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ДИАГНОСТИКА И КЛИНИЧЕСКОЕ ЗНАЧЕНИЕ «СКРЫТЫХ» СПЕКТРАЛЬНЫХ НАРУШЕНИЙ ОКСИГЕНАЦИИ КРОВИ У КУРИЛЬЩИКОВ С ОБОСТРЕНИЕМ БРОНХИАЛЬНОЙ АСТМЫ

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Diagnosis and Clinical Significance of «Hidden» Spectral Disorders of Blood Oxygenation Among Smokers with Exacerbation of Bronchial Asthma

Резюме

Цель — выявить и оценить клиническое значение «скрытых» нарушений оксигенации крови у курильщиков с обострением бронхиальной астмы. **Материалы и методы.** Обследовано 19 курильщиков(средний возраст 54,6±2,05 лет) с обострением смешанной (68 %) или аллергической (32 %) бронхиальной астмы. Пациентам проводились: спирометрия, пульсоксиметрия, СО-метрия выдыхаемого воздуха. **Результаты:** точность клинической оценки оксигенации крови у курильщиков с обострением бронхиальной астмы существенно возросла после коррекции уровня оксигемоглобина (SpO_2) на карбоксигемоглобин (HbCO)с помощью разработанной оригинальной программы ЭВМ, что позволило у пациентов с бронхиальной астмой своевременно диагностировать жизнеугрожающее обострение данного заболевания за счёт выявления «скрытой» дыхательной недостаточности.

Ключевые слова: *табакокурение, «скрытые» спектральные нарушения оксигенации крови, дыхательная недостаточность*

Конфликт интересов

Авторы заявляют, что данная работа, её тема, предмет и содержание не затрагивают конкурирующих интересов

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Abstract

The purpose of the study — to identify and evaluate the clinical significance of "hidden" disorders of blood oxygenation in smokers with exacerbation of bronchial asthma. **Materials and methods:** spirometry, pulse oximetry, CO-metry of exhaled air. To diagnose "hidden" disorders of blood oxygenation, including "hidden" violations of the spectral characteristics of the level of hemoglobin oxygen saturation, 19 male smokers (middle age 54,6±2,05 years) with exacerbation of mixed (68 %) or allergic (32 %) bronchial asthma were examined. **The results:** the accuracy of the clinical assessment of blood oxygenation in smokers increased significantly after the correction of the SpO_2 level to the level of carboxyhemoglobin with the help of a computer program developed by us, which made it possible to diagnose a clinically significant life-threatening exacerbation of this disease in smoking patients with bronchial asthma, since "hidden" respiratory insufficiency was detected in a timely manner.

Key words: *tobacco smoking, «hidden» violations of the spectral characteristics of the level of hemoglobin oxygen saturation, respiratory failure*

Conflict of interests

The authors declare no conflict of interests

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BA — bronchial asthma, CO — carbon monoxide, HbCO — carboxyhemoglobin, O_2 — oxygen, PY — pack-year, SpO_2 — transcutaneous level of hemoglobin saturation with oxygen

Introduction

Tobacco smoking is one of the known exogenous sources of carbon monoxide (CO) in human body. Carbon monoxide displaces oxygen (O_2) with the formation of carboxyhemoglobin (HbCO) that results in various impairments of the oxygen transport function of blood, therefore, it is necessary to define HbCO level in smokers, especially if they have chronic bronchial and obstructive pathology [1–3]. This diagnostic approach allows clarifying and objectifying the assessment of blood oxygenation disorders, in particular, in smokers with bronchial asthma (BA).

The prevalence of smoking in patients with bronchial asthma is high. It was established that 25–35 % of patients with bronchial asthma are active smokers [4, 5]. Tobacco smoke in some smokers with asthma leads to the neutrophilic transformation of airway inflammation with more frequent and more severe exacerbations of bronchial asthma [6, 7].

Transcutaneous two-wavelengths pulse oximetry is most widely used worldwide to assess blood oxygenation, however, it leads to a diagnostic error in smokers, since carboxyhemoglobin absorbs infrared light almost identically to oxyhemoglobin. As a result, the level of the oxygen saturation of hemoglobin in smokers according to transcutaneous two-wavelengths pulse oximetry is always overestimated [8–12].

The advanced two-wavelengths pulse oximeters allow monitoring blood oxygenation and conducting its spectral analysis to determine the percentage of blood oxygen saturation (SpO_2) in the ranges of 95–100 %, < 95 %, 90–94 %, 85–89 %, etc. [13]. However, the levels, as well as the spectral characteristics of hemoglobin oxygen saturation, without considering carboxyhemoglobin are always aberrant. The clinical significance of this aberration is confirmed by the data from the federal guidelines Carbon Monoxide Poisoning; they confirm that the level of HbCO in non-smokers is 1–2 %, whereas in smokers it ranges from 5 to 10 %, with average daily concentration of HbCO from 5 up to 15 % [14].

The reliable information about the exact level and spectral characteristics of SpO_2 is crucial for diagnosis and assessment of the severity of respiratory failure, in particular, in life-threatening asthma exacerbation. One of the most important diagnostic criteria for a life-threatening BA exacerbation is the blood oxygenation decrease below 92 %.

The objective of this study was to identify and to evaluate the clinical significance of the "occult" blood oxygenation impairments in smokers with asthma exacerbation.

Materials and Methods

For the diagnosis of the "occult" impairments of blood oxygenation, including "occult" impairments of the spectral characteristics of SpO_2, 19 male smokers aged (54.60 ± 2.05), with exacerbation of mixed (n = 13; 68 %) or allergic (n = 6; 32 %) asthma were examined. It was a cross-sectional study; informed consent

Table 1. *Clinical characteristics of smokers with bronchial asthma*

Signs	Smokers with bronchial asthma, n=19
Age, years	52,2±2,69
Men, %	100
Tobacco smoking, %	100
Disease duration, years	27,9±1,45
Duration of tobacco smoking, years	26,5±2,37
Mixed bronchial asthma, %	68
Allergic bronchial asthma, %	32
Allergens, %	100
Viral infection, %	15
Urticaria, %	7,3
Eosinophilia of blood and/or sputum, %	11
Arterial hypertension, %	17
Obesity, %	27
Angina pectoris II-III functional class, %	27
Type II diabetes mellitus with a target blood sugar level, %	14

was obtained. BA was diagnosed in accordance with the Clinical Guidelines for Asthma-2021 of the Ministry of Health of the Russian Federation [7]. Table 1 presents clinical characteristics of patients.

In all patients, carboxyhemoglobin level was analyzed using a Micro CO-monitor (Micro Medical, UK) by the carbon monoxide fraction in the exhaled air. HbCO was measured no earlier than 2 hours after smoking.

M. J. Jarvis et al. conducted a study to evaluate the accuracy of exhaled air CO measurement in comparison with gas chromatography results. The results obtained confirmed the high accuracy of HbCO evaluation by FECO measurement — the correlation coefficient in assessing the accuracy of HbCO measurement by these methods was 0.98 for "healthy" smokers and 0.92 for smoking patients with emphysema [1].

Ventilatory lung capacity was assessed using a Spirodoc SpO_2 spirometer (Italy).

Blood oxygenation was assessed using a 15-minute transcutaneous two-wavelength pulse oximetry at rest using a Spirodoc SpO_2 spirometer (Italy). The analysis of hemoglobin oxygen saturation, including spectral characteristics of SpO_2, was performed both without and with regard of carboxyhemoglobin. To adjust the results of monitoring blood oxygenation for HbCO, we used our proprietary Software for Carboxyhemoglobin Adjustment of Blood Oxygenation Monitoring Results During Transcutaneous Two-Wave Pulse Oximetry (https://elibrary.ru/item.asp?id=43888052&ysclid=l7ulwur86q612655985).

Software language and user interface are implemented in Java Script language using HTML and CSS. The software is provided as source code under the terms of the GNU General Public License. Implementing computer types — Intel, ARM, MIPS, operating system versions — Windows, Linux, FreeBSD.

Algorithm for using the software

1. Monitoring of blood oxygenation using transcutaneous two-wavelength pulse oximetry.
2. Extraction of the blood oxygenation dataset from the SpO_2 curve recorded by Spirodoc SpO_2 and its loading into the software.
3. Adjustment of blood oxygenation data for HbCO average level after the introduction of average HbCO value in the software.

Statistical processing of study results was carried out using a licensed Russian version of Statistica 13.3 software. Mann — Whitney U test was used to compare the parameters. The results are presented as (M ± m). The differences in the analyzed values were considered to be statistically significant at the level of α-error < 0.05.

Results and Discussion

A moderate BA exacerbation was observed in 5 patients (26 %), a severe exacerbation — in 8 patients (42 %), and a life-threatening exacerbation — in 6 patients (32 %) according to the level of peak expiratory flow and clinical signs of the severity of BA exacerbations. However, none of the examined patients demonstrated clinically significant decreased SpO_2 below 92 % (as measured by pulse oximetry with no subsequent adjustment for carboxyhemoglobin).

The main clinical signs of bronchial and obstructive pathology in smokers were: paroxysmal cough in 5 (27 %) individuals, episodes of labored breathing in 19 (100 %) individuals, shortness of breath at heavy physical activity in 7 (39 %) individuals, at moderate physical activity — in 10 (51 %) individuals, and shortness of breath at rest — in 2 (10 %) patients. Predominantly mucous sputum was observed in 4 (19 %) patients. All patients underwent chest X-ray to exclude pneumonia.

According to the pack-year (PY) parameter, 5 patients with asthma were identified as "absolute smokers" (PY > 10, 26 %) and in 10 — as "heavy smokers" (PY > 25, 53 %). In 4 patients (21 % of cases), smoking was less intense and less prolonged (PY ≤ 10). Mean carboxyhemoglobin level exceeded the upper limit of normal (< 1.12 %) and amounted to (2.40 ± 0.17)%. The pack-year parameter was at the level of (35.10 ± 5.15) due to the predominance of the "heavy" smokers category. The average duration of hospital stay was (11.10 ± 0.40) days.

Table 2. *Characteristics of lung ventilation in smokers with bronchial asthma*

Indicators, (M±m)	Smokers with bronchial asthma, n=19
VC, %	54,7±3,97
FVC, %	42,3±3,33
FEV_1, %	40,0±3,56
FEV_1/ VC, %	58,5±5,38
FEV_1/ FVC, %	67,9±4,11
COC_{25-75}, % MEF_{25-75}, %	32,5±4,33

Note: VC — vital capacity of the lungs; FVC — forced vital capacity of the lungs; FEV_1 — volume of forced exhalation in 1 sec.; MEF_{25-75} –middle expiratory flow of 25-75 % FVC

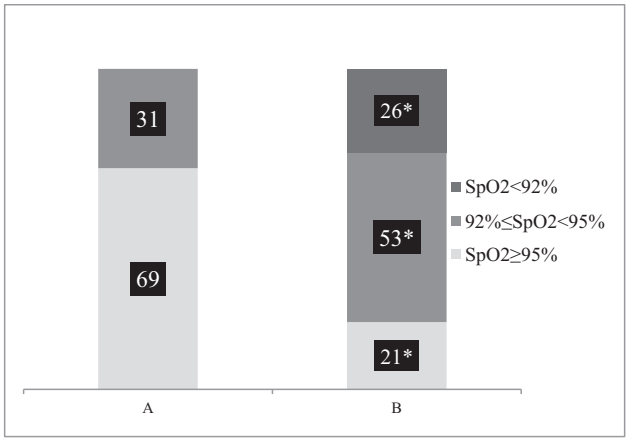

Figure 1. *Prevalence of normal (SpO2≥95 %), moderately reduced (92 %≤SpO2<95 %) and clinically significant reduced (SpO2<92 %) blood oxygenation without correction (A) and with correction for carboxyhemoglobin (B)*

Note: * — probability of α-error <0,05 when comparing indicators

All examined patients were found to have an obstructive respiratory dysfunction, with a decreased lung vital capacity (VC) and forced vital capacity (FVC), as well as the ratio of forced expiratory volume per 1 second (FEV_1) to VC (FEV_1/VC) and FVC (FEV_1/FVC), see Table 2. It is known that VC decreases in severe obstruction, and air-trapping that develops both during smoking and BA exacerbation contributes to a decrease in FVC.

When performing pulse oximetry without subsequent adjustment of the mean value of hemoglobin saturation with oxygen for carboxyhemoglobin, the saturation of hemoglobin with oxygen in all examined patients exceeded 92 %. It is worth mentioning, that normal mean SpO_2 values (SpO_2mean ≥ 95 %) were found in 13 (69 %), and moderately reduced mean values (92 % ≤ SpO_2mean < 95 %) — in 6 (31 %) smokers with asthma exacerbation.

Adjustment of hemoglobin oxygen saturation for HbCO (the mean value of carbon monoxide in the exhaled air used to determine carboxyhemoglobin level is presented in Table 3 below) allowed identifying "occult" impairments of blood oxygenation in 9 (48 %) patients. The prevalence of normal mean oxygenation values decreased from 69 to 21 %, and the prevalence of moderately decreased mean hemoglobin oxygen saturation increased from 31 to 53 %. Five (26 %) smokers demonstrated a decrease in SpO_2 below 92 %; it is typical for a life-threatening BA exacerbation (Figure 1).

As a result, the concept of BA exacerbation severity in the examined smokers with asthma has fundamentally changed: the prevalence of moderate exacerbation decreased from 26 (n = 5) to 21 % (n = 4), of severe — from 42 (n = 8) to 26 % (n = 5), and the prevalence of life-threatening exacerbation increased from 32 (n = 6) up to 53 % (n = 10) — p < 0.05 (Figure 2).

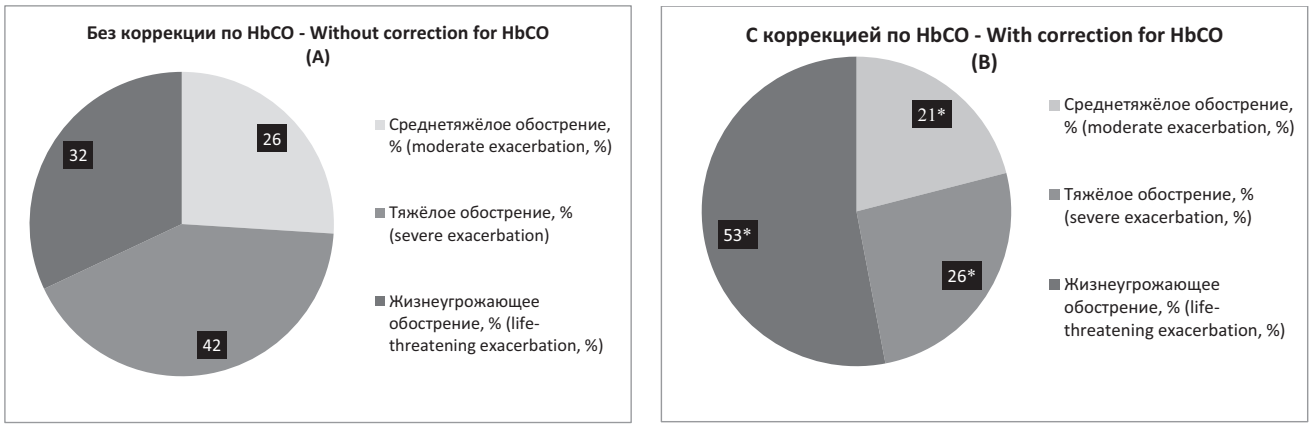

Figure 2. *Prevalence of severity of bronchial asthma exacerbation among smokers depending on the correction for carboxyhemoglobin*

Note. A — without correction for HbCO; B — with correction for HbCO; * — probability of α-error < 0.05 when comparing the parameters

Table 3. *Assessment of blood oxygenation in smokers with bronchial asthma with and without correction for carboxyhemoglobin*

Parameters	Without correction for HbCO, (M ± m)	With correction for HbCO, (M ± m)	p
F_ECO, ppm	-	15.60 ± 0.09	-
HbCO, %	-	2.40 ± 0.17	-
SpO_2min., %	93.80 ± 0.34	91.40 ± 0.39	< 0.001
SpO_2max., %	97.10 ± 0.24	94.60 ± 0.31	< 0.001
SpO_2mean, %	95.60 ± 0.29	93.20 ± 0.33	< 0.001
SpO_2 (< 95 %), %	20.70 ± 7.30	80.80 ± 8.53	< 0.001
SpO_2 (< 92 %), %	-	24.90 ± 7.82	-
SpO_2 (< 90 %), %	-	1.60 ± 0.75	-
SpO_2 (95–100 %), %	79.30 ± 7.30	19.20 ± 8.53	< 0.001
SpO_2 (95–100 %)mean, %	96.00 ± 0.20	95.50 ± 0.10	0.196
SpO_2 (90–95 %), %	20.70 ± 7.30	79.30 ± 8.37	< 0.001
SpO_2 (90–95 %)mean, %	93.80 ± 0.06	93.00 ± 0.24	0.022
SpO_2 (85–90 %), %	-	1.50 ± 0.75	-
SpO_2 (85–90 %)mean, %	-	89.50 ± 0.20	-

Note. F_ECO — fraction of carbon monoxide in exhaled air; HbCO — carboxyhemoglobin; SpO_2min., max., mean — minimum, maximum and average values of SpO_2; SpO_2(< 95 %) SpO_2 (< 92 %) SpO_2 (< 90 %), SpO_2 (95–100 %), SpO_2 (90–95 %), (85–90 %) — part of SpO_2 values related to the specified oxygenation spectra; SpO_2 (95–100 %)mean, SpO_2 (90–95 %)mean, SpO_2 (85–90 %)mean — the average level of SpO_2 in the indicated blood oxygenation spectra; p — the probability of α-error < 0.05 when comparing corrected and uncorrected for HbCO parameters of blood oxygenation

It is apparent that the accuracy of the clinical assessment of blood oxygenation in smokers after adjusting SpO_2 for HbCO level increased significantly and allowed diagnosing a clinically significant life-threatening exacerbation of asthma in smoking patients due to the timely detection of respiratory failure.

In addition to decreased mean, minimum and maximum SpO_2, adjustment of blood oxygenation monitoring data for HbCO allowed revealing significant changes in the basic spectra of blood oxygenation (Table 3).

In particular, the part of the normal values of blood oxygenation (95–100 %) decreased from 79.3 to 19.2 %. It should be noted that, for example, the proportion of decreased SpO_2 values (90–95 %) increased significantly from 20.7 to 79.3 % in combination with a decrease in the mean values of blood oxygenation in the indicated blood oxygenation spectra.

Conclusion

The negative effect of carbon monoxide on the oxygen transport function of blood is implemented due to hypoxic hypoxia (due to decreased partial pressure of O_2 in alveolar space), hemic hypoxia (due to excessive carboxyhemoglobin, HbCO), circulatory hypoxia (due to hemodynamic disorders), and tissue hypoxia (due to inactivation of enzymes that regulate tissue respiration). Further, the increase in HbCO level shifts the oxyhemoglobin dissociation curve to the left with a decrease in the rate of oxygen delivery to tissues. The higher HbCO, the more impaired the state of oxygen transport in a smoker is.

Due to elevated HbCO levels in all smokers, transcutaneous pulse oximetry is subject to diagnostic error due to similar absorption of infrared light by HbO_2 and HbCO; it leads to an "underestimation" of blood oxygenation disorders and, accordingly, to an "underestimation" of the severity of respiratory failure that occurs in some patients with chronic bronchial and obstructive pathology.

Therefore, timely detection and more accurate diagnosis of respiratory failure required adjustment for carboxyhemoglobin level after two-wavelength transcutaneous pulse oximetry. This determines the practical significance of this study. For practical adjustment of SpO_2 monitoring results we can use, for example, a computer program developed by us.

This diagnostic strategy is also important for the subsequent treatment the nature and extent of which largely depend on timely and more accurate assessment of respiratory failure.

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All the authors contributed significantly to this work, read and approved the final version of the article before publication

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Список литературы / References:

1. M Jarvis M.J. Russel M.A., Saloojee Y. Expired air carbon monoxide: a simple breath test of tobacco smoke intake. BMJ. 1980; 281 (16): 484-495.DOI: 10.1136/bmj.281.6238.484.
2. West J.B. Respiratory Physiology: The Essentials (eighth edition). J.B. West: England. 2013; 150p.
3. Фаткуллин К.В., Гильманов А.Ж., Костюков Д.В. Клиническое значение и современные методологические аспекты определения уровня карбокси- и метгемоглобина в крови. Практическая медицина. 2014; 3(14): 17-21.
   Fatkullin K.V., Gilmanov A.Zh., Kostyukov D.V. Clinical significance and modern methodological aspects of determining the level of carboxy- and methemoglobin in the blood. Practical medicine. 2014; 3(14): 17-21. [In Russian].
4. Cerveri I. The impact of cigarette smoking on asthma: a population-based international cohort study. Int. Arch. Allergy Immunol. 2012; 2(158): 75–183. DOI: 10.1159/000330900.
5. Титова О., Козырев А., Суховская О. Влияние различных факторов риска на течение и прогноз бронхиальной астмы. Врач. 2013; (6): 85-87.
   Titova O., Kozyrev A., Sukhovskaya O. The influence of various risk factors on the course and prognosis of bronchial asthma. Doctor. 2013; (6): 85-87. [In Russian].
6. Global Initiative for Asthma, GINA. 2022, 225p [Electronic resource]. URL: https://ginasthma.org/wp-content/uploads/2022/07/GINA-Main-Report-2022-FINAL-22-07-01-WMS.pdf (date of the application: 05.09.2022).
7. Клинические рекомендации по бронхиальной астме Минздрава РФ. 2021; 85 с. [Электронный ресурс] URL: http://disuria.ru/_ld/10/1037_kr21J45J46MZ.pdf?ysclid=l7un7hzve 9180338084 (дата обращения 05.09.2022).
   Clinical recommendations on bronchial asthma recommendations from the Ministry of Health. 2021; 85 p. [Electronic resource] URL: http://disuria.ru/_ld/10/1037_kr21J45J46MZ.pdf?ysclid =l7un7hzve9180338084 (дата обращения 05.09.2022). [In Russian].
8. Barker S.J., Tremper K.K. The effect of carbon monoxide inhalation on pulse oximeter signal detection. Anesthesiology. 1987; (67): 599-603. DOI: 10.1097/00000542-198705000-00014.
9. Руководство ВОЗ по пульсоксиметрии. 2009; 23 с. [Электронный ресурс] URL: https://mayak.help/wp-content/uploads/2016/05/WHO-Pulse-Oximetry-Training-Manual-Final-Russian.pdf (дата обращения: 24.01.2022).
   WHO Guidelines on pulse oximetry. 2009; 23 p. [Electronic resource] URL: https://mayak.help/wp-content/uploads/2016/05/WHO-Pulse-Oximetry-Training-Manual-Final-Russian.pdf (date of the application: 24.01.2021) [In Russian].
10. Wilson Iain. Pulse oximetry — Part 1/I. Wilson. Anaesthesia Tutorial Of The Week 123,-2nd March. 2009: 1-7p.
11. Buckley R.G., Aks S.E., Eshom J.L. et al. The pulse oximetry gap in carbon monoxide intoxication. Ann Emerg Med. 1994; (24): 252–255.
12. Gorge A. Guzman. Carbon Monoxide Poisoning. Critical Care Clinics. 2012; 28(4): 537-548.
13. Бузунов Р.В., Иванова И.Л., Кононов Ю.Л. и др. Компьютерная пульсоксиметрия в диагностике нарушений дыхания во сне. Ижевск, 2013; 40 с.
   Buzunov R.V., Ivanova I.L., Kononov Yu.L. et al. Computer pulse oximetry in the diagnosis of breathing disorders during sleep. Izhevsk, 2013; 40 p. [In Russian].
14. Клинические рекомендации ассоциации клинических токсикологов «Токсическое действие окиси углерода. Токсическое действие других газов, дымов и паров». 2020; 40 с. [Электронный ресурс] URL: http://www.toxicology.ru/docs/rek/09_26112020.pdf (дата обращения 20.07.2022).
   Clinical recommendations of the association of clinical toxicologists “Toxic effect of carbon monoxide. Toxic effects of other gases, fumes and vapours”. 2020; 40 p. [Electronic resource] URL: http://www.toxicology.ru/docs/rek/09_26112020.pdf (date of the application: 20.07.2022) [In Russian].