LIPID AND CARBOHYDRATE METABOLITES CHANGES IN EXHALED BREATH CONDENSATE AND BLOOD IN ACUTE EXACERBATION OF CHRONIC BRONCHITIS AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Abstract

Exhaled breath condensate (EBC) reflects the polyfunctionality of the lungs, the intensity and shifts of metabolic reactions.

The aim was to investigate the changes of some lipid and carbohydrate intermediate metabolites as well enzymes as both in EBC and blood in acute exacerbation of chronic bronchitis (AECB) and chronic obstructive pulmonary disease (AECOPD).

Methods: EBC was collected from in-patients with CB (n=12) and mild-moderate-severe COPD ($COPD_{1-2,3}$ — respectively) (n=49). We detected both in EBC and blood: total lipids (TL), phospholipids (TPhL) and cholesterol (TCL); free cholesterol (FCL) and etheric cholesterol (ECL), triglycerides (TG), free fatty acids (FFA), NH_3, lactic acid (LA); activity of pyruvate kinase (PK) and adenylate kinase (AK), pyruvic (PvA), succinic (ScA) and oxaloacetic acids (OaA) as well as EBC surface-active properties (SAP).

Results. Exhaled TL (eTL) were increased in CB, $COPD_{1,2}$ vs. the control and then were decreased in $COPD_3$ up to the control value. eTG were increased in $COPD_{2,3}$ by 18% vs. the control while eFFA were reduced in $COPD_{1,2,3}$ by 19% vs. the control. eTPhL were significantly enhanced in all groups without difference between them. SAP was significantly decreased in CB, $COPD_{1,2}$ but more in COPD3 (by 50% vs. the control). NH_3 level was significantly elevated both in EBC and blood vs. the control, but without difference between the groups. ScA in $COPD_{1,2}$ both in EBC and blood exceeded the control more than 5 times while AK activity in EBC and blood was significantly reduced (by 1,3 times) in mixed $COPD_{1,2}$ group.

Conclusions: The changes of these metabolites and enzymes occurred more in EBC and less in blood plus did not correlate with COPD severity (excluding SAP).

Keywords

Exhaled breath condensate, lipids, carbohydrates, surface-active properties, COPD.

Breath analysis is a non-invasive research procedure, which may provide specific information about pulmonary status and plays an important role in the diagnosis and management of lung diseases that makes exhaled breath condensate (EBC) attractive for clinicians. The exact site of origin of substances measured in EBC is unknown. Exhaled air in the form of droplets is converted to EBC [1-3] that contains aerosolized particles from airways lining fluid (ALF), including various non-volatile and over 200 volatile water-soluble compounds which can be measured from the cooled and condensed exhalant [4-6]. Molecules in EBC are due to bronchial and/or alveolar aerosols and evaporation from the epithelial surface airways. There are evidences [7-10] that changes in EBC content reflect biochemical and inflammatory processes in the respiratory tract pathology and help to gain insight into the composition of extracellular lining fluid and soluble exhaled gases [11-15]. Non-volatile substances present in the condensate arrive in respiratory droplets, whereas volatile solutes may be delivered in both respiratory droplets and in the gas phase of the exhaled air. The factors that determine the number and size of aerosol particles formed may include: ALF surface tension, distal airway surfactant (SRF) function, the velocity and humidity of inhaled air as well as airways anatomy and their caliber.

The studies [9] showed the presence a macromolecule in EBC, including proteins, oxidants, nucleotides, ions and a large number of mediators: adenosine, hydrogen peroxide, isoprostanes, prostaglandins (Pg), leukotriene and nitrogen oxides. These macromolecules may present a biomarkers of pathological process in COPD. The origin of these molecules which are determined in the EBC is different. It may be initially localized in the oral cavity and pharynx, tracheobronchial system and alveoli. Their proportional contribution to the level of a compound measured in EBC has not been sufficiently investigated. It is believed that main nonvolatile components of this fluid are the metabolic products of cells form the ALF.

We did not reveal the reports analyzing lipid and carbohydrate metabolites as well as enzymes changes both in EBC and blood in acute exacerbation of chronic bronchitis (AECB) and chronic obstructive pulmonary disease (AECOPD).

The aim of this study was to reveal some possible markers of non-respiratory (metabolic) lung dysfunction as well as to investigate the effect of AECOPD severity (the degree of airways limitation and exacerbation) on these metabolites and enzymes changes.

Material and methods

Clinical data of 15 healthy subjects and 12 patients with AECB as well as 49 AECOPD patients with different degree of severity in detail are summarized in Table 1. So, the purpose of CB examination (as the frequent prestage of COPD while without registration of airways obstruction) was to identify the effects of hypoxia in COPD on some studied EBC parameters. All COPD patients had three major symptoms of exacerbation (increased dyspnea, sputum volume and its purulence according to the Anthoninsen et al. criteria) within previous 1 week as well as airways obstruction with FEV_1<80% predicted and FEV_1/FVC ratio <0.7, which did not change marked over 3 months as well as was no spirometric response to bronchodilator. Post-bronchodilation spirometry was performed at the first day on hospital admission and before start to treatment.

As shown in Table 1, the control group (with normal pulmonary function) did not differ from CB and $COPD_1$ patients in terms of mean age, BMI and intensity of smoking. Compared with the control and CB, COPD1 patients had only decreased ventilation parameters, while COPD3 patients had a significantly lower BMI and a parameters of spirometry vs. $COPD_{1-2}$ groups. A significant increase in the number of exacerbations for the past year was found also in $COPD_3$ as compared with $COPD_{1,2}$. A higher CRP level in $COPD_{2,3}$ (p<0.05 vs. the control, CB and $COPD_1$) was reflected the intensification of low-grade systemic inflammation.

The ambulatory treatment usually included inhaled or nebulized ipratropium bromide and salbutamol as well as sometimes long active β_2-agonists. $COPD_1$ patients had never used systemic steroids (sCS) and inhaled steroids (ICS). Only 34% and 46% of $COPD_{2,3}$ patients respectively had the past history of intermittent ICS use in small or moderate doses of (usually 200-400 μg/day in terms of bydesonide), mostly with never prescribed sCS.

Inclusion criteria for study participants were the following: clinician-made diagnosis for ≥12 months of CB (no obstructive) as well as COPD (the presence of chronic progressive symptoms such as dyspnea, cough and wheeze) supported by spirometry evidence of fixed airflow limitation recorded at any time on maintenance therapy with bronchodilators and at least 2 episodes of CB or COPD exacerbations in the past two years requiring treatment with antibiotic. The participant excluded from the study if they had: existing comorbidities that complicated performing spirometry or that would its

Table 1. Baseline characteristics of patients on admission (X±SD)

Parameters	Control (n=15)	CB (n=12)	$COPD_1$ (n=24)	$COPD_2$ (n=12)	$COPD_3$ (n=13)
Mean age (years): males (%)	44±6 67	38±9 60	48±8 67	50±5* 83	54±5*,**,Δ, 86
Body mass index (kg/m²)	26.0±3.4	26.6±4.6	27.0±4.2	29.8±4.3*	24.5±5.0 **, Δ
Present smokers (%)	67	58	68	88	95**
Smoking history (packs/years)	6,6±4,0	7.7±4.6	14.2±9.0*,**	19.1±10.0*,**	32.6±9.4*,**,Δ
Mean duration of disease (years)	–	6±3	8±4	13±6*,**	13±9*,**
Number of exacerbations in the last year	–	2.0±0.9	2.5±1.0	2.8±1.0**	3.4±1.1**,***
post FVC (% pred.)	101±11	96±13	86±14*,**	56±13*,**,***	45±9*,**,***,Δ
post FEV_1 (% pred.)	88±16	76±12*	66±5*,**	45±6*,**,***	34±8*,**,***,Δ
post FEV_1/FVC	0.80±0.08	0.74±0.11	0.68±0.08*	0.46±0.07*,**,***	0.40±0.10*,**,***
C-reactive protein (% of positive reaction)	–	32	35	36	70**,***,Δ
Home therapy: inhaled steroids, oral steroids, inhaled long active anticholinergic or β_2-agonists	– – –	no no no	no no 20/24	2/12 no all	10/13 no all

** — p<0.05 vs the control; ** — p<0.05 vs CB; *** — p<0.05 vs $COPD_1$; Δ — p<0.05 vs $COPD_2$.*

confound; known other diseases (pneumonia; active pulmonary malignancies; gastro-esophageal reflux; hepatic, renal, vascular, neuromuscular and cardiac pathology as well as alcoholism). Chest radiography was carried out to all patients for excluding other diseases.

The control group was recruited from hospital staff and included fifteen healthy volunteers of comparable age, sex and smoking status with the observed patients. They were free from chronic respiratory symptoms, did not receive any regular medication and had normal spirometry values. The study was approved by the Belarusian State Medical University ethics committee and all patients gave their written informed consent.

The design of the collection method was based on the recommendations be ATS/ERS task force on EBC. Nose clips were not used during EBC sampling due to possible discomfort in COPD patients. EBC was collected in the morning (between 800 and 900) on the first-second day on admission to the clinic while the patient was breathing room air at constant room temperature and before clinical treatment, smoking as well as drinks or foods intake during the one hour before collection of EBC. After mouth rinsing (with distilled water and sodium bicarbonate 4%) subjects in sitting pose breathed tidally at a normal frequency for 15 minutes through glass tube. If the patients felt saliva in their mouth they were instructed to rinse their mouth again or swallow accumulated saliva when it was possible. Samples were excluded if gastric air was expelled during collection as well as if the positive result was detected by testing for salivary amylase. So, it was excluded only a two patients due to the presence of amylase in the condensate.

We use a specially designed glass tube [16] that was placed in condensing chamber that contained a double wall and was fell up by ice and cold water. Ambient air has not contacted with contents of condenser. So, glass tube was cooled by ice and cold water in this chamber and condensation was achieved at temperature ~40C. Approximately 5 ml of EBC was collected in a cold trap device. At the end of the collection, the tube was removed from the container and EBC was transferred to 5 ml sterile polypropylene tubes and immediately frozen. Then EBC stored at –200C until assay. Measurements were usually performed within 10 days of collection.

The total lipids (TL) content both in blood serum and EBC was detected according to P. Falch et al. [17]. Blood lipid's fractions were examined by thin layer chromatography on silica gel («Lachema», Czech). Separation of neutral lipids into the fractions was also carried out by the method of ascending thin layer chromatography on silica gel («Lachema»). The content of total phospholipids (TPhL) both in EBC and blood was determined according to W. Morison [18]. The color reaction of Lieberman-Burkhart was taken as the base for the quantitative determination of total cholesterol (TCL), free cholesterol (FCL) and etheric cholesterol (ECL). FCL and ECL fractions were preliminary isolated by thin-layer chromatography. Triglycerides (TG) in the blood were determined by using the «Lachema» kits while the level of unesterified fatty acids (FA) by the method of W. Duncobe [19]. According to the methods of S. Bestuzheva [20, 21] we detected: the surface-active properties (SAP) of EBC, the content of ammonia (NH3); intensity of glycolysis by the levels of lactic acid (LA), activity of pyruvic acid (PvA) and pyruvate kinase (PK); substrates of Krebs cycle — succinic acid (ScA) and oxaloacetic acid (OaA) as well as the percentage ratio of individual lipid's fractions both in EBC and serum. The blood sample collection was carried out in the morning on the second day of hospitalization. We chose this panel of lipid and carbohydrate metabolites as well as enzymes because we supposed that it could help to reveal a possible markers of metabolic lung dysfunction in AECOPD.

Statistical analysis. Levels of studied biochemical parameters in EBC and blood showed a normal distribution. Data are presented as mean ±SD. The relationships between variables are expressed as Spearman rank correlation coefficient (rs). To test for statistical differences between mean values t-test was used when appropriate. A p-value less than 0.05 was considered significant.

Results

It was revealed increase of mean level of exhaled TL (eTL) in CB, $COPD_{1,2}$ with subsequent decrease in COPD3 about up to the control value (Table 2). eTG was significantly elevated only in $COPD_{2,3}$ vs. the control. The level of exhaled free FA (eFFA) was decreased ($p<0.05$ vs. the control) in $COPD_{1,2,3}$ without difference between these groups. eFCL concentration did not change in all groups vs. the control. eTPhL level was increased in CB and $COPD_{1,2}$ vs. the control and then was decreased up to the control in $COPD_3$. So, we do not reveal a significant correlation between different EBC lipid's fractions and COPD severity. There was an increase of eNH3 level in all groups as compared with the control, but without difference between these groups. We revealed that SAP level was significantly decreased vs. the control in CB, in mixed $COPD_{1,2}$ group and more in $COPD_3$.

As seen in Table 3, mean TL and ECL levels in blood were significantly decreased only in $COPD_3$ vs. the control and CB. There was increase of blood NH3 level in all groups vs. the control, but without difference between these groups. The analysis showed that ePvA concentration was higher

(by 2.5 times; p<0.05) vs. the control in the mixed COPD group (9 patients with $COPD_{1,2}$ and 3 — with $COPD_3$). PvA blood level did not differ significantly from the control in the mixed COPD group (19 with $COPD_{1,2}$ and 5 with $COPD_3$). LA blood level in the mixed COPD group (21 with $COPD_{1,2}$ and 10 with $COPD_3$) was higher than in the control group (3.06+0.76 mM/L vs. 1.75+0.36 mM/L respectively; p<0.05). eLA concentration in the mixed COPD group (9 with $COPD_{1,2}$ and 3 with $COPD_3$) was close to the control values. OaA levels in $COPD_{1,2}$ patients also did not differ from the control both in EBC (n=12) and blood (n=22). eScA in patients with COPD1,2 (n=12) significantly exceeded the control values (0.048±0.014 and 0.010± 0.003 mM/L respectively). ScA blood concentration in mixed COPD group (21 patients with $COPD_{1,2}$ and 5 — with $COPD_3$) was also higher as compared with the control (0.42±0.17 and 0.06±0.02 mM/L respectively; p<0.05). eAK activity was significantly reduced (by 1.3 times) in mixed COPD group (12 patients with $COPD_{1,2}$ and 4 with $COPD_3$) vs. the control. We detected a similar significant AK decrease (by 32%) in the blood of 12 patients with $COPD_{1,2}$. PK activity in EBC and blood was not significantly differed from the values in the control. We noted a significant increase of ePgF2a level only in $COPD_3$ (p<0.05 vs. the control and CB).

Discussion

The results of our study suggest that changes of above mentioned intermediated metabolites and enzymes in EBC and blood both in AECB and AECOPD might reflect the extra/intra cellular metabolic abnormalities. Well known that lung use FA as bioenergy substrate. It was detected the increase of eFFA and eTG only in $COPD_{2,3}$. We did not reveal that levels of eFFA and eFCL were correlated with COPD severity. It can suppose that elevation of FFA provided the cells with additional energy in condition of chronic hypoxia in AECOPD. One of the reasons for lipids changes in EBC may be an intensification of lipid peroxidation processes and decrease activity of lung tissue enzymes in COPD [22]. It should be noted that FCL level was directly correlated between blood and EBC (p=0.73; p<0.05) but only in the control and then this association was lost during COPD development.

Our study demonstrated a local overproduction of some EBC lipids fractions (TL, TG, TPhL) during AECOPD, except $COPD_3$ in which eTL was less than in CB and $COPD_{1,2}$. A decrease of eTL level in $COPD_3$ was correlated with a significant SAP decrease. It can be assumed that changes in the level of these lipid's components in EBC and blood was caused by high energy expenditure (particularly due to increasing the work of breathing) in advanced COPD and with the fact that a significant part of the lipids is used to compensate for the increased expenditure of SRF. Our data support the fact that the lung plays an important role in the regulation of lipid metabolism. So, its disturbances in COPD resulting in SAP decreases and pulmonary failure progression. The consequence of it was an increased excretion of structural elements with vapors of exhaled air.

It can be assumed that growing EBC levels of TL, TG and TPhL was associated with elevated their «dumping» from the alveoli and bronchioles surface due to lung parenchyma destructive proces-

Table 2. Changes of EBC lipid metabolites and other parameters in the course of COPD development (X±SD)

Parameter	TL (g/L)	TG (%)	FFA (%)	FCL (%)	TPhL (mMp/L)	NH_3 (mmol/L)	SAP (%)	PgF_{2a} (pg/mL)
Control (n=15)	0.13±0.04	13.7±2.6	15.5±3.5	36.5±4.0	0.17±0.06	0.49±0.16	30.2±4.3	41.2±12.6 n=10
CB (n=12)	0.32±0.11*	14.1±3.1	14.8±4.0	39.7±4.2	0.29+0.09*	0.85±0.30*	19.8±5.7*	44.0±13.5 n=10
$COPD_1$ (n=24)	0.26±0.08*	14.5±3.2	12.0±2.6*	38.4±3.5	0.23+0.08*	0.95±0.34*	19.0±5.8* Σ n=15	47.5±12.0 Σ n=14
$COPD_2$ (n=12)	0.27±0.10*	16.1±1.4*	12.3±2.4*	37.5±4.3	0.24+0.07*	1.18±0.29*		
$COPD_3$ (n=13)	0.16±0.06**,***,Δ	16.0±3.0*	12.6±4.2*	37.2±5.4	0.18+0.06**,***,Δ	0.81±0.21*	15.1±4.6*	50.6±14.1*,** n=9

** — p<0,05 vs. the control; ** — p<0.05 vs. CB; *** — p<0.05 vs $COPD_1$; Δ — p<0.05 vs. $COPD_2$.*

Table 3. Changes of blood lipid metabolites and ammonia in the course of COPD development (X±SD)

Parameter	TL (g/L)	TG (mmol/L)	FFA (mEq/L)	TCL (g/L)	FCL (g/L)	ECL (g/L)	TPhL (mMp/L)	NH_3 (mmol/L)
Control (n=15)	5.0±1.12	1.33±0.41	0.18±0.06	5.0±0.31	0.59±0.11	1.47±0.26	3.0±0.68	1.18±0.38
CB (n=12)	5.20±1.48	1.56±0.55	0.22±0.07	5.31±0.52	0.66±0.20	1.64±0.31	3.45±0.80	2.17±0.70*
$COPD_1$ (n=24)	4.89±1.30	1.46±0.43	0.20±0.06	4.90±0.40	0.53±0.17	1.37±0.35	3.06±0.51	2.0±0.81*
$COPD_2$ (n=12)	4.56±1.37	1.32±0.52	0.19±0.02	4.80±0.45	0.47±0.13	1.35±0.29	2.98±0.60	2.52±0.92*
$COPD_3$ (n=13)	4.20±0.90*,**	1.32±0.59	0.22±0.07	4.69±0.48	0.48±0.11	1.22±0.27*,**	2.93±0.41	2.3±0.95*

** — p<0.05 vs control; ** — p<0.05 vs. CB.*

ses in AECOPD. Probably, volatile substances from the lower respiratory tract can be transported in the form of aerosols into EBC and that airways are more important source of exhale substrates than alveoli in COPD [4, 5]. However, the mechanisms and site of EBC particle formation are not clear understood jet.

Moderate disorders of lipid and phospholipid spectrum in EBC might be the result of complex action of unfavorable factors such as: chronic hypoxia, amplified inflammation and endogenous intoxication, impaired absorption of phospholipid hydrolysis products in intestine and a decrease of their synthesis in the liver as well as intensification of lipid peroxidation, peptidase and phospholipase activity [23, 24]. The production of respiratory droplets in COPD may variably depend on local turbulence (audible as rales or rhonchi) which tends to occur in the large airways and consequently less predictable.

We detected the increase of ScA (both in EBC and blood) and ePvA levels as well as blood LA in AECOPD. It was indicated increasing anaerobic processes of energy production in the condition of chronic hypoxia against the background of excessive working the respiratory muscle. Additionally, functioning the Krebs cycle becomes difficult (due to small oxygen consumption for oxidative processes) and followed a decrease of energy production as well as activation of the anaerobic pathways (primarily glycolysis) in AECOPD.

The elevation of ePvA concentration could also be explained by changing the permeability of the alveolar membranes and by the worsen consumption of PvA in Krebs cycle. A revealed change of ScA and PvA in EBC may be considered as indicators of existing adaptive metabolic lung disorders in AECOPD. So, a significant increase of ScA level (both in EBC and blood) was indicated the development of body oxygen starvation. It could be associated with increasing ScA synthesis, activation a fumarate-reductase reactions or with decreasing ScA utilization [25]. Additionally, a decrease AK activity both in EBC and blood could indicate a decrease of AMP and ADP phosphorylation. Thus, our data indicated that the aerobic-anaerobic relationships were disordered in AECOPD.

NH_3 as a volatile compound of EBC (mostly appearance due to catalytic degradation of urea in the mouth and airways) which is delivered to the condenser as gas [26, 27]. eNH_3 exceeded of the control value in CB and all COPD groups, but without the differences between them. Given that COPD patients have a high incidence of acid reflux [28, 29], this pathway for EBC acidification needs to be kept in mind. A several factors could be responsible for changing the eNH3 concentration. So, drying of the mouth secondary to action of some factors (such as hyperventilation, catecholamine release and medication) reduces oral NH_3 production while the presence of CO_2 in EBC enhances trapping of NH3 in the condensate [30]. It was detected that EBC are acidified during AECOPD that could suggest that it reflected excess acid production in the airways due to intensification of inflammation [31-33]. In conditions of acidosis (which is often in AECOPD), the amount of non-ionized NH3 (passing to EBC through the membranes) increases. We revealed that the expiration of NH_3 in EBC increases significantly in CB and $COPD_{1,2}$ while then eNH3 level was decreased slightly in COPD3. Such eNH3 elevation was associated with changing a metabolic process, which consists in stimulating the removal of excessed amounts of toxic ammonia from the lung parenchyma. A slight decrease of eNH_3 in $COPD_3$ was probably associated with its higher consumption for the neutralization of acid metabolites and for normalization the SRF synthesis. The blood NH3 concentration was also significantly exceeded the control values in CB and all COPD groups. This combination of elevated both blood and eNH3 levels in AECOPD was associated with impaired lung excretory function and indicated an elevated catabolism of proteins which was often correlated with BMI decrease in COPD3 patients. The correlation analysis did not reveal the associations between NH_3 level in blood and EBC. Our result contradicts the data of some authors [34, 35] who showed a decrease of eNH_3 level in COPD. Different methodology and different disease severity may explain this difference. Father investigation including a larger group of COPD patients with different illness severity are needed to clarify these discrepancies. Furthermore, because a considerable part of eNH_3 arises from the mouth, this observation should be taken into account when considering ammonia as a biomarker of COPD.

The analysis showed that eSAP was decreased as COPD progressed. It could be due to the following numerous factors: bronchial obstruction and followed local tissue hypoxia as well as disorders of pulmonary microcirculation, permeability of capillary wall, lipid supply of SRF biosynthesis and its spent removing through the respiratory tract; the action of the metabolic products of some microbes and activation of peroxidation and small bronchi intraluminal release of bioactive substances [36, 37]. eSAP significant reduction in advanced COPD against the background of not decreased eThL and eTL level was not illogicality. Probably, a fractional SRF composition was changed in AECOPD due to increasing the concentration of phospholipid fractions with low surface-active properties [38].

Oxidative stress is a major component of airway inflammation in AECOPD. Therefore, lipid peroxi-

dation appears to be the main mechanism for the larger PgF_{2a} formation in COPD. So, we as the other researchers [1, 9, 39] revealed a significantly higher concentration of $ePgF_{2a}$ in $COPD_3$, suggesting a higher level of oxidative stress and a greater lung injury at this advanced stage. Probably, the high concentration of EBC PgF_{2a} in $COPD_3$ allows to consider that inactivation of some biologic active substances goes not only by enzymatic splitting, but also by their secretion in the process of breathing.

There are some limitations in this study**.** So, the relative small size of COPD groups, not age-matched moderate-to-severe COPD groups with the control as well as estimation of these metabolites and enzymes in mixed groups (without their stratification according to COPD severity) made it difficult to compare EBC biologic parameters. It was also possible that there were some errors in the measurement of low these intermediated metabolites and enzymes concentration in EBC because of using the non-concentrated samples with very low values (that were near their detection limits) as well as these samples had a high variability of concentrations.

The lack of the correlation between the studied metabolites as well as enzymes in EBC and lung function tests could be due to different pathophysiological relevance of it and may be attributed to confounding factors (such as smoking or ICS use). So, there are also some evidences [40, 41] indicating that COPD patients treated with ICS may have values of some biomarkers lower than those of steroid native patients.

A number of questions remain to be answered, including the reason for the variability of these EBC intermediated metabolites and potential of their determination in clinical routine. So, the exact composition of airway surface fluids in the respiratory tract is still debated. The air that we exhale is saturated with water vapor and also contains significant numbers of small droplets of salty fluid. These droplets are believed to be generated by high velocity air flow, which creates shear forces that overcome the adhesion of the fluid to airflow surfaces, such events are much more likely to occur in AECOPD with remodeled airways due to chronic inflammation.

Not always unambiguous relationships of the individual indicators studied in EBC and blood made it difficult to interpret. Probably, to a certain extent it was due to the fact that metabolites from the functioning alveoli enter the EBC, but «non-working» alveoli are not considered. The independent role of the lungs in the metabolism of studied parameters in AECOPD was confirmed by the fact that changes in the content of these compounds in the blood did not clearly correlate with their EBC dynamics. Our data indicated a restructuring the oxidation-reduction reactions in COPD development aimed on providing the production of macroergic substrates in condition of significant decline in ventilator reserves, hypoxia and hypoxemia.

Conclusions

The changes of studied lipid and carbohydrate metabolites as well as enzymes were occurred more in EBC and less in blood in AECOPD and did not correlate with its severity (excluding SAP). Our «metabolic approach» to research these metabolites and enzymes both in EBC and blood may help to understand the internal changes of the lungs, the little-known aspects of pulmonary excretory function and pathophysiological mechanisms in COPD.

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ИЗМЕНЕНИЯ УРОВНЕЙ ЛИПИДНЫХ И УГЛЕВОДНЫХ МЕТАБОЛИТОВ В КОНДЕНСАТЕ ВЫДЫХАЕМОГО ВОЗДУХА И КРОВИ ПРИ ОБОСТРЕНИИ ХРОНИЧЕСКОГО БРОНХИТА И ХРОНИЧЕСКОЙ ОБСТРУКТИВНОЙ БОЛЕЗНИ ЛЕГКИХ

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Резюме. Конденсат выдыхаемого воздуха (КВВ) отражает полифункциональность легких, а также интенсивность и нарушения метаболических реакций.

Цель исследования — изучить изменения ряда промежуточных липидных и углеводных метаболитов, а также ферментов в КВВ и крови у пациентов с обострением хронического бронхита (ХБ) и хронической обструктивной болезни легких (ХОБЛ).

Материал и методы. КВВ собирался у 12 здоровых добровольцев, 12 пациентов с ХБ и 49 — с легкой-умеренной и тяжелой ХОБЛ (ХОБЛ$_{1,2,3}$ соответственно). Мы изучали в КВВ и крови содержание: общих липидов (ОЛ) и фосфолипидов (ОФЛ), свободного холестерола (СвХ) и эфиров холестерола (ЭХ), триглицеридов (ТГ), свободных жирных кислот (СЖК), аммиака (NH_3), молочной (МК), пировиноградной (ПВК), янтарной (ЯК) и щавелево-уксусной (ЩУК) кислот, активность пируват-киназы (ПК) и аденилат-киназы (АК), а также поверхностно-активные свойства КВВ (ПАС).

Результаты. Уровень ОЛ в КВВ был повышен при ХБ и ХОБЛ$_{1,2}$ при сравнении с контролем, а при ХОБЛ$_3$ снижался до контрольных величин. ТГ в КВВ статистически значимо повышались при ХОБЛ$_{1,2}$ на 18% по сравнению с контролем, а СЖК снижались при ХОБЛ$_{1,2,3}$ на 19% относительно контроля. Содержание ОФЛ и аммиака в КВВ было повышено во всех исследуемых группах пациентов без существенной разницы между ними. ЯК в КВВ и крови превысила контроль почти в 5 раз, тогда как активность АК в КВВ и крови была снижена в 1,3 раза по сравнению с контролем.

Выводы. Изменения вышеназванных метаболитов и ферментов чаще выявлялись в КВВ и реже в крови и прямо не коррелировали со степенью тяжести ХОБЛ (исключая динамику ПАС).

Ключевые слова: конденсат выдыхаемого воздуха, липиды, углеводы, поверхностно-активные свойства, ХОБЛ.