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Effect of medications of various groups on pro-inflammatory cytokine tnf- α level in induced sputum in patients with acute copd affected by lung Tb

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The article examined the application of different methods of treatment and their effect on the regional (in induced sputum) level of pro-inflammatory cytokine TNF- α in patients with chronic obstructive pulmonary disease (COPD) who had had lung TB. It highlights the beneficial use of the treatment of acute phase of COPD by combining β2 - agonist and an anticholinergic medication (Berodual) and doxofylline (Aerofyllin) for correction of the regional (endobronchial) cytokine imbalance of homeostasis.

Keyword: Tumor necrosis factor (TNF) alpha, chronic obstructive pulmonary disease, lung tuberculosis.

1. Introduction

Lung tuberculosis (TB) as an etiologic factor of chronic obstructive pulmonary disease (COPD) plays an integral role and remains a subject of scientific debate in modern phthisiopulmonology. If we consider the COPD as a universal reaction to all known and suspected risk factors [2], our extensive clinical expertise allows us to assert that recent lung TB can be considered as a risk factor of COPD progression [1, 9, 10].

Among the possible mechanisms of rapid progression of COPD in individuals who have had lung TB, the emphasis is placed on homeostasis imbalance which performs an important sanogenetic ("antimycobacterial") mission whereas in COPD it performs a pathogenic effect which maintains a chronic inflammatory process in bronchopulmonary system.

It must be noted that attempts to administer "anti-TNF-strategies" (etanercept, infliximab, adalimumab) in patients with COPD with recent lung TB have led to the development of serious complications - the reactivation of latent tuberculosis infection by reducing the subpopulation and functional activity of "antimycobacterial" CD4 + T memory cells capable of suppressing mycobacteria by synthesizing IFN-γ [6, 7]. Thus, the research in anti-cytokine therapy in COPD patients with recent TB seems quite a perspective.

The aim of this study is to evaluate the clinical effectiveness of combined therapy (β2 – agonist and an anticholinergic medication (Berodual) and doxofylline (Aerofyllin) for correction of regional (in induced sputum) level of pro-inflammatory cytokine TNF- α in patients with chronic obstructive pulmonary disease (COPD) with recent lung TB.

2. Methods and Resources

There were 98 male patients with COPD with recent lung TB of different forms under study. The 1st group consisted of 42 patients with COPD of I-II degree (stable stage of COPD, β2-agonists and xanthines were not administered).

For comparative assessment of clinical effectiveness of different groups of medications and their combinations, three more groups of patients were formed.

Thus, to assess the clinical anti -TNF-α- activity we have administered a combination drug Berodual as complex therapy to target acute I-II stages of COPD in individuals with recent lung TB (2nd group, 19 patients).

Berodual ("Boehringer Ingelheim Pharma GmbH & Co KG", Germany) is a metered -dose inhaler combining two components – fenoterol and ipratropium, administration 2 inhalations 3 times a day for 21 days. For clinical evaluation of anti -TNF-α- active drugs of the xanthine group (the third group, 21 patients) we administered doxofylline (Aerofyllin, ABC Farmaceutici, Turin, Italy; Table. 400 mg) 1 tab. 2 times a day for 21 days course. To assess the clinical activity of anti-cytokine combination of bronchodilator therapy (group 4th, 16 patients), we used a combination drug Berodual (2 inhalations 3 times a day for 21 days course) and Aerofyllin (1 tablet 2 times a day for 21 days course .)

The concentration of TNF-α in induced sputum (collected after a 15-minute inhalation of 3% hypertonic solution of chlorine via nebulizer) was determined by means of immunoenzyme method by applying commercial kits ProCon TNF- α ("Protein Contour ", Russia).

3. Results and Discussion

We have found out (Fig.) that patients with COPD affected by lung TB had the level of TNF-α in induced sputum at exacerbation of chronic nonspecific diseases (2nd - 4th group) 5,9-5,7 times higher ($p<0.001$) than in patients with stable course of disease (group 1).

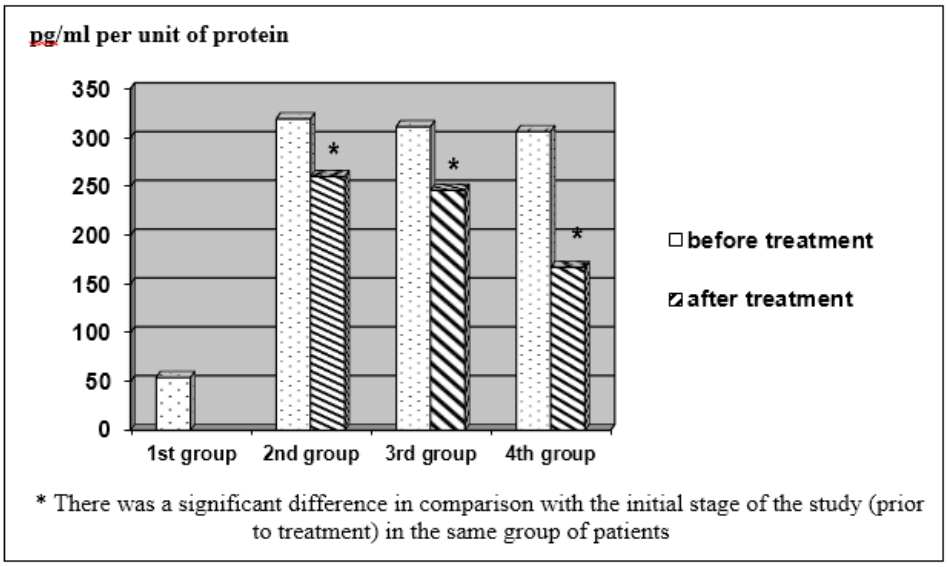

Fig 1: Dynamics of pro-inflammatory cytokine TNF-α in induced sputum under the influence of treatment in patients of the 2nd, 3rd and 4th groups pg/ml per unit of protein

It was also discovered that over the 3- week course of the combination drug Berodual (Group 2) the investigated indices significantly reduced by 18.3% ($p<0.001$) whereas with the application of Aerofyllin (Group 3) the investigated indices have increased to 20 8% ($p<0.001$), which is not significantly different from the corresponding phase of the study in patients of the third group who experienced Berodual. Thus, we have found that Aerofyllin and Berodual have a similar (anti -TNF-α- active) effect on the regional (endobronchial) cytokine level of COPD patients with recent lung TB.

Patients of group 4 under the influence of combined therapy of Berodual and Aerofyllin displayed the decrease of TNF-α levels in induced sputum by 45.4% ($p<0.001$), which may indicate a double effect of anti-cytokine (as

related to TNF-α) activity of each of the components of the complex therapy of Berodual and Aerofyllin.

4. Conclusions

Thus, having analyzed the scientific evidences we can draw the following conclusions:

1. During acute stages (of non-infectious nature) of COPD, patients with recent lung tuberculosis in comparison with stable COPD in these patients revealed an increase in multiple regional (endobronchial) levels of the proinflammatory cytokine TNF-α.
2. It was proved that the use of combined drug therapy in acute stages of COPD with application of β2- agonist and an anticholinergic drug (Berodual) and doxofylline (Aerofyllin) is rather beneficial with the purpose of regional correction of (endobronchial) Cytokine imbalance of homeostasis.

5. References

1. Klein S, Fontana L, Young VL. Absence of an effect of liposuction on insulin action and risk factors for coronary heart disease. N Engl J Med 2004; 350:2549-2557.
2. Borher BS, Reitledge BK, Schleimer RP. Interleukin-1 production by human lung tissue. J Immunol 2000; 139:2303–2307.
3. Rallidis LS, Paschos G, Liakos GK. Dietary a-linolenic acid and decreases C-reactive protein, serum amyloid A and interleukin 6 in dyslipidaemic patients. Atherosclerosis 2003; 167:237-242.
4. Keatings VM, Collins PD, Scott DM, Barnes PJ. Differences in interleukin-8 and tumor necrosis factor-alpha in induced sputum from patients with chronic obstructive pulmonary disease or asthma. Am J Respir Cirt Care Med 1996; 153:530-534.
5. Hamdi H, Mariette X, Godot V. Inhibition of anti-Tuberculosis T lymphocyte function with Tumor Necrosis Factor antagonists. Arthritis Res Ther 2006; 19(8):114.
6. Trebble T, Arden NK, Stroud MA. Inhibition of tumor necrosis factor alpha and interleukin 6 production by mononuclear cells following dietary fish-oil supplementation in healthy men and response to antioxidant co-supplementation. Br J Nutr 2003; 90:405-412.
7. Paquot N, Castillo MJ, Lefebvre PJ. No increased insulin sensitivity after a single intravenous administration of a recombinant human tumor necrosis factor receptor: Fc fusion protein in obese insulin-resistant patients. J Clin Endocrinol Metab 2000; 85:1316-1319.
8. Simpson RW, Shaw JE, Zimmer PZ. Simpson RW. The prevention of type diabetes – lifestyle change or pharmacotherapy? A challenge for the 21st century. Diabetes Res Clin Pract 2003; 59(3):165-180.
9. Page ST, Herbst KL, Amory JK. Testosteron administration suppresses adiponectin levels in men. J Androl 2005; 26:85-92.
10. Wang B, Jenkins JR, Trayhurn. Expression and secretion of inflammation-related adipokines by human adipocytes differentiated in culture: integrated response to TNF-alfa. Am J Physiol Endocrinol Metab 2005; 288:731-740.