Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 10, Issue, 07, pp.71116-71119, July, 2018

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

ISSN: 0975-833X

RESEARCH ARTICLE

THE CLINICAL AND FUNCTIONAL FEATURES OF DRUGRESISTANT PULMONARY TUBERCULOSIS INPATIENTS WITHCHRONIC OBSTRUCTIVE PULMONARY DISEASE

***Jeyhun M. Ismayilzada, Rafiq I. Bayramov, Urfana B. Nagiyeva and Rena I. Hamzayeva**

Azerbaijan Medical University, Department of Phthisiatry, Baku

ARTICLE INFO

Article History:
Received 27th April, 2018
Received in revised form
16th May, 2018
Accepted 19th June, 2018
Published online 30th July, 2018

Key Words:
Pulmonary tuberculosis,
Multidrug-resistant tuberculosis,
Chronic obstructive pulmonary disease.

ABSTRACT

Objectives: The present study reports the clinical and functional features of the current of drug-resistant pulmonary tuberculosis (TB) in patients withchronic obstructive pulmonary disease(COPD). **Material and Methods:** The present study reports the 180 patients who were examined in therapeutic departments of Tuberculosis Hospital No. 4 in Baku, which is the base of the Phthisiatry Department of the Azerbaijan Medical University from January 2013 to December 2017. **Results:** Among the examined were 33 women and 147 men aged 41 to 69 years. 110 patients (61%) had a widespread process in the lung, destructive changes were found in 126 (70%) patients. All patients were divided into two groups: the first group - 119 patients who had obstructive ventilation disorders in their pulmonary function test study, the 2nd group was formed from 71 patients with unchanged functional indices. Among the examined were 33 women and 147 men aged 41 to 69 years. 110 patients (61%) had a widespread process in the lung, destructive changes were found in 126 (70%) patients. Multidrug-resistant form was found in 36.1% of patients of the 1st and 20.5% in the 2nd group. The results of examination and treatment of patients with COPD testified to the severity and slow regress of clinical and radiological manifestations of the disease, the long-term preservation of bronchial patency disorders. All this led to the advisability of developing a basic of treatment program for patients with TB with COPD. **Conclusion:** The results obtained indicate a negative effect of bronchial obstruction on the tuberculosis process, which led to the development of a basic treatment program combining different methods for eliminating the causes of bronchial obstruction: adequate etiotropic chemotherapy, exposure to pathogenic agents, modern regimens of bronchodilator therapy, and smoking control.

Citation: ***Jeyhun M. Ismayilzada, Rafiq I. Bayramov, Urfana B. Nagiyeva and Rena I. Hamzayeva*, 2018.** "The clinical and functional features of drugresistant pulmonary tuberculosis inpatients withchronic obstructive pulmonary disease", *International Journal of Current Research*, 10, (07), 71116-71119.

INTRODUCTION

The problem of chronic obstructive pulmonary disease (COPD) in patients with pulmonary tuberculosis (TB) not sufficiently studied. The current of TB in patients of this category often leads to the rapid development of chronic forms and the formation of drug resistance, which is caused by the lack of adequate bronchodilator therapy, as well as the features of the functional and morphological changes in this disease. Annually 8, 6 million new cases and 1, 3 million deaths are attributed to tuberculosis (Word Health Organization Global tuberculosis report, 2016). The epidemiological situation of tuberculosis continues to be tense, there is a persistent tendency towards an increase in the number of patients with multidrug-resistant tuberculosis (MDR), and the clinical structure continues to play an important role in rapidly progressive and widespread forms of tuberculosis (TB) (Dharmadhikari, 2014; World Health Organization, 2011 and Alikhanova, 2014). One of the reasons of burden of a disease and depression of results of treatment of patients is bronchial obstruction.COPD occurs in TB patients is often, particularly in men older than 40 years. Both diseases have similar risk factors: smoking, low socio-economic status of the individual, the disturbance of the immune defense.Use only of antituberculous therapy doesn't lead to appreciable improvement of bronchial obstruction .Data of single researches with use of references of Global Initiative for Chronic Obstructive Lung Disease (GOLD) showed a possibility of increasing the results of treatment of patients with the TB (GOLD, 2017 and Ismayilzada, 2017). However, in TB practice modern standards of treatment of bronchial obstruction weren't widely adopted. The individualized program of treatment including different methods of elimination of the reasons is necessary for patients with a combination of a pulmonary TB and COPD.

Corresponding author: **Jeyhun M. Ismayilzada,**
Azerbaijan Medical University, Department of Phthisiatry, Baku
DOI: https://doi.org/10.24941/ijcr.30929.07.2018

MATERIAL AND METHODS

180 patients who were on treatment in therapeutic departments of TB dispensary No. 4, which is the base of the Phthisiatry Department of the Azerbaijan Medical University participated in a research on the basis of the voluntary informed consent. The study was in accordance with the ethical standards of the bioethical committee, developed in accordance with the Helsinki Declaration of the World Medical Association «Ethical Principles of Medical Research Involving Human Subjects" with the amendments of 2013 and the "Rules of Ethical Conduct of Medical Workers" approved by the Order (№137) of the Ministry of Health of the Republic of Azerbaijan dated 29.12. 2011.94 patients with infiltrative, 26 - disseminated, 53 fibro-cavernous and 7 with cirrhotic TB were diagnosed. Among the examined were 33 women and 147 men aged 41 to 69 years. 110 patients (61%) had a widespread process in the lung, destructive changes were found in 126 (70%) patients. In accordance with the purpose of the study, the patients were divided into two groups: the first group consisted of 119 people who had obstructive ventilation disorders in the pulmonary function testing (functional vital capacity (FVC), forced expiratory volume (FEV1)study, the 2nd group was formed from 71 patients with unchanged functional indices.

The mean values of the functional indices in the patients of the 1st group were statistically significantly different from those of the patients of the 2nd group. Examination of patients was conducted according to the developed diagnostic program which besides the standard volume of a research in a phthisiology included questioning on a questionnaire of the main respiratory symptoms and the diary of introspection. The questionnaire included a block of questions about the presence of nonspecific etiological factors leading to the formation of COPD: hereditary predisposition for lung diseases, inhalation effects (tobacco smoke, occupational dusts, indoor air pollution due to stove heating and cooking with bio-organic fuel), age, gender, socio-economic status, nutrition of the patient. The diagnosis of COPD was established according to the recommendations of GOLD (2016) on diagnosis, treatment, the presence of risk factors for COPD and postbronchilatory values of the ratio of FEV1 to FVC <70%. Spirometry with bronchodilator test (inhalation sympathomimetic with short-acting β2-agonist Ventolin "GlaxoSmithKline") (gsk) - 2 doses = 200 μg) was used with measurement of bronchodilation response after 15 minutes. The spirometry study was performed using the Bodytest device (Erich Jaeger, Germany) and SPM – 300(Bionet, South Korea) in accordance with the criteria proposed by the joint group of experts of the American Thoracic and European Respiratory Society (ATS / ERS) (Miravitlles, 2016).

The actual values of the spirographic indexes, the registration of the P-FEV curve were compared with the proper values developed by the experts of the European Community of Coal and Steel (1983) [8-10]ˏ and evaluated the changes in indicators according to the GOLD recommendations. Samples were subjected to microscopy and culture on Lowenstein-Jensen (LJ), Xpert® MTB/RIF (Cepheid, Sunnyvale, CA, USA) and MGIT™ (BD, Sparks, MD, USA) media. All culture-positive isolates were subjected to drug susceptibility testing (DST) on LJ medium for first-line anti-tuberculosis drugs (isoniazid, rifampicin, streptomycin, ethambutol and pyrazinamide), and MDR-TB isolates were further subjected to DST for second-line anti-tuberculosis drugs (ofloxacin, capreomycin, amikacin, prothionamide, cycloserine and para-amino-salicylic acid). The obtained results were subjected to statistical processing on a personal computer using the application package Microsoft Office Excel 2007 and StatSoft Statistic 6.1, the license agreement BXXR006D092218FAN11. Significance of differences tested using Pearson U - Mann-Whitney test. The statistical significance of differences was taken at $p < 0.05$.

DISCUSSION

It was established that contact with domestic polluters, occupational dusts, information on hereditary predisposition to lung diseases, intensive smoking (the index of a smoker more than 10 packs / year), the age of a patient over 40 years old increased by 1.4-2.1 times the risk of bronchial obstruction in patients with pulmonary tuberculosis. The proportion of patients exposed to non-specific factors turned out to be greater in the 1st group - 65.9% (in the 2nd group - 51.9%, $p < 0.03$).Simultaneous influence of two factors was registered in every 4-5th patient of the 1st and 2nd groups (29.3 and 21.0%, respectively, $p > 0.05$).The most common risk factor for developing COPD in the subjects was smoking cigarettes. The groups were not significantly different in terms of the number of smokers (51.1 and 42.0%, respectively), but the average for the 1st group of the smoker was significantly higher than that of the 2nd group ((19.6 ± 1.5) and $(11, 9 \pm 1.6)$ packs / years, respectively, $p < 0.01$).Comparison of the patients of the studied groups by the main clinical and functional characteristics showed that in the 1st group compared with the 2nd group, respectively, the syndrome of intoxication (79.9 and 61.7%), cough (82.5 and 50.6%), dyspnea (55.5 and 16.0%), physical changes in the lungs (48.5 and 7.4%), changes in the hemogram (67.2 and 42%, 0%),The results obtained indicated a predominance in the 1st group in comparison with the 2nd group of persons with a widespread tuberculosis process (67.7 and 41.9%, respectively, $p < 0.01$), with destructive changes (72.9 and 61, 7%), with bacterial excretion (67.7 and 48.1%, $p < 0.002$), with drug resistance of mycobacterium tuberculosis (69.0 and 43.6%, $p < 0.003$).

Multidrug-resistant form was found in 36.1% of patients of the 1st and 20.5% in the 2nd group. It should be noted that the drug resistance to isoniazid and rifampicin in all cases was combined with resistance to other ant tuberculosis drugs. In the 1st group, frequent complications were expressed ($p<0.03$): hemoptysis in 12.2% of patients, pulmonary insufficiency - in 46.3% (in the second group - 3.7 and 0%, respectively).The results of examination and treatment of patients with COPD testified to the severity and slow regress of clinical and radiological manifestations of the disease, the long-term preservation of bronchial patency disorders. All this led to the advisability of developing a basic of treatment program for patients with TB with COPD. The main component of the program is adequate etiotropic chemotherapy, which is based on domestic and international recommendations for the treatment of patients with TB. Broncholytic therapy of TB patients with COPD (FEV1 / FVC <70%) was performed according to the developed schemes, based on international and domestic recommendations for the treatment of COPD. In all patients with different forms of MDR TB combined with COPD, the effect of successful bronchodilation on the course of the underlying disease, on the indices of abacillation was evaluated (Table 1).

Table 1. The indices of abacillation in patients of different clinical groups during the 3-month therapy

Nosological forms and bronchial obstruction	The main group of patients with excretion of bacilli,%		Comparison group of patients with excretion of bacilli,%	
	Before treatment	After treatment	Before treatment	After treatment
Infiltrative TB				
FEV1>70%	67,4±3,76	0,6±1,23*	68,3±3,12	8,6±1,43*
FEV1=69-50%	73,6±3,12	1,1±1,46*	72,8±2,65	12,7±1,02*
FEV1< 50%	79,5±4,04	3,8±1,87*	78,1±3,04	20,6±2,12*
Fibrous-cavernous TB				
FEV1>70%	70,1±3,1	12,3±3.6*	71,5±2,78	18,7±3,54*
FEV1=69-50%	87,5±3,87	22,4±2,76*	84,4±4,12	34,4±3,47*
FEV1< 50%	91,1±4,06	30,6±2,32*	88±3,76	45,7±3.14*

Note: ** - the differences were significant with the original data, p <0, 05*
FEV1- *forced expiratory volume in the first second*

Table 2. The dynamics of bronchial patency with different initial severity of bronchial obstruction

Dynamics of pulmonary function	Initial bronchial obstruction, n=32	Moderate bronchial obstruction, n=48	Significant bronchial obstruction, n=39	p_{1-2}	p_{1-3}
	n (%)	n (%)	n (%)		
	1	2	3		
Improving	18(56,25)	21 (43,8)	13(33,3)	<0,02	<0,005
including normalization of bronchial patency	18(56,25)	13(27)	0	<0,0004	<0,0001
worsening	5(15,6)	3(6,2)	0	<0,002	<0,008
No dynamics	7(21,9)	24(50)	26(66.7)	<0,0001	<0,0001

Note: p - the achieved level of significance of the difference between the parameters of initial and significant bronchial obstruction

Patients of the main group received modern bronchodilation therapy in a step type, depending on the severity of bronchial obstruction (starting with short-acting β2-agonists and anticholinergics, long-acting β2-agonists and anticholinergics, as well as inhaled glucocorticosteroids). Patient comparison groups received only euphillin, with much less efficacy of bronchodilation. The data presented in the table demonstrate not only more pronounced indicators of bacilli excretion in patients with severe bronchial obstruction, but also a statistically significant decrease in bacilli excretion with successful bronchodilation, which again confirms the need for therapy not only for the underlying disease in patients with MDR TB , but also for the treatment of COPD. Patients with initial, moderate bronchial obstruction and FEV1 / FVC> 70% received therapy with predominantly short acting β2-agonists. The data obtained agree with the data of the researchers, who established that as the tuberculosis process calms down, the severity of obstructive disorders decreases. Obviously, during the treatment process, there is an effect on the reversible components of obstruction caused by tuberculous inflammation.

Dynamics of the state of bronchial patency, depending on the initial degree of manifestation of bronchial obstruction, are presented in Table 2. Thus, we can conclude that the functional mechanisms of bronchial obstruction may regress under the influence of basic treatment, and organic - defined by the expression of tissue changes in the structure of the lung, bronchus and does not fade under the influence of treatment. The choice of bronchodilator was carried out according to the therapeutic algorithm developed by us, taking into account the results of the individual bronchodilator test. In the cases shown, nebulizer therapy was prescribed with the use of bronchodilators, mucolytics. The educational part of the program included individual interviews with patients about the need to stop smoking, information about COPD, teaching the patient to use inhalers and general approaches to COPD therapy. Thus, the results obtained indicate a negative effect of bronchial obstruction on the tuberculosis process, which led to the development of a basic treatment program combining different methods for eliminating the causes of bronchial obstruction: adequate etiotropic chemotherapy, exposure to pathogenetic agents, modern regimens of bronchodilator therapy and smoking control.

REFERENCES

Alikhanova N., Akhundova I., Seyfaddinova M., Mammadbayov E., Bayramov R. et al. First national survey of anti-tuberculosis drug resistance in Azerbaijan and risk factors analysis. *Public Health Action*, 2014; 2: 17–23.

Celli B.R., Decramer M., Wedzicha J.A. et al. An official American Thoracic Society/European Respiratory Society statement: research questions in COPD.*Eur. Respir. J.* 2015; 45 (4): 879-905. DOI:10.1183/09031936.00009015.

Dharmadhikari A.S. et al. Rapid impact of effective treatment on transmission of multidrug-resistant tuberculosis //Int.J.Tuberc.Lung Dis. – 2014. – Vol. 18, №9. – P. 1257-1266.

GOLD. Global Strategy for the Diagnosis, Management and prevention of COPD, 2017. Available at: *http: // goldcopd.org / gold – 2017 – global – strategy – dignosis – management – prevention – copd /*

Ismayilzada J.M. Dependence of functional changes of respiratory sistem from structural changes in patients with chronic destructive tuberculosis in association with chronic obstructive pulmonary disease - 27 National Congress on Respiratory Diseases. St. Petersburg; 2017. P. 145.

Miller M.R., Hankinson J., Brusasco V. et al. Standardization of spirometry. *Eur. Respir. J.* 2005; 26: 319-338.

Miravitlles M., Vogelmeier C., Roche N. et al. A review of national guidelines for management of COPD in Europe. *Eur. Respir. J.* 2016; 47 (2): 625-637. DOI: 10.1183/ 13993003.01170-2015.

Pellegrino R., Viegi G., Brusasco V. et al. Interpretative strategies for lung function tests. Eur. Respir. J. 2005; 26: 948-968.

Word Health Organization Global tuberculosis report, 2016.

World Health Organization. Roadmap to prevent and combat drug-resistant tuberculosis. The Consolidated Action Plan to Prevent and Combat Multidrug-and Extensively Drug-Resistant Tuberculosis in the WHO European Region, 2011–2015.Copenhagen, Denmark: WHO, 2011.

****