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Systemic and Local Metabolic Changes in Interstitial Lung Injury

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ABSTRACT

Background. *Interstitial lung injury is accompanied by significant metabolic disturbances affecting both local pulmonary structures and systemic homeostasis. However, the relationship between these changes remains insufficiently studied.*

Material and methods. *The study was performed on 64 rats with experimentally induced interstitial lung injury via chronic tobacco smoke exposure. Metabolic parameters were assessed in serum and bronchoalveolar fluid, including phospholipid fractions and lipid metabolism indices. Lipids were extracted by the Folch method and analyzed using thin-layer chromatography. All procedures complied with international ethical standards.*

Results. *Experimental interstitial lung injury was associated with significant metabolic disturbances at both local and systemic levels. In bronchoalveolar fluid and blood, a decrease in structural membrane components and an increase in membrane degradation products were observed, indicating destabilization of cellular membranes. In addition, pronounced alterations in lipid metabolism were detected, including elevated levels of total cholesterol, triglycerides, and low-density lipoproteins, along with a decrease in high-density lipoproteins. Pharmacological correction contributed to partial normalization of the studied parameters, with the most significant effect observed in combined therapy, where values approached those of intact animals. Pharmacological correction partially restored metabolic balance, with the most pronounced effect observed under combined therapy, approaching values of intact animals.*

Conclusion. *Interstitial lung injury is accompanied by interconnected local and systemic metabolic disturbances that contribute to disease progression. Combined pharmacological correction demonstrates a pronounced normalizing effect, highlighting its potential as an effective therapeutic strategy.*

Key words: *Interstitial lung injury, metabolic changes, bronchoalveolar fluid, lipid metabolism, inflammation, oxidative stress, pharmacological correction, experimental model.*

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INTRODUCTION

Interstitial lung diseases (ILDs) represent a heterogeneous group of disorders characterized by inflammation, diffuse damage of the alveolar epithelium, and progressive remodeling of the pulmonary interstitium, often leading to fibrosis and impaired gas exchange. These conditions are associated with significant morbidity and mortality worldwide and remain a major challenge in modern pulmonology [8].

Interstitial lung injury is a key pathogenetic component underlying many forms of ILDs. It is characterized by persistent inflammation, activation of immune cells, epithelial and endothelial damage, and excessive deposition of extracellular matrix components, ultimately resulting in fibrotic transformation of lung tissue [4]. Chronic inflammation and dysregulated repair processes play a central role in disease progression, contributing to irreversible structural and functional impairment of the lungs.

Hypoxia is considered one of the most important drivers of metabolic disturbances in interstitial lung injury. Reduced oxygen availability leads to mitochondrial dysfunction, altered energy metabolism, and activation of hypoxia-inducible pathways, which further amplify inflammation and fibrosis [10]. In addition, oxidative stress caused by excessive production of reactive oxygen species contributes to cellular damage, lipid peroxidation, and disruption of membrane integrity [5].

Increasing evidence suggests that metabolic alterations are not merely secondary phenomena but actively participate in the pathogenesis of interstitial lung injury. Changes in cellular metabolism affect membrane composition, signaling pathways, and immune responses, thereby influencing disease progression [11]. Disturbances in lipid metabolism, in particular, have been shown to impair surfactant function, enhance inflammatory signaling, and promote fibrotic remodeling of lung tissue [2].

Importantly, metabolic changes in interstitial lung injury occur at both local and systemic levels. Local alterations within lung tissue reflect direct damage to alveolar structures and surfactant systems, whereas systemic metabolic disturbances indicate broader involvement of the organism, including changes in circulating metabolites, inflammatory mediators, and vascular function [7]. The interaction between these levels remains insufficiently understood but may play a crucial role in the progression and severity of the disease.

Despite the growing body of research, most studies have focused on isolated aspects of the disease, either local pulmonary changes or systemic metabolic alterations. A comprehensive evaluation integrating both levels is still lacking and represents an important direction for further investigation [2].

Therefore, the aim of this study was to investigate systemic and local metabolic changes in experimental interstitial lung injury and to evaluate the effectiveness of pharmacological correction.

Lipid and phospholipid metabolism plays a fundamental role in maintaining the structural and functional integrity of lung tissue. Phospholipids are essential components of cellular membranes and constitute the major fraction of pulmonary surfactant, which is critical for reducing alveolar surface tension and maintaining normal respiratory function. Under physiological conditions, a balanced lipid composition ensures membrane stability, optimal permeability, and proper functioning of membrane-bound enzymes and receptors [9].

Under pathological conditions, including interstitial lung injury, significant disturbances in lipid and phospholipid metabolism occur. These changes are characterized by degradation of structural phospholipids, accumulation of lysophospholipids, and alterations in membrane fluidity and permeability. Such disturbances lead to surfactant dysfunction, increased vulnerability of cells to damage, and disruption of cellular homeostasis [6].

Furthermore, disorders of lipid metabolism are closely associated with key pathogenetic mechanisms such as inflammation, oxidative stress, and hypoxia. Increased lipid peroxidation results in the formation of reactive intermediates that damage cellular structures and amplify inflammatory signaling pathways. At the same time, alterations in phospholipid composition can affect intracellular signaling, immune responses, and processes of cell proliferation and apoptosis, thereby contributing to the progression of interstitial lung injury and fibrotic remodeling.

Importantly, these alterations are not limited to the lungs but also involve systemic metabolic pathways. Circulating lipid fractions reflect the overall metabolic state of the organism and may influence vascular function, immune regulation, and the severity of inflammatory responses. Therefore, an integrated assessment of lipid and phospholipid metabolism at both local and systemic levels is essential for a comprehensive understanding of disease pathogenesis and for the development of targeted therapeutic strategies [3].

The aim of the study: To investigate systemic and local metabolic changes, including lipid and phospholipid alterations, in experimental interstitial lung injury

and to evaluate the effectiveness of pharmacological correction.

MATERIALS AND METHODS

The study was conducted on 64 white outbred rats weighing 150–200 g, in which experimental interstitial lung injury was induced by chronic exposure to tobacco smoke in a Kurland chamber for 2 months. All experimental procedures were carried out in accordance with international ethical standards for animal research (Strasbourg Convention, 1986).

After model induction, pharmacological correction was performed using ecdisten, acetylcysteine, and polyoxidonium, administered per os for 15 consecutive days, both as monotherapy and in combination.

To assess metabolic alterations, both local and systemic parameters were evaluated. Bronchoalveolar fluid and blood serum were analyzed to determine phospholipid composition and lipid metabolism indices. Lipids were extracted using the Folch method, followed by separation of phospholipid fractions (phosphatidylcholine, phosphatidylethanolamine, sphingomyelin, and lysophosphatidylcholine) by thin-layer chromatography. Quantitative analysis was performed based on lipid phosphorus content.

In addition, systemic lipid metabolism parameters, including total cholesterol, triglycerides, low-density lipoproteins (LDL), and high-density lipoproteins (HDL), were measured using a biochemical analyzer.

Statistical analysis of the obtained data was carried out using standard methods, with significance assessed at $p < 0.05$.

RESULTS

Rats with interstitial pneumonia demonstrated significant disturbances in lipid metabolism. The levels of total cholesterol, triglycerides, and LDL were significantly increased by 70.3%, 178.0%, and 13%, respectively, compared to the intact group. At the same time, the level of HDL decreased by 1.96-fold. HDL plays a key role in reverse cholesterol transport and has anti-atherogenic properties; therefore, its reduction may indicate the development of lipid metabolism disorders.

Thus, the obtained data indicate pronounced violations lipid metabolism in rats with interstitial pneumonia. Correction of these disturbances represents a promising therapeutic approach. In this regard, pharmacological correction using ecdisten, acetylcysteine, and polyoxidonium was evaluated.

Treatment with ecdisten led to a significant decrease in total cholesterol and triglycerides by 22.46% and 30.1% ($p < 0.05$), respectively, compared to the control group. LDL levels showed a tendency to decrease (from 32.2±0.7 to 30.2±0.8 mmol/L), although the change was not statistically significant ($p > 0.05$). HDL levels significantly increased by 58.8% ($p < 0.05$).

In groups receiving combined therapy (ecdisten, acetylcysteine, and polyoxidonium), the most pronounced corrective effect was observed, particularly in the triple combination group. In this group, the levels of total cholesterol, triglycerides, and LDL were markedly reduced, while HDL levels approached those of the intact group (15.5±1.1 vs. 16.7±0.8 mmol/L).

Dyslipidemia in pneumonia should be considered as an important component of the inflammatory process, reflecting its complex and dual nature. These metabolic disturbances not only result from inflammation but may also contribute to its progression. Therefore, correction of lipid metabolism represents a critical therapeutic target aimed at preventing the transition from adaptive responses to pathological processes.

In conclusion, interstitial pneumonia is associated with pronounced dyslipidemia characterized by increased total cholesterol, triglycerides, and LDL levels, along with decreased HDL levels. The results of the present study demonstrate that combined pharmacological therapy with ecdisten, acetylcysteine, and polyoxidonium provides the most effective correction of these disturbances, suggesting a potential synergistic effect of these agents.

As shown in the table, treatment with ecdisten reduced the level of lysophosphatidylcholine (LPC) by 19.7% ($p < 0.05$) compared to the control group. At the same time, the level of phosphatidylcholine (PC) increased by 14.2% ($p < 0.05$). No significant changes in sphingomyelin (SM) and phosphatidylethanolamine (PE) levels were observed following ecdisten treatment compared to the control group. The combination of ecdisten and acetylcysteine significantly reduced LPC and SM levels by 21.1% and 4.9%, respectively, compared to the control group. In this group, PE and PC levels significantly increased by 13.7% and 16.7%, respectively.

The combination of ecdisten with polyoxidonium produced a more pronounced effect, reducing LPC levels by 36.6% and increasing PC levels by 24.9% compared to the control group. Changes in SM and PE were less pronounced, increasing by 4.2% and 16.7%, respectively ($p < 0.05$).

The most significant changes in phospholipid composition were observed in the group receiving combined therapy with ecdisten, acetylcysteine, and polyoxidonium. In this group, LPC levels decreased by 38.03%,

while PC levels increased by 29.2% compared to the control group.

Thus, the results of the study demonstrate that combined therapy with ecdisten, acetylcysteine, and polyoxidonium has a more pronounced corrective effect on blood phospholipid composition than monotherapy. Disturbances in lipid metabolism in interstitial pneumonia are not only a consequence of inflammatory and hypoxic tissue damage but also an active component of pathogenesis contributing to fibrosis progression.

The study of lipid metabolism opens new perspectives for the diagnosis and pathogenetic treatment of interstitial pneumonia, including the application of lipidomic approaches, targeted therapy, and nutraceutical strategies.

DISCUSSION

The results of the present study demonstrate that experimental interstitial lung injury is accompanied by pronounced metabolic disturbances involving both phospholipid composition and systemic lipid metabolism. These alterations reflect not only structural damage to pulmonary tissue but also broader metabolic dysregulation at the organism level.

One of the key findings of this study is the disruption of phospholipid balance, characterized by an increase in LPC and a decrease in major structural phospholipids such as PC and PE. LPC is known to be a marker of membrane degradation and cellular damage, and its accumulation indicates enhanced phospholipid breakdown under conditions of oxidative stress and inflammation. At the same time, the reduction of PC, a major component of pulmonary surfactant, suggests impairment of surfactant function, which may contribute to decreased alveolar stability and impaired gas exchange. These local changes are closely associated with systemic disturbances in lipid metabolism, including increased levels of total cholesterol, triglycerides, and LDL, along with decreased HDL. Such a pattern of dyslipidemia reflects activation of inflammatory pathways and may contribute to endothelial dysfunction, impaired microcirculation, and progression of fibrotic processes. HDL, which plays a protective role through reverse cholesterol transport and anti-inflammatory effects, was significantly reduced, further indicating the severity of metabolic imbalance.

Importantly, the observed metabolic alterations appear to be interconnected. Damage to cellular membranes and surfactant systems at the local level may lead to the release of lipid components into circulation, thereby influencing systemic lipid metabolism. Conversely, systemic dyslipidemia may exacerbate pulmonary inflammation and tissue remodeling, creating a vicious cycle that promotes disease progression. Pharmacological correction demonstrated significant efficacy in modulating these changes. Monotherapy with ecdisten showed moderate improvement, particularly in reducing LPC levels and partially restoring PC content. However, combined therapy, especially the triple combination of ecdisten, acetylcysteine, and polyoxidonium, produced the most pronounced effects, leading to normalization of both phospholipid composition and lipid metabolism parameters. This suggests a synergistic mechanism of action involving antioxidant, membrane-stabilizing, and immunomodulatory effects.

These findings are consistent with recent studies emphasizing the role of metabolic disturbances in the pathogenesis of interstitial lung diseases. Lipid metabolism is increasingly recognized as an active participant in inflammatory and fibrotic processes rather than a secondary phenomenon. Targeting these metabolic pathways may therefore represent a promising therapeutic strategy.

In conclusion, the present study highlights the importance of integrated assessment of phospholipid and lipid metabolism in interstitial lung injury. The identified changes provide insight into disease mechanisms and support the potential of combined pharmacological approaches aimed at restoring metabolic balance and preventing disease progression.

CONCLUSION

Experimental interstitial lung injury is associated with significant disturbances in both phospholipid composition and systemic lipid metabolism, reflecting the close interaction between local pulmonary damage and systemic metabolic imbalance. These alterations play an important role in disease progression by contributing to membrane destabilization, inflammation, and fibrotic remodeling.

Pharmacological correction demonstrated a beneficial effect on the studied parameters, with the most pronounced improvement observed under combined therapy. The use of ecdisten, acetylcysteine, and polyoxidonium in combination provided the most effective normalization of metabolic disturbances, suggesting a synergistic mechanism of action. The findings of this study highlight the importance of targeting metabolic pathways as a promising approach for the diagnosis and treatment of interstitial lung injury.

REFERENCES

1.Barnes PJ. Inflammatory mechanisms in patients with chronic airway diseases. Nat Rev Immunol. 2023;23(3):159–175. doi:10.1038/s41577-022-00782-8. PMID: 36221011.

2.Distler JHW, Györfi AH, Ramanujam M, et al. Shared and distinct mechanisms of fibrosis. Nat Rev Rheumatol. 2021;17(12):705–730. doi:10.1038/s41584-021-00689-6. PMID: 34671152.

3.Kim YJ, Lee H, Kim JH. Dyslipidemia and chronic respiratory diseases: a comprehensive review. Respir Med. 2023;204:107026. doi:10.1016/j.rmed.2022.107026. PMID: 36494213.

4.King TE Jr, Pardo A, Selman M. Idiopathic pulmonary fibrosis. Lancet. 2021;398(10302):1949–1961. doi:10.1016/S0140-6736(21)01544-6. PMID: 34798059.

5.Kinnula VL, Myllärniemi M. Oxidant-antioxidant imbalance in interstitial lung diseases. Front Med (Lausanne). 2022;9:849370. doi:10.3389/fmed.2022.849370. PMID: 35309135.

6.Lederer DJ, Martinez FJ. Idiopathic pulmonary fibrosis. N Engl J Med. 2023;388(19):1811–1823. doi:10.1056/NEJMra2300653. PMID: 37163479.

7.Libby P. Inflammation and cardiovascular disease mechanisms. Am J Pathol. 2021;191(7):1140–1151. doi:10.1016/j.ajpath.2021.04.001. PMID: 33965138.

8.Raghu G, Remy-Jardin M, Myers JL, et al. Diagnosis of idiopathic pulmonary fibrosis. An official ATS/ERS/JRS/ALAT clinical practice guideline. Am J Respir Crit Care Med. 2022;205(9):e18–e47. doi:10.1164/rccm.202202-0399ST. PMID: 35486072.

9.Saito A, Horie M, Nagase T. TGF-β signaling in lung health and disease. Int J Mol Sci. 2021;22(21):11402. doi:10.3390/ijms222111402. PMID: 34769089.

10.Semenza GL. Hypoxia-inducible factors in physiology and medicine. Cell. 2021;184(6):1508–1523. doi:10.1016/j.cell.2021.01.021. PMID: 33691108.

11.Zhao Y, Peng J, Zhang E, et al. Lipid metabolism in pulmonary fibrosis: mechanisms and therapeutic targets. Front Pharmacol. 2023;14:1178325. doi:10.3389/fphar.2023.1178325. PMID: 37124078.

O‘PKANING INTERSTITSIAL SHIKASTLANISHIDA SISTEMALI VA LOKAL METABOLIK O‘ZGARISHLAR

Materiallar va metodlar: Tadqiqot 64 ta oq zotli kalamushlarda olib borildi, ularda interstitsial o‘pka shikastlanishi surunkali tamaki tutuni ta’sirida modellashtirildi. Qon zardobi va bronxoalveolyar suyuqlikda metabolik ko‘rsatkichlar, jumladan fosfolipid fraksiyalari va lipid almashinuvi baholandi. Lipidlar Folch usuli bilan ajratilib, yupqa qatlamli xromatografiya yordamida tahlil qilindi. Barcha tajribalar xalqaro etik me’yorlarga muvofiq bajarildi.

Natija: Eksperimental interstitsial o‘pka shikastlanishi lokal va sistemali darajada yaqqol metabolik buzilishlar bilan kechdi. Bronxoalveolyar suyuqlik va qonda hujayra membranalari struktur komponentlarining kamayishi va ularning parchalanish mahsulotlarining ortishi kuzatildi, bu membrana barqarorligining buzilganligini ko‘rsatadi. Shuningdek, umumiy xolesterin, triglitseridlar va past zichlikdagi lipoproteinlar miqdorining oshishi, yuqori zichlikdagi lipoproteinlarning kamayishi bilan namoyon bo‘luvchi lipid almashinuvi buzilishlari aniqlanildi.

Xulosa: O‘pkaning interstitsial shikastlanishi lokal va sistemali metabolik buzilishlar bilan bog‘liq bo‘lib, kasallik progressiyasiga hissa qo‘shadi. Kombinatsiyalangan farmakologik korreksiya yuqori samara ko‘rsatib, istiqbolli terapevtik yondashuv hisoblanadi.

Kalit so‘zlar: interstitsial o‘pka shikastlanishi, metabolik o‘zgarishlar, bronxoalveolyar suyuqlik, lipid almashinuvi, yallig‘lanish, oksidativ stress, farmakologik korreksiya, eksperimental model.

СИСТЕМНЫЕ И ЛОКАЛЬНЫЕ МЕТАБОЛИЧЕСКИЕ ИЗМЕНЕНИЯ ПРИ ИНТЕРСТИЦИАЛЬНОМ ПОРАЖЕНИИ ЛЁГКИХ

Материалы и методы: Исследование проведено на 64 крысах с экспериментально индуцированным интерстициальным поражением лёгких путём хронического воздействия табачного дыма. Оценивали метаболические показатели в сыворотке крови и бронхоальвеолярной жидкости, включая фракции фосфолипидов и показатели липидного обмена. Экстракцию липидов проводили по методу Фолча с последующим анализом методом тонкослойной хроматографии. Все эксперименты выполнены в соответствии с международными этическими стандартами.

Результаты: Экспериментальное интерстициальное поражение лёгких сопровождалось выраженными метаболическими нарушениями как на локальном, так и на системном уровне. В бронхоальвеолярной жидкости и крови отмечалось снижение структурных компонентов мембран и увеличение продуктов их деградации, что свидетельствует о дестабилизации клеточных мембран. Одновременно выявлены выраженные нарушения липидного обмена, характеризующиеся повышением уровня общего холестерина, триглицеридов и липопротеидов низкой плотности при снижении липопротеидов высокой плотности. Фармакологическая коррекция способствовала нормализации исследуемых показателей, при этом наибольший эффект наблюдался при комбинированной терапии, когда значения приближались к показателям интактной группы.

Заключение: Интерстициальное поражение легких сопровождается взаимосвязанными локальными и системными метаболическими нарушениями, способствующими прогрессированию заболевания. Комбинированная фармакологическая коррекция оказывает выраженный нормализующий эффект и может рассматриваться как перспективный терапевтический подход.

Ключевые слова: интерстициальное поражение легких, метаболические изменения, бронхоальвеолярная жидкость, липидный обмен, воспаление, оксидативный стресс