diagnosed tuberculosis patients who had not had tuberculosis in the past. The risk of drug resistance and multidrug resistance in cases with a history of anti-tuberculous drug use was significantly higher than that in cases without a history of antituberculous drug use, which was

consistent with the literature reports at home and abroad. Some studies have shown that there is a significant difference in drug resistance among newly diagnosed tuberculosis patients, the drug resistance rate of newly diagnosed tuberculosis patients is 13%[6], and the drug resistance rate of retreated tuberculosis patients is as high as 40%[7].

The presence of tuberculosis cavity lesions is a risk factor for drug resistance, which is consistent with Meng Suyan[3] and other reports[8]. Kim HJ et al. found that the structure of the cavity focus is special[9], because the drug is not easy to penetrate into the cavity, so it is difficult to reach the effective treatment concentration to kill Mycobacterium tuberculosis in the cavity[10], and then it is more likely to mutate to cause drug resistance[11]. Patients with cavity in chest CT should be vigilant[12], drug sensitivity test should be carried out as soon as possible, sensitive drugs should be used[13], and the dose should be increased in a safe range in order to ensure the curative effect and prevent the occurrence of drug resistance and even multidrug resistance.

For patients with drug-resistant pulmonary tuberculosis, we should find as early as possible, and take individualized treatment as soon as possible combined with the results of drug sensitivity[14], which is of great help to block the spread of drug-resistant bacteria and prevent its development to widespread drug-resistant pulmonary tuberculosis[15,16]. Strengthening the standardized treatment of newly diagnosed pulmonary tuberculosis patients and improving the cure rate of newly diagnosed pulmonary tuberculosis is the basis17 for the prevention of multi-drug resistant pulmonary tuberculosis patients[18].

In the future tuberculosis prevention and control work, we should strengthen the propaganda and education of tuberculosis treatment principles[19]: early, regular, whole process, appropriate amount, combination, strengthen the supervision and management of tuberculosis patients, Advise patients to take medicine on time, according to the amount, according to the course of treatment, in conditional areas as far as possible to carry out drug sensitivity test[20], according to the results of drug sensitivity, choose an effective treatment plan[7,21]. Try our best to achieve high cure rate of newly treated patients, reduce the number of relapsed patients, reduce the occurrence of drug-resistant cases.

5. Conclusion

Retreatment and cavity in chest CT are the main risk factors of drug resistance in patients with pulmonary tuberculosis. we should focus on the population with the above risk factors of drug-resistant tuberculosis and take effective intervention measures as soon as possible from the source. Prevention of the spread and prevalence of drug-resistant tuberculosis.

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