

THE PHARMA INNOVATION - JOURNAL

Topographic characteristics of the level of osteoprotegerin in cadaver blood of patients with copd affected by lung tuberculosis

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Patients with chronic obstructive pulmonary disease (COPD) with recent lung tuberculosis (TB) were studied on the question of regional level of osteoprotegerin (in cadaver blood from various vascular regions in the study of postmortem). It was found out that patients with COPD had no significant effect of the recent TB and it didn't influence the level of the investigated indicator in various vascular regions. Thus, among COPD patients the osteoprotegerin level in induced sputum, according to previous studies, is formed by the local cytokine synthesis (at the tissue level of the bronchi), but not by means of increasing its level in the blood entering the pulmonary circulation through the inferior vena cava (IVC).

Keyword: Osteoprotegerin, chronic obstructive pulmonary disease, lung tuberculosis.

1. Introduction

Among the diseases that have a direct impact on the course of chronic broncho-obstructive pathology the emphasis is placed on lung TB which acts as a clinical marker of a sharp decline in multiple protective "barriers" of the respiratory system [3]. The Important pathogenetic mechanism of both chronic obstructive pulmonary disease (COPD) and lung TB is the imbalance of cytokine homeostasis which acts on the one hand as an important factor of chronicity and progression of COPD and on the other hand as an important component of antimycobacterial defense mechanism in patients with TB [4].

Disorders in both systemic and regional cytokine potential are considered as one of key mechanisms of the development of systemic manifestations of COPD including a reduction in bone mineral density (detectable in all patients) [4]. The latter is characterized by an increased number of fractures of various locations which significantly impair the quality of life of patients

causing pain, disruption of respiratory function, mobility limitation, and may be associated with mortality of COPD patients [5]. In this context, the problem of preventing the progression of osteoporosis in patients with COPD can be considered as an important task of modern pulmonology [7].

In the last decade, a great number of research in systemic effects of COPD has significantly enriched with scientific facts about the role in the development of osteoporosis system cytokines, growth factors, transcription factors and various regulatory proteins and enzymes as well as the least studied group of local factors united in RANKL / RANK / OPG [2, 6, 8].

As it is stated above, it's quite a perspective to develop the further study of pathogenetic entity of cytokine - mediated mechanisms of COPD progression in individuals with recent lung TB, since it is the basis for the research of new methods of differentiated pathogenetic therapy of chronic obstructive pulmonary disease including

reduction of the risk of development and progression of osteopenic syndrome.

The aim of the study was to explore the level of osteoprotegerin in cadaver blood from various vascular regions in patients with COPD complicated by recent lung TB.

2. Methods and Resources

There were 20 dead bodies under examination: the 1st (the 3rd) group comprised 16 cadavers who had had COPD (GOLD stage III-IV) and the 2nd (the 4th) group consisted of 18 cadavers who had had COPD (GOLD stage III-IV) complicated by recent TB. The subject of research was the cadaver blood belonging to the 3rd and 4th group. Death in patients of the 3rd and 4th groups occurred with short agonal period. Blood samples from all the dead bodies was collected from various vascular regions within the period of up to 6 hours after the death.

Concentration of Osteoprotegerin in blood serum was analyzed by means of immunoenzymometric method using commercial kits such as Human Osteoprotegerin (OPG) ELISA Kit Company Biomedica Medizinprodukte GmbH & Co KG (Austria). Evaluation of the results was carried out photometrically.

3. Results and Discussion

Taking into account that adults' osteoprotegerin mRNA is highly expressed in various tissues, including the lungs, liver, heart, kidneys, bones, etc. [5], we carried out a postmortem study of osteoprotegerin level in cadaver blood from various vascular regions in patients with ante mortem COPD (GOLD stage III-IV), and COPD (GOLD stage III-IV complicated by recent TB. It must be emphasized that with the view of the factor of postmortem index deviations (a progressive decrease from the moment of death), the assessment was performed in the ratio of the level of cytokine % "on the periphery" - in v. subclavia, conventionally taken as 100%.

Results of the study of osteoprotegerin levels in cadaver blood from various vascular regions in patients of the 1st and 2nd groups are presented in the table.

We have determined (Table) that patients of either group 1 (not affected by lung TB in past history) or patients of group 2 (affected by lung TB) in cadaver blood both had cytokine osteoprotegerin. With regard of this fact lung TB didn't cause serious influence on the ratio of the indices of various vascular regions: the differences between the indices of cytokines in patients of the 1st and 2nd groups in the respective vascular regions were unreliable.

Noteworthy is the maximum increase in the vascular region of the hepatic veins (v.v.hepaticae) in the individuals of the 1st and 2nd groups as well as a significant increase of osteoprotegerin level after the passage of blood through the liver. Accuracy of the deviations between the index of the portal venous blood and the blood of the hepatic veins was <0.02 and <0.001 in patients of the 1st and 2nd groups. These facts are evidences of the active role of the liver in the synthesis of osteoprotegerin.

Thus, the results of postmortem research prove that a substantial increase of osteoprotegerin levels in induced sputum, as stated above [1], is formed by the local (at the tissue level of the bronchi) cytokine synthesis, but not because of its level increase in the blood which entered the pulmonary circulation through the inferior vena cava. These particular facts suggest that in order to correct the regional (bronchial tissue, endobronchial) level of osteoprotegerin the optimal way of drug delivery will be inhalative or endobronchial.

4. Conclusions

1. Elevated levels of osteoprotegerin in induced sputum in patients with COPD, as it was revealed earlier [1], is formed by the local (at the tissue level of bronchi) cytokine synthesis, but not because of the increase of its level in blood entering the pulmonary circulation through the inferior vena cava.
2. The optimal way of delivering drugs to correct regional (bronchial tissue, endobronchial) osteoprotegerin level is through inhalations or by means of endobronchial treatment in combination of fiber-optic bronchoscopy.

Table 1: Topographic characteristics of osteoprotegerin level in cadaver blood from various vascular regions of patients of the 1st and 2nd groups are presented with the view of the factor of postmortem change index (progressive decline), the calculation was performed in % to the level of cytokines on the "periphery" - in v. subclavia, conventionally taken as 100%.

Vascular region	Statist. data	Group 1	Group 2
v.subclavia	M ± m	100 ± 0	100 ± 0
	n	16	18
ventriculus dexter	M ± m	113 ± 5	117 ± 5
	n	16	18
	p	–	> 0,5
ventriculus sinister	M ± m	108 ± 3	103 ± 6
	n	16	18
	p	–	< 0,5
v.v.hepaticae	M ± m	117 ± 6	121 ± 5
	n	16	18
	p	–	> 0,5
v.portae	M ± m	97 ± 5	92 ± 5
	n	16	18
	p	–	< 0,5
v.mesenterica superior	M ± m	95 ± 4	96 ± 4
	n	16	18
	p	–	> 0,5
v.mesenterica inferior	M ± m	98 ± 3	92 ± 5
	n	16	18
	p	–	< 0,5
v.v.pancreaticae	M ± m	87 ± 3	83 ± 4
	n	16	18
	p	–	< 0,5
v.lienalis	M ± m	104 ± 4	103 ± 5
	n	16	18
	p	–	> 0,5
v.cava inferior to the level of hepatic venous return	M ± m	110 ± 3	114 ± 5
	n	16	18
	p	–	< 0,5

Note: p – accuracy of differences calculated in comparison with the corresponding vascular region in patients of group 1.

5. References

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