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THE EFFECT OF REPAGLINIDE AND METFORMIN ON EXTERNAL RESPIRATORY FUNCTION IN PATIENTS WITH DIABETES AND ISCHEMIC HEART DISEASE ASSOCIATED WITH OBESITY

Saule B. Zhautikova[1], https://orcid.org/0009-0000-5712-7369

Nailya M. Urazalina[2], https://orcid.org/0000-0003-0200-1763

Diana B. Tolubayeva[3], https://orcid.org/0000-0003-3119-7814

[1] NCJSC «Karaganda Medical University», Karaganda, the Republic of Kazakhstan;
[2] NCJSC «Semey Medical University», Semey, the Republic of Kazakhstan;
[3] Medical Center Hospital of the President,s affairs Administration of the Republic of Kazakhstan, Astana, the Republic of Kazakhstan.

Abstract

Introduction: Over the past 20 years, numerous studies have examined the state of the bronchopulmonary system in type 2 diabetes mellitus (T2DM), but findings remain inconsistent. Some researchers report decreased external respiratory function (ERF) linked to metabolic shifts and disease complications, while others associate it with vascular pathology. There is also evidence of increased pulmonary ventilation in diabetes. The implementation of optimal glucose-lowering therapies to prevent complications, including pulmonary issues, remains a key concern in modern medicine.

The aim of the study is to evaluate the functional state of the external ventilation system in patients with type 2 diabetes mellitus in combination with coronary heart disease and obesity during treatment with repaglinide and metformin.

Materials and Methods: A 3–3.5-year observational study included 120 patients. The effect of repaglinide or metformin on patients with diabetes and concomitant diseases such as coronary heart disease and obesity has been studied. The data was analyzed using the following methods: computer spirometry and fiber-optic bronchoscopy.

Results: Patients with T2DM, especially those with IHD and obesity, showed both restrictive and obstructive pulmonary disorders, impaired gas exchange, and ventilation-perfusion mismatch. Repaglinide improved respiratory parameters, while metformin led to worsened spirometry indicators and increased bronchial resistance in most cases. Bronchoscopic findings confirmed nonspecific bronchial mucosal changes in 29.4% of patients.

Conclusion: Bronchopulmonary impairments in T2DM are primarily due to reduced ERF and increased bronchial resistance. Repaglinide appears more effective than metformin or gliclazide in improving respiratory function.

Keywords: *type 2 diabetes mellitus (T2DM), type 2 diabetes mellitus (T2DM) combined with obesity, functional state of external respiration, computerized spirography, repaglinide, metformin.*

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Резюме

ВЛИЯНИЕ РЕПАГЛИНИДА И МЕТФОРМИНА НА ФУНКЦИЮ ВНЕШНЕГО ДЫХАНИЯ У ПАЦИЕНТОВ С САХАРНЫМ ДИАБЕТОМ И ИШЕМИЧЕСКОЙ БОЛЕЗНЬЮ СЕРДЦА, АССОЦИИРОВАННОЙ С ОЖИРЕНИЕМ

Сауле Б. Жаутикова[1], https://orcid.org/0009-0000-5712-7369

Найля М. Уразалина[2], https://orcid.org/0000-0003-0200-1763

Диана Б. Толубаева[3], https://orcid.org/0000-0003-3119-7814

[1] НАО «Медицинский университет Караганды», г. Караганда, Республика Казахстан;
[2] НАО «Медицинский университет Семей», г. Семей, Республика Казахстан;
[3] Больница Медицинского центра Управления делами Президента Республики Казахстан, г. Астана, Республика Казахстан.

Введение: За последние 20 лет в многочисленных исследованиях изучалось состояние бронхолегочной системы при сахарном диабете 2 типа (СД2), но результаты остаются противоречивыми. Некоторые исследователи сообщают о снижении функции внешнего дыхания (ФВД), связанном с метаболическими сдвигами и осложнениями заболевания, в то время как другие связывают это с сосудистой патологией. Имеются также данные об усилении легочной вентиляции при сахарном диабете. Внедрение оптимальной сахароснижающей терапии для предотвращения осложнений, включая проблемы с легкими, остается ключевой задачей современной медицины.

Целью исследования является оценка функционального состояния системы внешней вентиляции легких у пациентов с сахарным диабетом 2 типа в сочетании с ишемической болезнью сердца и ожирением на фоне лечения репаглинидом и метформином.

Материалы и методы: В наблюдательном исследовании, продолжавшемся 3-3,5 года, приняли участие 120 пациентов. Было изучено влияние репаглинида или метформина на пациентов с сахарным диабетом и сопутствующими заболеваниями, такими как ишемическая болезнь сердца и ожирение. Полученные данные были проанализированы с использованием следующих методов: компьютерной спирометрии и волоконно-оптической бронхоскопии.

Результаты: У пациентов с СД2, особенно с ИБС и ожирением, наблюдались как рестриктивные, так и обструктивные заболевания легких, нарушение газообмена и несоответствие вентиляции и перфузии. Репаглинид улучшал показатели дыхания, в то время как метформин в большинстве случаев приводил к ухудшению показателей спирометрии и повышению бронхиального сопротивления. Результаты бронхоскопии подтвердили неспецифические изменения слизистой оболочки бронхов у 29,4% пациентов.

Заключение: Бронхолегочные нарушения при СД2 в первую очередь обусловлены снижением ФВД и повышением бронхиального сопротивления. Репаглинид, по-видимому, более эффективен в улучшении дыхательной функции, чем метформин или гликлазид.

Ключевые слова: *сахарный диабет 2 типа (СД2), сахарный диабет 2 типа (СД2) в сочетании с ожирением, функциональное состояние внешнего дыхания, компьютерная спирография, репаглинид, метформин.*

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Түйіндеме

РЕПАГЛИНИД ПЕН МЕТФОРМИННІҢ СЕМІЗДІККЕ БАЙЛАНЫСТЫ ҚАНТ ДИАБЕТІ ЖӘНЕ КОРОНАРЛЫҚ АРТЕРИЯ АУРУЛАРЫ БАР НАУҚАСТАРДА ТЫНЫС АЛУ ФУНКЦИЯСЫНА ӘСЕРІ

Сауле Б. Жаутикова[1], https://orcid.org/0009-0000-5712-7369

Найля М. Уразалина[2], https://orcid.org/0000-0003-0200-1763

Диана Б. Толубаева[3], https://orcid.org/0000-0003-3119-7814

[1] «Қарағанды медицина университеті» КЕАҚ, Қарағанды қ., Қазақстан Республикасы;
[2] «Семей медицина университеті» КЕАҚ, Семей қ., Қазақстан Республикасы;
[3] Қазақстан Республикасы Президенті Іс Басқармасының Медициналық орталығының ауруханасы, Астана қ., Қазақстан Республикасы.

Кіріспе: соңғы 20 жыл ішінде көптеген зерттеулер 2 типті қант диабетіндегі (T2DM) бронхопульмональды жүйенің жағдайын зерттеді, бірақ нәтижелер сәйкес келмейді. Кейбір зерттеушілер метаболизмнің өзгеруіне және аурудың асқынуына байланысты сыртқы тыныс алу функциясының (ERF) төмендеуі туралы хабарлайды, ал басқалары оны тамырлы патологиямен байланыстырады. Сондай-ақ қант диабеті кезінде өкпенің желдетілуінің жоғарылағаны туралы деректер бар. Асқынулардың, соның ішінде өкпе ауруларының алдын алу үшін глюкозаны төмендететін оңтайлы емдеу әдістерін енгізу қазіргі медицинаның негізгі мәселесі болып қала береді.

Зерттеудің мақсаты - репаглинид пен метформинмен емдеу кезінде жүректің ишемиялық ауруы мен семіздікпен бірге 2 типті қант диабетімен ауыратын науқастарда сыртқы желдету жүйесінің функционалдық жағдайын бағалау.

Материалдар мен әдістер: 3-3, 5 жылдық бақылау зерттеуіне 120 пациент қатысты. Репаглинидтің немесе метформиннің қант диабеті және жүректің ишемиялық ауруы және семіздік сияқты қатар жүретін аурулары бар науқастарға әсері зерттелді. Деректер келесі әдістер арқылы талданды: компьютерлік спирометрия және талшықты-оптикалық бронхоскопия.

Нәтижелер: T2DM бар емделушілерде, әсіресе ЖИА және семіздікпен ауыратын науқастарда өкпенің шектеуші және обструктивті бұзылыстары, газ алмасуының бұзылуы және желдету-перфузия сәйкессіздігі байқалды. Репаглинид тыныс алу параметрлерін жақсартты, ал метформин спирометрия көрсеткіштерінің нашарлауына және көп жағдайда бронхқа төзімділіктің жоғарылауына әкелді. Бронхоскопиялық зерттеулер пациенттердің 29,4% - ында бронхтың шырышты қабығындағы спецификалық емес өзгерістерді растады.

Қорытынды: T2DM-Дегі Бронхопульмональды бұзылулар, ең алдымен, ERF төмендеуіне және бронхқа төзімділіктің жоғарылауына байланысты. Репаглинид метформинге немесе гликлазидке қарағанда тыныс алу қызметін жақсартуда тиімдірек болып көрінеді.

Түйінді сөздер: *2 типті қант диабеті (T2DM), 2 типті қант диабеті (T2DM) семіздікпен, сыртқы тыныс алудың функционалды күйімен, компьютерленген спирографиямен, репаглинидпен, метформинмен біріктірілген.*

Дәйексөз үшін: *Жаутикова С.Б., Уразалина Н.М., Толубаева Д.Б.* Репаглинид пен метформиннің семіздікке байланысты қант диабеті және коронарлық артерия аурулары бар науқастарда тыныс алу функциясына әсері // Ғылым және Денсаулық. 2025. Т.27 (3), Б. 36-41. doi: 10.34689/SH.2025.27.3.004

Introduction

With the development of diabetes and related diseases in diabetes, the study of the effect of metabolic control on the function of external respiration is relevant. Research in this area is mixed. Some studies find a link between hyperglycemia and respiratory disorders, while others do not [11, 6]. At the same time, it is obvious that the longer a person is ill, the worse the lung indicators are: their work and structure are changing. Below are some studies that evaluate how different forms of diabetes and its stages affect the lungs.

Scientists from Denmark have found that fasting sugar levels and certain biochemical parameters (CK1 and CK2) are associated with the development of diabetes [14]. In addition, high blood sugar levels are known to cause breathing problems [4]. Every 1% reduction in blood sugar (HbA1c) reduces the risk of cardiovascular disease by 4%. At the same time, scientists have not come to a consensus on how much sugar affects the complications of diabetes.

The choice of medications for diabetes is quite wide [9, 10, 11]. Although there are clear treatment regimens [8, 12], the real quality of patient care is still not up to par [5].

The aim of the study is to evaluate the functional state of the external ventilation system in patients with type 2 diabetes mellitus in combination with coronary heart disease and obesity during treatment with repaglinide and metformin.

Materials and methods

The study, which was conducted for 3-3.5 years, involved 120 patients with type 2 diabetes mellitus with a duration of 6 years or more.

The study was conducted over a 3-year period, from May 2022 to May 2025, at Karaganda Medical University, located in Karaganda, Kazakhstan. The research protocol was approved by the university's Ethics Committee (Protocol No. 5, dated May 19, 2022). All participants provided written informed consent prior to inclusion in the study. The university administration was informed about the course of the study and did not raise any objections to the publication of its results in open access.

The average age of patients with type 2 diabetes mellitus (T2DM) was 53.74 ± 2.48 years. The mean duration of diabetes was 9.2 ± 0.61 years. In patients with T2DM combined with ischemic heart disease (IHD) and obesity, the average age was 60.1 ± 2.98 years.

Inclusion criteria:

– Age between 30 and 70 years;

– Confirmed diagnosis of T2DM;

– Ability to provide written informed consent.

Exclusion criteria:

– Acute infectious diseases;

– Severe somatic or mental disorders;

– Refusal to participate in the study.

Subject of the study: The functional state of the external respiratory (pulmonary ventilation) system in these patients during treatment with repaglinide and metformin.

For the convenience of the study, the patients were divided into two main groups. There are 60 people with type 2 diabetes in the first group. They were divided into two groups of 30 people: some were treated with repaglinide (Novonorm, Novo Nordisk, Denmark), others with metformin (Glucophage, Merck Serono, France). The second group also had diabetics (with complications), and they were also divided into 2 subgroups: repaglinide treatment and metformin treatment.

The treatment was carried out with two drugs, according to Figure 1.

Repaglinide		Metformin
a dose of 0.5; 1 or 2 mg		in tablets of 0.5, 0.85 g, 1 g
The drug is taken in a dose of 0.5; 1 or 2 mg before each meal; the daily dose is 6-10 mg, if necessary, it can be increased to 16 mg		Metformin is taken with meals, gradually increasing its dose to the therapeutic dose. Subsequently, the drug is used 3 times a day at 500 mg or 2 times a day at 850 mg

Figure 1. Dosage and Drug Information.

A good result of treatment is considered if fasting sugar is less than 7.8 mmol / l, and after eating - less than 10. After a while, HbA1c should decrease to less than 7.5%. Repaglinide helps produce insulin more naturally, is well tolerated, and allows for flexible sugar control.

Instrumental and functional research methods are used according to Table 1:

Table 1.

Instrumental and functional research methods.

Parameter	Computer spirography	Fiberoptic bronchoscopic examination of the bronchi
Method	Automated spirometric breath analyzer “AD-02”	Fiberoptic bronchoscope BF-P20 (Olympus, Japan)
Testing conditions	Morning, seated position, fasting, quiet environment	Morning, fasting, under local anesthesia
Purpose	Bronchospasm detection [11, 19]	Assessment of bronchial mucosa and inflammation severity
Classification used	According to the “Guidelines for the Use of Spirographic Indicators” (1986)	Lemoine I.M. (2002)

Results

According to the conducted research, two main results were obtained:

- People with type 2 diabetes have poorly ventilated lungs — this is due to the fact that gases do not pass well through the wall between the alveoli and capillaries.

- Patients with type 2 diabetes who also have coronary heart disease and obesity have both narrowing of the

airways and problems with lung stretching, which disrupts the supply of air and blood to the lungs.

Against the background of repaglinide treatment, there is a dynamic change in the indicators in patients with type 2 diabetes - the CTE increased by 11.5%, the CTE by 13.1%, the ventricular rate by 9.31%, the FGD50 by 11.83% and the FGD75 by 10.1%, while the Tiffno index decreased by 5.43% and the FGD75 by 23.7% ($p<0.05$). Also, there was a decrease in the indicators of the heart rate, except for the FGD and FGD50. The values are shown in Figure 2.

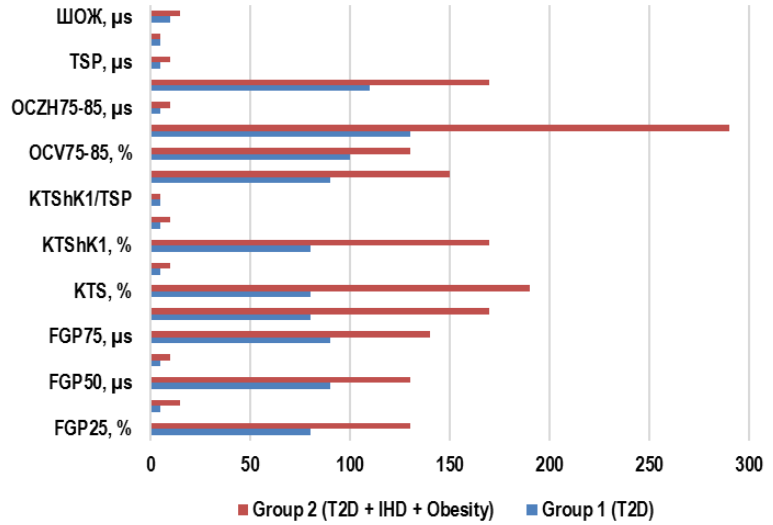

Figure 2. External Respiratory Function Parameters: Repaglinide Groups.

The following results were revealed during treatment with metformin:

- After treatment with metformin, respiratory function improved in only 2 out of 30 patients with type 2 diabetes and coronary heart disease. In the remaining 28 patients, respiratory parameters worsened, and air resistance in the bronchi increased.

- In patients with type 2 diabetes and minor changes in the lungs, there was a deterioration in air permeability in the large airways — this is seen by a decrease in exhalation volume in 1 second by 7.1%, the Tiffen index by 10%, as well as FGP25 and FGP50 by 7.04% and 10.5%. These data coincided with the results of bronchoscopy: in 29.41% of patients, nonspecific changes in the bronchial mucosa were found. The values are shown in Figure 3.

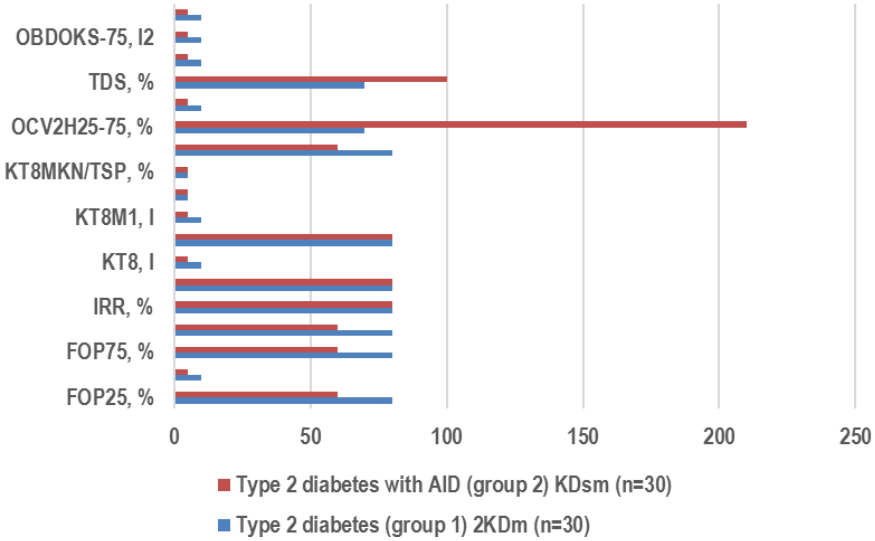

Figure 3. External Respiratory Function Parameters: Metformin Groups.

As a result of the conducted study of treatment with repaglinide and metformin, it can be said that a positive trend is observed in the treatment with repaglinide. Metformin has also effect on patients with diabetes mellitus and concomitant diseases. Central respiratory tract patency disorders were detected in all patients.

Discussion

Type 2 diabetes mellitus (T2DM) represents a rapidly growing global health challenge, increasingly recognized not only for its well-documented macro- and microvascular complications but also for its profound and often insidious impact on the respiratory system. Impaired respiratory function in T2DM patients contributes significantly to reduced quality of life, diminished exercise tolerance, and increased susceptibility to pulmonary infections and other complications. The presence of coronary heart disease (CHD) and obesity further acts as a critical aggravating circumstance, synergistically compounding the respiratory challenges faced by these individuals. The current study reinforces the growing understanding that patients with T2DM frequently exhibit restrictive alveolar

hypoventilation, a finding consistent with a burgeoning body of established literature highlighting a progressive decrease in lung diffusion capacity. This impairment is critically linked to the pathological accumulation of advanced glycation end products (AGEs) and subsequent glycosylation of basement membrane proteins within the pulmonary capillaries, leading to thickening of the alveolar-capillary barrier and impaired gas exchange efficiency [1]. Furthermore, chronic low-grade inflammation and oxidative stress, hallmarks of T2DM, contribute to interstitial fibrosis and microvascular damage in the lung parenchyma, collectively resulting in the observed ventilatory limitations and reduced pulmonary compliance.

Beyond the direct effects of diabetes, our data compellingly confirm that patients presenting with the complex triad of T2DM, CHD, and obesity demonstrate a more severe and multifaceted respiratory impairment, encompassing both restrictive and obstructive changes, alongside significantly impaired ventilation-perfusion ratios. This observation strongly aligns with recent evidence underscoring the profound pathophysiological alterations in lung tissue that arise from the intricate interplay of metabolic, inflammatory, and cardiovascular disorders [3]. Obesity, a pervasive comorbidity, contributes substantially through both mechanical and metabolic mechanisms. Mechanically, excess adipose tissue around the chest wall and abdomen leads to reduced functional residual capacity, expiratory reserve volume, and overall lung volumes, increasing the work of breathing and reducing compliance. Metabolically, adipose tissue acts as an active endocrine organ, secreting pro-inflammatory adipokines (e.g., leptin, TNF-alpha, IL-6) that can directly contribute to systemic and pulmonary inflammation, fibrosis, and impaired airway mechanics. Concurrently, coronary heart disease significantly impacts cardiorespiratory interactions. Left ventricular dysfunction and incipient heart failure, common in CHD, can lead to chronic pulmonary venous hypertension, resulting in interstitial edema, increased lung stiffness, and further impairment of gas exchange. These cardiogenic pulmonary effects often mimic or exacerbate the restrictive patterns seen in diabetes, creating a complex clinical picture where cardiac and pulmonary dysfunctions are inextricably linked. The synergistic negative effects of these comorbidities render the patient cohort particularly vulnerable to severe respiratory compromise.

A comparative analysis of hypoglycemic therapy effectiveness, central to our study's aim of evaluating the functional state of the external ventilation system in patients with type 2 diabetes mellitus in combination with coronary heart disease and obesity during treatment with repaglinide and metformin, revealed nuanced and distinct effects on spirometric parameters. Repaglinide, a short-acting insulin secretagogue, showed a positive, albeit partial, impact on bronchial patency, evidenced by increases in CTE, CTHP, FGD50, and FGD75. This observation, while promising, should be interpreted cautiously as direct, contemporary studies specifically investigating repaglinide's long-term effects on detailed respiratory function are remarkably scarce. Nevertheless, this partial improvement aligns with the known pleiotropic effects of meglitinides, including their rapid and transient insulin release, which might lead to more physiological glucose excursions, as well as their potential to positively influence microcirculation and reduce oxidative stress and inflammation [2, 7]. These mechanisms, while not primarily targeting the lungs, could theoretically contribute to improved bronchial dynamics and lung compliance, thereby accounting for the observed benefits in specific spirometric parameters. However, the "limited effect on obstructive components" suggests that while repaglinide may offer some benefit in specific aspects, it does not appear to reverse significant structural airway remodeling or long-standing obstructive pathology.

Conversely, most patients on metformin therapy exhibited a deterioration in spirometric parameters and an increase in bronchial resistance. This outcome, while seemingly counterintuitive given metformin's well-established systemic benefits in metabolic control, cardiovascular protection, and even broad anti-inflammatory properties, highlights a critical area for further investigation concerning its direct pulmonary effects in highly comorbid populations. Metformin's primary mechanism of action involves the activation of AMP-activated protein kinase (AMPK), leading to reduced hepatic glucose production and improved insulin sensitivity in peripheral tissues. While it exerts systemic anti-inflammatory and vascular protective effects, these beneficial actions may not sufficiently translate into direct, measurable improvements in macroscopic spirometric parameters in the complex setting of established lung damage from chronic T2DM, CHD, and obesity. Indeed, more recent reports have sometimes associated metformin with a neutral or even negative effect on pulmonary function in patients with a burdened medical history [1, 11, 12], suggesting its pulmonary benefits may not be as direct or universal as its systemic advantages, or perhaps its effects on some specific pathways in the lung are less favorable compared to its overall metabolic impact. This differential effect underscores the complexity of managing multi-morbid patients where general metabolic improvements do not always guarantee improvements in all organ systems.

The unique contribution and scientific novelty of this study, therefore, lie in its direct, focused comparative assessment of the long-term impact of two specific and commonly prescribed oral hypoglycemic agents – repaglinide and metformin – on detailed spirometric indicators within a carefully defined cohort burdened by T2DM and significant comorbidities like CHD and obesity. While existing research broadly discusses diabetes-related pulmonary complications, often from an epidemiological or pathophysiological standpoint, our study provides a granular, head-to-head analysis of the differential effects of these two widely used drugs on specific respiratory parameters. This allows for a deeper understanding of how repaglinide, despite its moderate overall effect, can contribute to partial improvements in bronchial patency, whereas metformin appears to have a less favorable or even negative impact on these specific pulmonary functions in this complex patient group. Our findings offer a contemporary analysis of these established therapies, providing valuable preliminary insights into personalized diabetes management strategies where pulmonary complications are a significant concern, emphasizing that not all beneficial systemic antidiabetic drugs confer similar pulmonary advantages.

Despite these important findings, the study has several limitations. The relatively small sample size and single-center design may limit the generalizability of our results. The follow-up duration, while allowing for assessment of long-term effects, might not have been sufficient to capture the full spectrum of progressive pulmonary changes or drug-induced adaptations. Furthermore, the study primarily relied on spirometric

parameters, and the absence of more advanced lung function tests (e.g., diffusing capacity for carbon monoxide - DLCO), specific imaging (e.g., HRCT scans), or mechanistic biomarkers (e.g., inflammatory markers in bronchoalveolar lavage fluid or lung tissue biopsies) precludes a deeper understanding of the underlying biological changes. Future research should address these limitations by conducting larger, multicenter randomized controlled trials with extended follow-up periods. Such studies should incorporate comprehensive pulmonary function testing, advanced imaging modalities, and biomarker analysis to elucidate the precise cellular and molecular mechanisms underlying the observed drug-specific effects on lung tissue. Additionally, investigating the impact on patient-reported outcomes, quality of life, and exercise capacity, as well as exploring other emerging antidiabetic drugs, would provide a more holistic understanding of their role in mitigating respiratory complications in T2DM patients with multiple comorbidities.

Conclusion

1. In patients with type 2 diabetes, lung dysfunction was detected, provoked by poor ventilation of the respiratory tract, leading to resistance in the bronchi. Patients in the first group suffered from a "restrictive type of hypoventilation." A process where gases pass poorly through the wall of the alveoli and capillaries, and oxygen enters the bloodstream worse.

2. The second group also had restrictive and obstructive type of respiratory disorders. In addition, the relationship between ventilation (air intake) and blood supply to the lungs was disrupted.

3. Metformin helps to improve blood sugar reduction.

4. Repaglinide, unlike other drugs, helped improve lung function. It is especially useful for type 2 diabetic patients with respiratory disorders.

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Literature:

1. *Deng Y., et al.* Effects of metformin on respiratory diseases: Current evidence and future perspectives. Frontiers in Pharmacology, 2022. 13, 856711. (DOI: 10.3389/fphar.2022.856711)

2. *Kalra S., Gupta Y., Kumar A.* Repaglinide: An Overview. Journal of the Association of Physicians of India, 2015. 63(4), 60–63.

3. *Kim H.L., et al.* Impact of obesity and metabolic syndrome on respiratory function: A narrative review. Journal of Obesity & Metabolic Syndrome, 2021. 30(2), 101–110. DOI: 10.7570/joms.2021.30.2.101

4. *Kostovski M., Simeonovski V., Mironska K., Tasic V., Gucev Z.* Metabolic Profiles in Obese Children and Adolescents with Insulin Resistanceю. Open Access Maced J Med Sci. 2018. 15. 6(3):511-518 https://oamjms.eu/index.php/mjms/article/view/oamjms.

5. *Król E., Rutkowski B.* Influence of Metformin on Pulmonary Function in Diabetic Patients. Polish Archives of Internal Medicine, 2015. 125(3), 182–189.

6. *Kolahian S., Leiss V., Nürnberg B.* Diabetic lung disease: fact or fiction? Rev Endocr Metab Disord. 2019 Sep. 20(3):303-319. doi: 10.1007/s11154-019-09516-w. PMID: 31637580; PMCID: PMC7102037.

7. *Lee J.S., et al.* The pleiotropic effects of meglitinides in cardiovascular and renal protection. International Journal of Molecular Sciences, 2020. 21(11), 3845. (DOI: 10.3390/ijms21113845)

8. *Long C., Fan W., Liu Y., Hong K.* Stress hyperglycemia is associated with poor outcome in critically ill patients with pulmonary hypertension. Front Endocrinol (Lausanne). 2024 Feb 23;15:1302537. doi: 10.3389/fendo.2024.1302537. PMID: 38464971; PMCID: PMC10924302.

9. *Li M., Chi X., Wang Y. et al.* Trends in insulin resistance: insights into mechanisms and therapeutic strategy. Sig Transduct Target Ther. 2022. 7, 216. https://doi.org/10.1038/s41392-022-01073-0

10. *Li W., Ning Y., Ma Y. et al.* Association of lung function and blood glucose level: a 10-year study in China. BMC Pulm Med. 2022. 22, 444 https://doi.org/10.1186/s12890-022-022

11. *Suleman S., Madsen A.L., Ängquist L.H., Schubert M., Linneberg A., Loos R.J.F., Hansen T., Grarup N.* Genetic Underpinnings of Fasting and Oral Glucose-stimulated Based Insulin Sensitivity Indices. J Clin Endocrinol Metab. 2024 Oct 15;109(11):2754-2763. doi: 10.1210/clinem/dgae275. PMID: 38635292; PMCID: PMC11479690.

12. *Sharma A., Müller K., Zhang Y., Ivanov D.* A comprehensive review on diabetic cardiomyopathy: Pathophysiology, imaging assessment and potential metabolic-targeted strategies. European Journal of Endocrinology, 2025. 192(6), R127–R150. https://doi.org/10.1530/EJE-25-0147

13. *Peng Y., Zhong GC., Wang, L. et al.* Chronic obstructive pulmonary disease, lung function and risk of type 2 diabetes: a systematic review and meta-analysis of cohort studies. BMC Pulm Med. 2020. 20, 137. https://doi.org/10.1186/s12890-020-1178-y

14. *Zhao Y., et al.* Mechanisms of impaired lung function in diabetes mellitus: An updated review. Frontiers in Physiology, 2022. 13, 856711. (DOI: 10.3389/fphys.2022.856711)

Information about the authors:

Urazalina Nailya - Candidate of Medical Sciences, Associate Professor of the Department of physiological disciplines named after honored scientist of the republic of Kazakhstan, professor T.A. Nazarova, NJSC "Semey Medical University", Semey, Kazakhstan; phone: 8 777 907 55 89, e-mail: hakim_15@mail.ru, https://orcid.org/0000-0003-0200-1763,

Tolubayeva Diana - Doctor *PhD "Medical Center Hospital of the President affairs Administration of the Republic of Kazakhstan" Astana,* https://orcid.org/0000-0003-3119-7814; e-mail: dianajianna@gmail.com; Cell phone +7 701 299 34 06.

***Corresponding author:**

Zhautikova Saule - Professor of the Department of Physiology of NJSC «Karaganda Medical University», https://orcid.org/0009-0000-5712-7369; Karaganda, Kazakhstan.

Address: Gogol str. 40, Karaganda 100000, Kazakhstan.

e-mail: Zhautikova@qmu.kz;

Cell phone +7 701 299 34 07