

UDC 616.248.1-085-084.001.5

L. M. Kuryk

State Organization «National Institute of Phthisiology and Pulmonology named after F. G. Yanovsky NAMS of Ukraine»

Efficiency ginkgolides and bilobalides in complex correction of erythrocyte homeostasis in asthma patients

Key words: asthma in adults, blood rheology, biophysical parameters of erythrocyte membrane morphological characteristics of red blood cells, ginkgolides, bilobalides.

Blood rheology due to a set of functional state of blood cells (mobility, deformability, aggregative activity of red blood cells, white blood cells and platelets), blood viscosity (concentration of proteins and lipids), blood osmolarity (glucose concentration) [1, 4, 19]. The key role in the formation of blood rheological parameters belonging to red blood cells, which constitute 98 % of the total volume of blood cells [3, 7, 12]. The progression of any disease is accompanied by functional - structural changes in certain blood elements. Of particular interest are changes in erythrocyte membrane which is a model of the molecular organization of the plasma membrane. From the structural organization of the membrane of red blood cells depend largely on their aggregative activity and deformation, which are critical components in the microcirculation [10].

A large number of papers devoted to blood hemorheology in chronic obstructive pulmonary disease, found reduction parameters characterizing the deformation of red blood cells, namely their ability to deformation and osmotic stability. Oxygen binding properties of blood play an important role in physiological mechanisms maintain equilibrium between the processes of free radical oxidation and antioxidant protection in the body. These properties determine the nature of blood and the magnitude of the diffusion of oxygen to the tissues ,

depending on the need for it and its efficiency, contributes to the prooxidant – antioxidant status, manifesting in different situations or antioxidant or prooxidative properties [14, 16, 20]. Thus, the deformability of red blood cells is not only a determinant of oxygen transport to peripheral tissues and to ensure their needs are there, but the mechanism that affects the performances of the antioxidant defense and, ultimately, the entire support organization prooxidant – antioxidant balance the whole body.

In patients with asthma decreased ability of red blood cells to deform, their increased viscosity is the result of thickening of the basement membrane, leading to a decline in the delivery of oxygen to tissues, abnormal red blood cells that play a critical role in the development of microcirculatory disorders and peripheral hypoxia. [6, 9, 15, 22]. The world is constantly conducted research and the search for new effective medication and no medication comprehensive treatments to improve the flow and timing of rehabilitation of patients with asthma.

Among the herbal drugs have drawn our attention to herbal products containing extracts of *Ginkgo biloba* leaves. The many facets of their pharmacodynamic effects, very low toxicity and safety make it possible to find new indications for clinical use. To date, global studies have shown that *Ginkgo* extract is a potent inhibitor of the formation of nitric oxide in

inflammation of tissues. Also, experimental evidence suggests vazorelaxing effects data are available on its antiaggregatory properties of inhibition of thrombus formation in venous and arterial. In tests on human volunteers found that ginkgo extract has no effect on blood pressure, hematocrit value, the number of circulating white blood cells and platelets as well as platelet aggregation properties. However, the observed decrease in aggregation ability of red blood cells and improve blood flow through the capillaries [23, 29]. Standardized ginkgo extract in vitro inhibits by 69 % the adhesion of neutrophils to the endothelium of the great saphenous vein of a man who rises 5–6 times during hypoxia . In addition, the drug inhibits the subsequent activation of neutrophils and secretion of superoxide anion them. As a result, blocked the adhesion and activation of neutrophils. Results immunopharmacological studies indicate that biologically active substances of Ginkgo actively influence neurotransmitter processes. In addition, an extract of Ginkgo shows a specific effect on the noradrenergic system in the cerebral cortex and β_2 -adrenergic receptors [28].

Therefore, the **main aim of this study** was to study the influence of ginkgolides and bilobalides ability the rheological blood -based deforming properties of red blood cells and acid - base and blood gas status in patients with asthma.

Materials and methods

Thirty patients with asthma were examined in remission of the disease, from 28 to 68 years (mean age $(41,2 \pm 6,0)$ years). When the diagnosis is taken into account medical history, clinical symptoms, indicators of respiratory function, reversibility of obstruction in a sample of bronchodilators. Selection of patients by severity of asthma was conducted in accordance with the criteria Decree № 128 of Ministry of Health of Ukraine of 19.03.2007 «On approval of clinical protocols of care in the specialty «Pulmonology» [18]. As controls were examined 15 healthy volunteers had no clinically significant severe pathology. All patients received standard basic therapy remission, which included the use of inhaled corticosteroids and β_2 -agonist, short acting to reduce asthma symptoms. For the purpose of comparative evaluation, all patients were divided into groups: 15 patients (group I) received basic treatment of the disease in the remaining 15 patients (group II) used in the treatment of drug, which includes ginkgolides and bilobalides immediately after treatment exacerbation, daily for 90 days orally 1 capsule 2 times a day after meals. Age and sex composition of patients, the degree of severity of asthma in all groups were comparable. Research ventilatory lung function was conducted with all patients according to the analysis spirogram curve «flow-volume» forced expiratory volume and total bodypletyzmohrafy on the unit «Master Scope» and «MasterScreen BodyDiff» company «Erich Jaeger» (Germany) [8]. The study of biophysical parameters of erythrocytes and serum were carried out assessment of performance [5, 11, 17, 21]:

- the degree of deformation of red blood cells (points);
- the relative charge membrane (VZME) (v. Fr.)
- the relative membrane potential gradient (VHMP) erythrocytes (v. Fr.)
- crystal optical characteristics of blood serum (the liquid crystalline nature and lattice structuring of serum);

- sorption capacity of red blood cells (SYEE) %;
- the percentage of hemoglobin saturated with O₂ (SaO₂ %).

Gradient of relative membrane potential of erythrocytes was carried out with determination in blood Δ Ph solution is not buffered saline 0,9% NaCl. Determination of the relative charge of erythrocytes was performed using mathematical calculations. Sorption capacity of red blood cells (SYEE) was determined using a dye – methylene blue. Units – per cent (%). We determined the amount of methylene blue associated with the cells (Cb), the amount of dye remaining in solution (Cbs), which made it possible to calculate the distribution coefficient of methylene blue between the cell and the environment (Q). Assessment of erythrocyte deformation and crystal optical properties of serum were carried out using the edge of dehydration and body fluids by electron microscope «NU 2» company «VEB Carl Zeiss» MRS of photosystem 60. The presence of comorbidity in remission was taken into account. Research SaO₂ was performed using pulse oximeters UTAS OXI 200. Serum crystal optical parameters measured on the scale.

Scale crystallization serum:

- 0 – Basic morphotype (filamentary structures, medium and large spherulites);
- 1 – mixed structure, which includes the following subtypes : (fan, with secondary fragments needle);
- 2 – «vitreous structure» (amorphization) the appearance of the structures of the «bundle».

Scale of assessment of the extent of deformation of red blood cells:

- 0 – no deformation ;
- 1 – 10–29 % misshapen red blood cells;
- 2 – 30–69 % misshapen red blood cells;
- 3 – deformed 70% or more red blood cells.

Performance of gas composition and acid - base balance (ABB) capillary blood micromethod evaluated using the analyzer ABL₅ («Radiometer») [24 – 27]. Analyzed the following parameters:

- pH;
- pressure of carbon dioxide (pCO₂, mmHg.)
- real plasma bicarbonate (HCO₃⁻, mmol/l);
- plasma standard bicarbonate (SBC, mmol/l);
- standard excess bases (SBE, mmol/l);
- oxygen tension (pO₂, mm. Hg.)
- saturation of hemoglobin (Hb, g/L) oxygen (SO₂, %) .

Statistical analysis of the data was performed using the licensed software products that are included in the software package Microsoft Office Professional 2000, a personal computer IBM Celeron program Excel [2, 13]. Work carried out by public funds.

Results and discussion

As a result of this work revealed the following. At baseline in patients with baseline asthma therapy, observed changes in deformation capacity and osmotic resistance of red blood cells, namely, the value was VHMPE ($0,351 \pm 0,042$), VZME – ($0,149 \pm 0,005$), the degree of deformation of red blood cells was ($3,0 \pm 0,0$) points, i. E., peripheral blood was 70 % or more pathological morfoform, and only 30 % dyskoocytes. Blood serum had signs of hypoxic anisotropy with loss

of structure – $(3,0 \pm 0,0)$ points, which was significantly different from the picture serum of healthy group $(0,1 \pm 0,0)$ points. As well as the work of an analysis of sorption capacity erythrocytes, which provides information about the status of their regenerative capacity, which varies in degree of change of the barrier properties of the plasma membrane. Increased sorption capacity of red blood cells is considered an indicator of cell membrane damage and disruption. Factors that influence it are endogenous intoxication, hypoxia, and the state of proteins and lipids of erythrocyte membranes. After reducing the charge on the red cell membrane and increase her graded membrane potential, by increasing its permeability, respectively , and increased the sorption capacity of red blood cells – $(77,4 \pm 12,3)$ %, healthy person – $(31,0 \pm 4,6)$ % distribution coefficient of methylene blue between the cell and the environment (Q) was $(1,12 \pm 0,08)$, healthy individuals $(0,75 \pm 0,01)$. In re-examination, after 3 months of observation, changes in the estimated parameters is not the case (Table 1).

In the analysis of the initial parameters of patients who received additional treatment with drugs, which include ginkgolides and bilobalides also showed a reduction in deformation capacity and osmotic resistance of red blood cells , namely, the value was increased to VHMP (0,355 \pm 0,042), VZME reduced to $(0,151 \pm 0,005)$, the degree of deformation of red blood cells was $(2,2 \pm 0,0)$ balls, crystal optical characteristics of blood serum were $(2,0 \pm 0,0)$ points sorption capacity of red blood cells was increased relative to the norm $(78,2 \pm 12)$ % distribution coefficient of methylene blue between the cell and the environment (Q) group was $(1,15 \pm 0,09)$ (Table 2).

After treatment, deformation capacity and osmotic cell resistance improved, namely, significantly reduced the gradient to membrane potential $(0,202 \pm 0,022)$, erythrocyte membrane to the charge $(0,245 \pm 0,009)$, also decreased circulating pathologically deformed shape (degree of deformation – $(1,5 \pm 0,0)$ points), increased serum liquid crystal ordering to $(1,1 \pm 0,01)$ points. Sorption capacity of red blood

cells was significantly decreased to $(41,2 \pm 5,1)$ %, the distribution coefficient of methylene blue between the cell and the environment (Q) – $(0,84 \pm 0,06)$.

Table 3 shows comparative data of biophysical parameters of deformation capacity and osmotic resistance of erythrocytes of patients in both groups. Significant difference between the control group and treated with medication, which includes ginkgolides and bilobalides, seen in terms VHMP, VZME, the degree of deformation of red blood cells, crystal optical structuring of serum and in the sorption capacity of red blood cells and the distribution coefficient between methylene blue. Significant difference in the estimated parameters persisted in both groups compared to the control group of healthy donors.

After analyzing the data on acid – base and blood gas status in patients with asthma, the presence of compensated respiratory acidosis, which was confirmed by the growth pressure of carbon dioxide (pCO_2), plasma standard bicarbonate (SBC) and reduced oxygen tension (pO_2) and hemoglobin oxygen saturation (SO_2) repeated examination in patients with asthma receiving standard therapy, no significant changes compared to the beginning of the observation is not the case (Table. 4).

When comparing the results of the second survey of patients who received the drug, which includes ginkgolides and bilobalides, set the normalization of acid - base status of blood and gas, more detailed information is presented in Table 5.

By comparing the final data (first group – 3 months of observation, the second group - after the end of treatment), it was found that the use of medication in treatment, which includes ginkgolides and bilobalid, helps to normalize acid-base and blood gas status, namely reduce the tension of carbon dioxide and bicarbonate level of standard plasma, increase oxygen tension and hemoglobin oxygen saturation (Table 6).

Conclusions

As a result of the work found that in patients with bronchial asthma observed deterioration of rheological proper-

Table 1
Dynamics of deformation capacity and osmotic resistance of red blood cells in patients with asthma and to the monitoring group ($M \pm m$)

Indicators	Healthy donors (n = 15)	I group before the treatment (n = 15)	I group after 3 months of observation (n = 15)
VHMP, v. o.	$0,013 \pm 0,001$	$0,351 \pm 0,042^*$	$0,325 \pm 0,019^*$
VZME, v. o.	$0,31 \pm 0,005$	$0,149 \pm 0,005^*$	$0,145 \pm 0,004^*$
The degree of deformation of erythrocyte membranes, points	$1,3 \pm 0,1$	$3,0 \pm 0,0^*$	$2,1 \pm 0,01^*$
Erythrocytes, $10^{12}/l$	$3,01 \pm 0,0$	$3,41 \pm 0,2$	$3,1 \pm 0,01$
Crystal optical properties serum, points	$0,1 \pm 0,0$	$3,0 \pm 0,0^*$	$2,0 \pm 0,01^*$
Hb, g/l	$134,5 \pm 2,3$	$148,1 \pm 0,1$	$133,1 \pm 0,1$
Sorption capacity of red blood cells, %	$31,0 \pm 4,6$	$77,4 \pm 12,3^*$	$67,6 \pm 10,2^*$
Partition coefficient of methylene blue between erythrocytes and environment (Q)	$0,75 \pm 0,01$	$1,12 \pm 0,08^*$	$1,01 \pm 0,06$

Note: • – index difference compared with the group of healthy subjects demonstrated statistically ($p < 0,001$).

Table 2
Dynamics of deformation capacity and osmotic resistance of red blood cells in patients with bronchial asthma group II during treatment ($M \pm m$)

Indicators	Healthy donors (n = 15)	II group before the treatment (n = 15)	II group after treatment (n = 15)
VHMPE	0,013 ± 0,001	0,355 ± 0,042*	0,202 ± 0,022**
VZME	0,31 ± 0,005	0,151 ± 0,005*	0,245 ± 0,009**
The degree of deformation of erythrocyte membranes, points	1,3 ± 0,1	2,2 ± 0,0*	1,5 ± 0,01*
Erythrocytes, $10^{12}/l$	3,01 ± 0,0	3,51 ± 0,2	3,9 ± 0,2
Crystal optical properties serum, points	0,1 ± 0,1	2,0 ± 0,0*	1,1 ± 0,01**
Hb, g/l	134,5 ± 2,3	145,1 ± 0,1	134,1 ± 0,1
Sorption capacity of red blood cells, %	31,0 ± 4,6	78,2 ± 12,2*	41,2 ± 5,1*
Partition coefficient of methylene blue between erythrocytes and environment (Q)	0,75 ± 0,01	1,15 ± 0,09*	0,84 ± 0,06**

Notes: * – difference in rate in the treatment group demonstrated statistically ($p < 0,05$); • – index difference compared with the group of healthy individuals demonstrated a statistically ($p < 0,05$).

Table 3
Dynamics of deformation capacity and osmotic resistance of red blood cells in patients with asthma during treatment ($M \pm m$)

Indicators	Healthy donors (n = 15)	I group (control) (n = 15)	II group after treatment (n = 15)
VHMPE	0,013 ± 0,001	0,325 ± 0,019*	0,202 ± 0,022**
VZME	0,31 ± 0,005	0,145 ± 0,004*	0,245 ± 0,009**
The degree of deformation of erythrocyte membranes, points	1,3 ± 0,1	2,1 ± 0,01*	1,5 ± 0,01*
Erythrocytes, $10^{12}/l$	3,01 ± 0,0	3,1 ± 0,01	3,9 ± 0,2
Crystal optical properties serum, points	0,1 ± 0,1	2,0 ± 0,01*	1,1 ± 0,01**
Hb, g/l	134,5 ± 2,3	133,1 ± 0,1	134,1 ± 0,1
Sorption capacity of red blood cells, %	31,0 ± 4,6	67,6 ± 10,2*	41,2 ± 5,1*
Partition coefficient of methylene blue between erythrocytes and environment (Q)	0,75 ± 0,01	1,01 ± 0,06	0,84 ± 0,06**

Notes: * – Index difference between the groups during treatment demonstrated statistically shown ($p < 0,05$); • – index difference compared with the group of healthy individuals statistically shown ($p < 0,05$).

ties of blood, including by the functional state of erythrocyte level. Namely, in asthma occurs decrease in osmotic resistance and deformation capacity of red blood cells with abnormal formation of their morfoform (decreased red cell membrane charge relative increase of the relative potential gradient on it), hypoxic anisotropy serum, and due to the increase of sorption capacity and exchange coefficient

between the cell and the medium increases intracellular fluid and reduces the number of active hemoglobin in her, and consequently, the conditions associated to the development of hypoxia. This is confirmed compensated respiratory acidosis (increase pressure of carbon dioxide (pCO_2), plasma standard bicarbonate (SBC) and reduced oxygen tension (pO_2) and hemoglobin oxygen saturation (SO_2)). Application

Table 4

The evolution of the CBS and the gas composition of the blood in patients of the I group in the process of observation and compared with a group of healthy donors ($M \pm m$)

Indicators	Healthy donors (n = 15)	I group before the treatment (n = 15)	I group after 3 months of observation (n = 15)
HCO_3^- , mmol/l	$23,8 \pm 0,4$	$24,3 \pm 0,2$	$24,1 \pm 0,2$
PCO_2 , mmHG	$36,8 \pm 0,2$	$37,6 \pm 0,1^*$	$37,4 \pm 0,1^*$
PO_2 , mmHG	$64,7 \pm 0,2$	$63,3 \pm 0,2^*$	$63,5 \pm 0,2^*$
pH	$7,41 \pm 0,007$	$7,41 \pm 0,004$	$7,41 \pm 0,004$
SO_2 , %	$98,6 \pm 0,7$	$94,7 \pm 1,2^*$	$96,1 \pm 1,3^*$
SBE, mmol/l	$-0,7 \pm 0,4$	$1,2 \pm 0,5$	$1,9 \pm 0,5$
SBC, mmol/l	$23,5 \pm 0,2$	$24,6 \pm 0,2^*$	$24,5 \pm 0,2^*$

Notes: * – statistically significant difference in the group during treatment ($p < 0,05$); • – statistically significant difference compared with the group of healthy donors ($p < 0,05$).

Table 5

The evolution of the CBS and the gas composition of the blood in patients of the II group during treatment and compared with a group of healthy individuals ($M \pm m$)

Indicators	Healthy donors (n = 15)	II group before the treatment (n = 15)	II group after treatment (n = 15)
HCO_3^- , mmol/l	$23,8 \pm 0,4$	$24,8 \pm 0,2$	$23,9 \pm 0,1$
PCO_2 , mmHG	$36,8 \pm 0,2$	$37,8 \pm 0,1^*$	$36,7 \pm 0,2^*$
PO_2 , mmHG	$64,7 \pm 0,2$	$63,2 \pm 0,2^*$	$64,1 \pm 0,5^*$
pH	$7,41 \pm 0,007$	$7,40 \pm 0,004$	$7,41 \pm 0,004$
SO_2 , %	$98,6 \pm 0,7$	$94,3 \pm 1,2^*$	$97,1 \pm 1,3^*$
SBE, mmol/l	$-0,7 \pm 0,4$	$1,1 \pm 0,5$	$1,0 \pm 0,5$
SBC, mmol/l	$23,5 \pm 0,2$	$24,8 \pm 0,2^*$	$23,8 \pm 0,2^*$

Notes: * – difference in rate in the treatment group demonstrated statistically ($p < 0,05$); • – index difference compared with the group of healthy individuals statistically shown ($p < 0,05$).

Table 6

The evolution of the CBS and the gas composition of the blood of patients with bronchial asthma during treatment and compared with a group of healthy individuals ($M \pm m$)

Indicators	Healthy donors (n = 15)	I group after 3 months of observation (n = 15)	II group after treatment (n = 15)
HCO_3^- , mmol/l	$23,8 \pm 0,4$	$24,1 \pm 0,2$	$23,9 \pm 0,1$
PCO_2 , mmHG	$36,8 \pm 0,2$	$37,4 \pm 0,1^*$	$36,7 \pm 0,2^*$
PO_2 , mmHG	$64,7 \pm 0,2$	$63,5 \pm 0,2^*$	$64,1 \pm 0,5^*$
pH	$7,41 \pm 0,007$	$7,41 \pm 0,004$	$7,41 \pm 0,004$
SO_2 , %	$98,6 \pm 0,7$	$96,1 \pm 1,3$	$97,1 \pm 1,3^*$
SBE, mmol/l	$-0,7 \pm 0,4$	$1,9 \pm 0,5$	$1,0 \pm 0,5$
SBC, mmol/l	$23,5 \pm 0,2$	$24,5 \pm 0,2^*$	$23,8 \pm 0,2$

Notes: * – difference is statistically compared with the index after treatment demonstrated statistically ($p < 0,05$); • – index difference compared with the group of healthy individuals statistically shown ($p < 0,05$).

of ginkgolides and bilobalides, against the basic treatment of asthma allows you to: improve blood rheology of acid-base status and gas due to the functional state of blood cells (deformability and osmotic resistance of red blood cells) and normalize its acid-base status and gas (lower carbon dioxide tension and standard bicarbonate levels in blood plasma , increase oxygen tension and hemoglobin oxygen saturation).

References

1. Александров, О. В. Состояние микроциркуляторного кровообращения у больных бронхиальной астмой [Текст] / О. В. Александров, А. М. Алехина Ю. А. Шубин // Сов. мед. – 1982. – № 10. – С. 30–35.
2. Бабич, П. Н. Применение современный статистических методов в практике клинических исследований. Сообщение третье. Отношение шансов: понятие, вычисление, интерпретация [Текст] / П. Н. Бабич, А. В. Чубенко, С. Н. Лапач // Укр. мед. часопис. – 2005. – № 2, Т. 46. – С. 113–119.
3. Волынский, Ю. Д. Анализ взаимоотношений между легочным и системным кровообращением в пульмонологии [Текст] / Ю. Д. Волынский // Легочная гипертензия при хронических неспецифических заболеваниях легких. – Л., 1988. – С. 94–99.
4. Гаврилюк, В. К. Клиническая классификация дыхательных и гемодинамических нарушений при заболеваниях легких [Текст] / В. К. Гаврилюк [и др.] // Укр. пульмонол. журн. – 2003. – № 1. – С. 133–136.
5. Жидкие кристаллы и биологические структуры [Текст] / Под ред. Г. Брауна, Д. Уолкена. – М. : Мир, 1982. – 198 с.
6. Зинчук, В. В. Роль кислородосвязывающих свойств крови в поддержании прооксидантно-антиоксидантного равновесия организма [Текст] / В. В. Зинчук, М. В. Борисюк // Успехи физиологических наук. – 1999. – № 3. – С. 38–48.
7. Кириллов, М. М. Влияние медикаментозной терапии бронхиальной астмы на систему микроциркуляции и гемостаз [Текст] / М. М. Кириллов, И. В. Присяжнюк, Т. Г. Шаповалова // Пульмонология. – 2002. – Т. 12, № 2. – С. 17–21.
8. Клемент, Р. Ф. Функционально-диагностические исследования в пульмонологии [Текст] : методические рекомендации / Р. Ф. Клемент, Н. А. Зильбер. – СПб., 1993. – 150 с.
9. Коваль, Н. Н. Система красной крови как фактор компенсации дыхательной недостаточности у больных с хроническими неспецифическими заболеваниями легких: Автореф. дис. ... д-ра мед. наук. – М., 1984. – 40 с.
10. Коломоець, М. Ю. Функціональні властивості еритроцитів у хворих на бронхіальну астму [Текст] / М. Ю. Коломоець, Г. І. Шумко // Укр. пульмонол. журн. – 2003. – № 2. – С. 209.
11. Курик, М. В. Мицелярность и фрактальные кластера биологических структур [Текст] / М. В. Курик // Вестник АН ССР. – 1991. – № 56. – С.17–19.
12. Лаврова, О. В. Результаты клинико-функционального и гемореологического исследования на ранних этапах развития бронхиальной астмы [Текст] / О. В. Лаврова // Акт. проблемы пульмонологии. – 1991. – С. 102–106.
13. Лапач, С. Н. Статистические методы в медико-биологических исследованиях с использованием Excel [Текст] / С. Н. Лапач, А. В. Чубенко, П. Н. Бабич. – К. : Морион, 2001. – 320 с.
14. Лукьяннова, Л. Д. Современные проблемы гипоксии [Текст] / Лукьяннова Л. Д. [и др.] // Вестник РАМН. – 2000. – № 9. – С. 3–11.
15. Мажак, К. Деякі аспекти дестабілізації мембрани еритроцитів у хворих на бронхіальну астму [Текст] / К. Мажак [та ін.] // 10-й Конгрес СФУЛТ. – 2004. – С. 256–257.
16. Минеев, В. Н. Влияние физической нагрузки на мембрано-рецепторный комплекс эритроцитов и диффузионную способность легких при бронхиальной астме [Текст] / В. Н. Минеев, Ю. Д. Рабик, С. Ф. Клименкова // Сборник резюме 14-го Национального конгресса по болезням органов дыхания. – М., 2004. – 120 с.
17. Морфология биологических жидкостей человека [Текст] / Под ред. В. Н. Шабалина, С. Н. Суматохиной. – М. : Христозом, 2001. – 304 с.
18. Про затвердження клінічних протоколів надання медичної допомоги за спеціальністю «Пульмонологія» [Текст] : Наказ МОЗ України від 19.03.2007 р. № 128. – К., 2007. – 146 с.
19. Роль тромбоцитов в патогенезе бронхиальной астмы [Текст] / Под ред. А. Г. Чучалина. – М. : Агар, 1997. – Т. 1. – С.102–117.
20. Структура и функции биологических мембран [Текст] / Под ред. П. Г. Богач, М. Д. Курского. – К. : Вища школа, 1981. – 336 с.
21. Шатохина, С. Н. Диагностическое значение профильной дегидратации сыворотки крови: структурная форма информации [Текст] / С. Н. Шатохина, В. Н. Шабалин // Лаборатория. – 1999. – № 4. – С. 3–5.
22. Banerjee, R. The diagnostic relevance of red cell rigidity [Text] / R. Banerjee, K. Nageshwar, R. Puniyani // Clin. Hemorheol. Microsc. – 1988. – Vol. 19 (1). – P. 21–24.
23. Beek, T. A. Ginkgolides and bilobalide: Their physical, chromatographic and spectroscopic properties [Text] / T. A. van Beek [et al.] // Bioorg. Med. Chem. – 2005. – Vol. 13. – P. 5001–5012.
24. Gay, S. E. Cardiopulmonary exercise testing in unexplained dyspnea [Text] / S. E. Gay [et al.] // Clinical exercise testing. – Basil. Switzerland : Karger, 2002. – P. 81–88.
25. Haby, M. M. An exercise challenge for epidemiological studies of childhood asthma: validity and repeatability [Text] / M. M. Haby [et al.] // Eur. Respir. J. – 1995. – Vol. 8. – P. 729–736.
26. Hansen, J. E. Relations of Oxygen Uptake to Work in Normal Men and Men with Circulatory Disorders [Text] / J. E. Hansen [et al.] // Am. J. Cardiol. – 1987. – Vol. 59. – P. 669–674.
27. Jones, N. L. Exercise limitation in health and disease [Text] / N. L. Jones, K. J. Killian // N. Engl. J. Med. – 2000. – Vol. 343. – P. 632–641.
28. Kuribara, H. An anxiolytic-like effect of Ginkgo biloba extract and its constituent, ginkgolide-A, in mice [Text] / H. Kuribara [et al.] // J. Natural Products. – 2003. – Vol. 66. – P. 1333–1337.
29. Shen, J. Ginkgo biloba extract (EGb761) inhibits mitochondria-dependent caspase pathway and prevents apoptosis in hypoxia-reoxygenated cardiomyocytes [Text] / J. Shen [et al.] // Chin. Med. – 2012. – Vol. 30. – P. 1232–1240.
30. Vogensen, S. B. Preparation of 7-substituted ginkgolide derivatives: potent platelet activating factor (PAF) receptor antagonists [Text] / S. B. Vogensen [et al.] // J. Med. Chem. – 2003. – Vol. 46. – P. 601–608.

ЕФФЕКТИВНОСТЬ ГИНКГОЛИДОВ И БИЛОБАЛИДОВ В КОМПЛЕКСНОЙ КОРРЕКЦИИ НАРУШЕНИЙ ЕРИТРОЦИТАРНОЙ ЗВЕНА ГОМЕОСТАЗА У БОЛЬНЫХ БРОНХІАЛЬНОЙ АСТМОЙ

Л. М. Курик

Резюме

Цель исследования. Исследование влияния гинкголидов и билобалидов на реологические свойства крови на основе определения деформирующих свойств эритроцитов и кислотно-основного состояния (КОС) и газового состава крови у больных бронхиальной астмой (БА).

Материалы и методы. Было обследовано 30 больных БА в фазе ремиссии, от 28 до 68 лет (средний возраст $(41,2 \pm 6,0)$ года).

В качестве контроля были обследованы 15 здоровых добровольцев, не имевших тяжелой клинически значимой патологии. Все больные получали стандартную базисную терапию периода ремиссии, включая применение ингаляционного глюкокортикоидного препарата, а также β_2 -агониста короткого действия для уменьшения симптомов астмы. С целью сравнительной оценки все больные были разделены на группы: 15 больных (I группа) получали базовое лечение, у остальных 15 больных (II группа) применяли в комплексной терапии препарат, в состав которого входили гинкголиды и билобалиды. Препарат назначался сразу после окончания курса лечения обострения, в течение 90 дней ежедневно по 1 капсуле 2 раза в сутки после еды. Исследование вентиляционной функции легких проводили всем больным по данным спирограммы, анализу кровой «поток–объем» форсированного выдоха и общей плеизмографии тела на аппарате «Master Scope» и «MasterScreen BodyDiff» фирмы «Erich Jaeger» (Германия). Исследование относительного градиентного мембранныго потенциала эритроцитов проводили с помощью ионометра «OR-264/1» (Венгрия). Исследование степени деформации эритроцитов крови проводили с использованием метода краевой дегидратации биологических жидкостей и оценивали с помощью электронного микроскопа «NU 2» фирмы «VEB Carl Zeiss» с фотосистемой MPS 60. Статистическую обработку полученных данных выполняли с помощью лицензионных программных продуктов, входящих в программный пакет Microsoft Office Professional 2000, на персональном компьютере IBM Celeron в Excel.

Результаты. В результате проведенной работы установлено, что у больных БА наблюдается ухудшение реологических свойств крови, в том числе за счет функционального состояния ее эритроцитарного звена. А именно: при БА происходит снижение осмотической резистентности и деформационной способности эритроцитов крови с образованием патологически измененных морфоформ (снижение относительного заряда эритроцитарной мембраны, нарастание относительного градиентного потенциала на ней), наблюдается гипоксическая анизотропия сыворотки крови, а за счет роста сорбционной емкости и коэффициента обмена между клеткой и средой возрастает объем внутриклеточной жидкости и уменьшается количество активного гемоглобина в ней, следовательно – создаются условия для сопутствующего развития гипоксии. Это подтверждается компенсированным респираторным ацидозом (ростом парциального давления углекислого газа (pCO_2), стандартного бикарбоната плазмы (SBC) и снижением напряжения кислорода (pO_2) и насыщения гемоглобина кислородом (SaO_2)). Применение гинкголидов и билобалидов на фоне базисной терапии БА позволяет улучшить реологию крови за счет улучшения функционального состояния форменных элементов (деформируемость и осмотическая устойчивость эритроцитов) и нормализовать ее КОС и газовый состав (снизить pCO_2 и уровень SBC, повысить уровни pO_2 и SaO_2).

Ключевые слова: бронхиальная астма у взрослых, реологические свойства крови, биофизические показатели эритроцитарной мембранны, морфофункциональные характеристики эритроцитов крови, гинкголиды, билобалиды.

Научно-практический журнал «Астма и аллергия», 2014, № 2
 Л. М. Курик,
 канд. мед. наук, ст. научн. сотр.,
 ГУ «Национальный институт фтизиатрии и пульмонологии
 им. Ф. Г. Яновского НАМН Украины»,
 отделение пульмонологии
 03680, Украина, Киев, ул. Н. Амосова, 10
 тел.: 044 275 30 21

EFFICIENCY OF GINKGOLIDES AND BILOBALIDES IN COMPLEX ERYTHROCYTE LINK HOMEOSTASIS CORRECTION IN ASTHMATIC PATIENTS

L. M. Kuryk

Abstract

Objective. To study the influence of ginkgolides and bilobalides on the rheological properties of blood, based on the definition of deforming properties of erythrocytes and acid-base status (ABS) and arterial blood gas (ABG) in patients with bronchial asthma.

Materials and methods. We examined 30 patients with asthma in remission of the disease, from 28 to 68 years (mean age 41.2 ± 6.0 years). As a control, were examined 15 healthy volunteers who had no clinically significant severe pathology. All patients received standard basic therapy remission period, included the use of inhaled corticosteroids preparation and β_2 -agonist short action to reduce the symptoms of asthma. For the purpose of comparative evaluation of all the patients were divided into two groups: 15 patients (I group) received basic treatment of the disease in the remaining 15 patients (II group) were used in a complex drug therapy, which consists of ginkgolides and bilobalides immediately after treatment exacerbation within 90 days of daily oral 1 capsule 2 times a day after meals. Study of pulmonary ventilation function in all patients according spirogram analysis curve «flow-volume» and forced expiratory total bodyplethysmography on the «Master Scope» and «Master Screen Body Diff» company «Erich Jaeger» (Germany). Investigation of the relative gradient of the membrane potential of erythrocytes was performed using ionometers «OR-264/1» (Hungary). Study of the degree of deformation of red blood cells were carried out using the edge dehydration of biological fluids and with an electron microscope «NU 2» firm «VEB Carl Zeiss» photosystem 60 MPS. Statistical data processing was performed using licensed software, included in the software package Microsoft Office Professional 2000 on a personal computer IBM Celeron in Excel.

Results. As a result of the work was found, that in patients with asthma has worsened blood rheology, including through its functional state of erythrocyte level. Namely, there is a decrease in asthma osmotic resistance and deformability of red blood cells to form abnormal morfoform (reduction in the relative charge of the relative increase in the erythrocyte membrane potential gradient on it), hypoxic anisotropy serum, and due to the increase of the sorption capacity and exchange coefficient between the cell and environment, the intracellular fluid volume increases and decreases the amount of active hemoglobin in it, and hence, the conditions for concurrent development of hypoxia. This is confirmed by a compensated respiratory acidosis (increase in partial pressure of carbon dioxide (pCO_2), plasma standard bicarbonate (SBC) and a decrease in oxygen tension (pO_2) and hemoglobin oxygen saturation (SaO_2)). Application of ginkgolides and bilobalides with basic therapy of asthma improves blood rheology by the functional state of blood cells (deformability and osmotic resistance of red blood cells) and normalize its ABS and ABG (reduce pCO_2 and SBC, increase the pO_2 and SaO_2).

Key words: asthma in adults, blood rheology, biophysical indicators of the erythrocyte membrane, morphofunctional characteristics of red blood cells, ginkgolides, bilobalides.

Theoretical and practical J. «Asthma and Allergy», 2014, 2

L. M. Kuryk

PhD, Senior Researcher,

GU «National Institute of Phthysiology and Pulmonology

Named after F. G. Yanovsky NAMS of Ukraine»,

Pulmonology Department,

03680, Ukraine, Kiev, 10 Amosova str.

tel.: 044 275 30 21