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Radionuclide methods in assessing pulmonary perfusion and ventilation in patients with connective tissue dysplasia

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ABSTRACT

Aim. To perform a scintigraphic assessment of the bronchopulmonary system and pulmonary microcirculation in patients with connective tissue dysplasia.

Materials and methods. The study included 31 male patients of conscription age with connective tissue dysplasia (CTD), diagnosed according to the 2019 clinical guidelines (average age (19.6 ± 2.6 years)), and 25 practically healthy individuals comparable in gender and age, who formed a control group. All patients underwent planar pulmonary ventilation – perfusion scintigraphy with determination of pulmonary alveolar – capillary permeability.

Results. In patients with CTD, the apical to basal perfusion gradient (U/L_Q) was on average 24% lower than in the control group ($p = 0.046$), and alveolar – capillary permeability was higher in both lungs, both at minute 10 and at minute 30.

Conclusion. Static pulmonary ventilation – perfusion scintigraphy allows to identify functional disorders in patients with CTD at the preclinical stage: a decrease in the perfusion gradient on average by 24% compared with the control group and an increase in alveolar – capillary membrane permeability.

Keywords: connective tissue dysplasia, pulmonary ventilation – perfusion scintigraphy

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Радионуклидные методы в оценке легочной перфузии и вентиляции у пациентов с дисплазией соединительной ткани

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РЕЗЮМЕ

Цель. Провести сцинтиграфическую оценку состояния бронхоальвеолярной системы и легочной микроциркуляции у пациентов с дисплазией соединительной ткани.

Материалы и методы. В исследование включен 31 пациент мужского пола призывного возраста с дисплазией соединительной ткани (ДСТ), диагностированной согласно клиническим рекомендациям 2019 г., средний возраст 19,6 ± 2,6 лет, и 25 практически здоровых лиц, сопоставимых по полу и возрасту, составивших группу контроля. Всем пациентам выполняли вентиляционно-перфузионную сцинтиграфию легких в планарном режиме с определением скорости альвеолярно-капиллярной проницаемости.

Результаты. У пациентов с ДСТ апикально-базальный градиент перфузии (U/L_Q) имел более низкие значения по сравнению с группой контроля в среднем на 24% ($p = 0,046$) и более высокие значения альвеолярно-капиллярной проницаемости в обоих легких, как на 10-й, так и на 30-й мин.

Заключение. Вентиляционно-перфузионная сцинтиграфия в статическом режиме позволяет на доклиническом этапе выявить функциональные нарушения у пациентов с ДСТ: снижение градиента перфузии по сравнению с группой контроля в среднем на 24% и повышение проницаемости альвеолярно-капиллярной мембраны.

Ключевые слова: дисплазия соединительной ткани, вентиляционно-перфузионная сцинтиграфия легких

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Источник финансирования. Авторы заявляют об отсутствии финансирования при проведении исследования.

Соответствие принципам этики. Все пациенты подписали информированное согласие на участие в исследовании. Исследование одобрено этическим комитетом СибГМУ (протокол № 8903 от 20.12.2021).

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INTRODUCTION

Connective tissue dysplasia (CTD) is an inherited condition manifested through defects of the ground substance and fibrous tissue structures. It underlies morphological and functional disorders in various organs and systems and is characterized by a progressive course, which determines the features of associated pathological conditions. Social and clinical significance of these pathological manifestations is determined, on the one hand, by high prevalence of the disease due to accumulation of genetic defects in the population and by a significant impact of anthropogenic and abiotic factors and on the other hand –

by the progressive nature of clinical manifestations, characterized by multi-organ lesions with a risk of severe complications at late stages, up to death of the patient [1, 2].

The main period for a clinical debut of CTD is adolescence, when an increase in the volume of connective tissue corresponds to growth and development of the body [3]. Phenotypic manifestations of CTD are usually divided into groups depending on organs and systems involved in it. The first systematized data on lesions of the respiratory tract in undifferentiated CTD were published in 1994. [3].

The authors identified a group of dysplasia-associated changes of respiratory organs, which were determined by genetic defects in fibrillogenesis. This group included tracheobronchomegaly, tracheobronchomalacia, Williams – Campbell syndrome, pulmonary hypoplasia, bronchiectasis, pulmonary emphysema, and tracheobronchial dyskinesia. The morphofunctional state of the respiratory system in CTD is characterized by both increased elasticity of the bronchial tree and alveolar lung tissue and by extrapulmonary manifestations, such as thoracoabdominal syndrome and lability of the autonomic nervous system and immune system. Later, spontaneous pneumothorax as a consequence of bullous emphysema was included in the group of dysplasia-associated respiratory changes [4, 5].

Some authors believe that the mainstay for impaired binding and supporting function of the connective tissue in CTD is genetic weakness of all lung structures (bronchi, blood vessels, alveoli) that is manifested through several clinical syndromes in the postnatal period under the influence of external factors [5]. Dysplasia is often accompanied by a decreased tone of the bronchial wall with subsequent development of tracheobronchial dyskinesia and bronchiectasis [6]. The most important extrapulmonary factors determining the state of respiratory organs in CTD are chest wall and spinal deformity, weakness of respiratory muscles, features of breathing regulation, and the state of pulmonary hemodynamics [7, 8].

Radiology techniques are known to occupy a prominent place in the diagnosis of bronchopulmonary pathology. However, generally accepted radiology methods allow to detect changes in the lung parenchyma at relatively late stages of the disease. To assess morphofunctional changes at the preclinical stage of the disease, the use of radionuclide methods is promising. They are easy to reproduce and highly sensitive in evaluating both pulmonary ventilation and perfusion [9–11]. At the same time, when studying pathological changes in the lungs, the most complete information can be obtained using combined ventilation–perfusion scintigraphy, which significantly complements the data on the state of the capillary blood flow with lung ventilation parameters, which is essential for the diagnosis of early functional disorders [12].

Therefore, the aim of the study was to perform a scintigraphic assessment of the bronchopulmonary system and pulmonary microcirculation in patients with CTD.

MATERIALS AND METHODS

The study is based on the results of the examination of a group of persons subject to mandatory enlistment in the Armed Forces of the Russian Federation at the Military Medical Commission of Tomsk. The study included 31 male patients aged 16–22 years. The average age was 19.7 ± 2.7 years, the body mass index was 18.2 ± 2.2.

CTD was detected by the anamnestic data to identify previously diagnosed diseases typical of CTD, the clinical examination to identify external signs of systemic connective tissue involvement, including the anthropometric study, and the findings of instrumental methods of examination. Undifferentiated CTD was revealed in all patients. The severity of the disease was assessed using the phenotype table proposed by T.I. Kadurina and V.N.Gorbunova [4]. Exclusion criteria were patients' inability to participate or disagreement with the protocol requirements, bronchopulmonary diseases, acute diseases, and exacerbation of chronic diseases. The control group encompassed 25 healthy non-smoking volunteers, comparable in gender and age with the patients of the experimental group.

All the individuals underwent planar pulmonary ventilation – perfusion scintigraphy with determination of alveolar – capillary permeability according to the previously developed technique [9]. The ventilation – perfusion ratio (V / Q ratio) was determined by dividing the percentage of the accumulated inhaled radioaerosol by each lung separately by the similar parameter of the perfusion radiopharmaceutical (RPC).

Scintigraphic studies were performed using the Forte gamma camera (Philips Medical Systems, Netherlands). Image registration and gamma scan processing were carried out using the JETStream Workspace 3.0 software (PMS, Netherlands).

Statistical data analysis was performed using Microsoft Office and STATISTICA 10.0 software packages (StatSoft Inc, USA). Quantitative data were presented as the mean (*M*) and the standard deviation (*SD*). The Mann – Whitney test was used to compare independent quantitative variables. The differences were considered statistically significant at $p < 0.05$.

The study was conducted in accordance with the principles set out in the Declaration of Helsinki and approved by the Ethics Committee at Siberian State Medical University and the Ethics Committee at Cardiology Research Institute. All patients signed an informed consent to participate in the study.

RESULTS AND DISCUSSION

The results of the scintigraphic studies are presented in the Table. In the patients with CTD, the mean V / Q value for the right lung was 0.97 ± 0.06 and for the left lung – 1.04 ± 0.07, and these values did not differ from the ones in the control group. The apical to basal ventilation gradient (U/L_V) also did not differ from that in the control group, while the perfusion gradient U/L_Q was 24% lower than in the control group ($p = 0.046$) and averaged 0.52 ± 0.14.

Three physiological processes are involved in effective external respiration: pulmonary ventilation, pulmonary perfusion, and gas diffusion through the alveolar – capillary membrane. In various pathological conditions in the lungs, these processes can be impaired. To assess the disorders, it is necessary to use methodological approaches allowing to determine diagnostically significant parameters, which include the V / Q ratio, alveolar – capillary permeability, etc. [9, 13–15].

In assessing the results of ventilation – perfusion scintigraphy in patients with CTD, the V / Q ratio corresponded to the control values for both lungs (Table). In CTD patients, a decrease only in U / L_Q (0.52 ± 0.14; $p = 0.046$) was observed, while the U / L_V gradient was not significantly different from that in the control group (Table). Concordance of the main functional units of the lungs in patients with CTD was quite satisfactory, and a drop in U / L_Q was probably associated with vasoconstriction, which contributed to a decrease in the blood flow to poorly ventilated lung areas.

Table

Scintigraphic parameters of pulmonary perfusion and ventilation in patients with connective tissue dysplasia and in the control group, *M* ± *SD*

Parameter		Control group, *n* = 25	Experimental group with CTD, *n* = 31					
			RL	MW test (*p*) 1–2	LL	MW test (*p*) 1–4	RL + LL	MW test (*p*) 1–6
		1	2	3	4	5	6	7
V/Q		0.98 ± 0.03	0.97 ± 0.06	NS	1.04 ± 0.07	NS	–	–
U/L_Q		0.68 ± 0.03	–	–	–	–	0.52 ± 0.14	0.046
U/L_V		0.66 ± 0.04	–	–	–	–	0.63 ± 0.11	NS
ACP, %	10 min	10.6 ± 2.9	18.73 ± 8.51	0.005	15.56 ± 8.58	0.006	–	–
	30 min	21.3 ± 4.3	33.17 ± 9.87	0.001	30.32 ± 9.96	0.004	–	–

Note: NS – nonsignificant; CTD – connective tissue dysplasia; *n* – number of patients in the group; RL – right lung; LL – left lung; MW test – Mann – Whitney test; *p* – significance of differences between the groups; V / Q – ventilation – perfusion ratio; U / L_Q – apical to basal perfusion gradient; U / L_V – apical to basal ventilation gradient; ACP – alveolar – capillary permeability.

It is known that alveolar air and pulmonary capillary blood flow are separated by the alveolar – capillary membrane, which provides gas transport according to the laws of diffusion, and pulmonary diffusing capacity depends on both lung capacity and the corresponding gas exchange surface. To assess alveolar – capillary permeability (ACP) of the lungs, we proposed and used an improved method of pulmonary ventilation – perfusion scintigraphy, which included the use of planar ventilation scintigraphy, assessment of radiopharmaceutical washout from the entire affected / intact lung, as well as examination in the posterior – anterior imaging plane of ACP in RPC washout and its registration at minute 10 and then at minute 30 after RPC inhalation [9, 15].

The study revealed an increase in the ACP rate in patients with CTD both in the right and left lung at minute 10 (18.73 ± 8.51% ($p = 0.005$), 15.56 ± 8.58% ($p = 0.007$), respectively) and at minute 30 of the study (33.17 ± 9.87% ($p = 0.001$), 30.32 ± 9.96% ($p = 0.004$), respectively), compared with the control group (Table).

Therefore, a significant increase in the RPC washout rate in patients with CTD was revealed, compared with the control group, which indicates increased ACP. The observed decrease in the U / L_Q perfusion gradient in CTD can be explained by the involvement of the vasoconstrictor mechanism in the development of alveolar hypoxia. A statistically significant increase in the ACP rate in both lungs, compared with the control group, is probably a compensatory response of the alveolar – capillary network aimed at increasing gas exchange [12, 14]. At the same time, the increase in ACP can be determined both by an increase in gas exchange surface area, typical of primary emphysema in patients with CTD, and by hyperventilation syndrome, often observed in this group of patients [16].

CONCLUSION

Planar ventilation – perfusion scintigraphy allows to detect functional disorders in patients with CTD at the preclinical stage: a decrease in the U / L_Q perfusion gradient on average by 24%, compared with the control group, and an increase in ACM.

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Authors contribution

Vesnina Zh.V. – collection of the material, analysis of the obtained material, statistical processing of the data, interpretation of the data, drafting of the manuscript. Anashbaev Zh. Zh. – carrying out of radionuclide studies, processing of scintigraphy findings, database filling. Teteneva A.V. – conception of the study, review of the literature, analysis of the disease under investigation. Krivonogov N.G. – development of the radionuclide technique, methodological support, analysis of the findings. Bespalova I.D. – coordination of patient selection, clinical substantiation of the diagnostic method and design of the study, collection of the data (clinical section). Sazonova S.I. – literature search, provision of material facilities for radionuclide studies. Serdyukov N.A. –coordination of patients (obtainment of the informed consent to participate in the study), theoretical and clinical confirmation of the findings. Potapov K.V. – selection of patients, collection of raw data for filling the clinical patient database.

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