The content of lactate in muscle tissue of different types in the early post-mortal period

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A – research concept and design, B – data collection, C – data analysis and interpretation, D – article writing, E – critical review of the article, F – final approval of the article

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It's known from the basics of clinical biochemistry and pathophysiology, lactate is the end product of anaerobic glycolysis. During exercise lactate leaves the muscles and is converted by the liver into pyruvate or metabolized by brain tissue and heart muscle. The level of lactate in muscle tissue from the standpoint of forensic examination to determine the age of death (PDC) during the early postmortem period (PMP) has not been previously studied.

***The aim of the study** was to study the postmortem patterns of lactate content in muscle tissue (MT) of various types to increase the accuracy of determining the age of death.*

***Materials and methods.** Determination of lactate content was performed in homogenates of myocardial muscles, esophagus, diaphragm and intercostal muscles in early PMP (3-13 hours after death) in 30 human corpses. MT collection was performed in sectional biopsy using special tools, preparation of MT homogenates – according to standard methods with subsequent determination of lactate content in MT homogenates by enzymatic photometric method.*

***Results**. Analysis of postmortem changes in lactate content in MT, depending on the time periods of the prescription of death coming (PDC)revealed that after 3 hours. since the onset of death, the highest content was in the intercostal muscles, the lowest – in the MT of the esophagus (respectively – (6,847 ± 0,042) mmol/g and (3,266 ± 0,031) mmol/g, p<0,001. in MT of different types was characterized by fluctuations with increasing terms of PDC, in addition, our time series became the basis for substantiating the quantitative time dependences and construction of appropriate nomograms for forensic diagnosis of PDC by lactate content in MT.*

***Conclusions.** It is proved that the lactate content naturally (and nonlinearly) changed in all studied homogenates of MT, but the initial and final level of lactate content differs depending on the type of MT. In addition, the dynamics of changes in lactate content in the time period 3÷13 hours. from the moment of death, depending on the type of MT also varies. The quantitative analytical and graphical dependences of the change in the lactate content in MT in the early PMP revealed in the study allowed to substantiate the corresponding nomograms.*

Key words: *early postmortem period, prescription of death coming, muscle tissue, lactate*

Pol Med J, 2021; XLIX (290); 391–393

Zawartość mleczanu w tkance mięśniowej różnego typu we wczesnym okresie pośmiertnym

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Znany z podstaw biochemii klinicznej i patofizjologii mleczan jest końcowym produktem beztlenowej glikolizy. Podczas wysiłku mleczan opuszcza mięśnie i jest przekształcany przez wątrobę w pirogronian lub metabolizowany przez tkankę mózgową i mięsień sercowy. Stężenie mleczanu w tkance mięśniowej z punktu widzenia badania kryminalistycznego określającego wiek zgonu (PDC) we wczesnym okresie pośmiertnym (PMP) nie był wcześniej badany.

***Celem pracy** było zbadanie pośmiertnych wzorców zawartości mleczanu w tkance mięśniowej (MT) różnego typu w celu zwiększenia dokładności określania wieku zgonu.*

***Materiały i metody.** Oznaczenie zawartości mleczanu wykonano w homogenatach mięśnia sercowego, przełyku, przepony i mięśni międzyżebrowych we wczesnym PMP (3-13 godzin po śmierci) w 30 zwłokach ludzkich. Pobranie MT wykonano w biopsji sekcyjnej przy użyciu specjalnych narzędzi. Przygotowanie homogenatów MT przeprowadzono zgodnie ze standardowymi metodami, a następnie oznaczono w nich zawartość mleczanu metodą enzymatyczno-fotometryczną.*

***Wyniki.** Analiza zmian pośmiertnych zawartości mleczanu w MT w zależności od okresów PDC wykazała, że po 3 godzinach. od początku zgonu najwyższą zawartość występowały w mięśniach międzyżebrowych, najmniejszą w MT przełyku (odpowiednio – (6847 ± 0,042) mmol / gi (3,266 ± 0,031) mmol / g, p <0,001. w Różne typy MT charakteryzowały się fluktuacjami wraz ze wzrostem warunków PDC, dodatkowo nasze szeregi czasowe stały się podstawą do uzasadnienia ilościowych zależności czasowych i konstrukcji odpowiednich nomogramów do diagnostyki sądowej PDC przez zawartość mleczanów w MT.*

***Wnioski.** Udowodniono, że zawartość mleczanu w sposób naturalny (i nieliniowy) zmieniała się we wszystkich badanych homogenatach MT, ale początkowy i końcowy poziom zawartości mleczanu różni się w zależności od rodzaju MT. Dodatkowo dynamika zmian zawartości mleczanu w okresie 3÷13 godzin. od momentu śmierci, w zależności od rodzaju MT również się zmienia. Ujawnione w badaniach ilościowe zależności analityczne i graficzne zmiany zawartości mleczanu w MT we wczesnym PMP pozwoliły uzasadnić odpowiednie nomogramy.*

Słowa kluczowe*: wczesny okres pośmiertny, przepisywanie nadchodzącej śmierci, tkanka mięśniowa, mleczan.*

Pol Merkur Lekarski, 2021; XLIX (290); 391–393

As it is known from fundamentals of biochemistry and pathophysiology, lactate is the end product of anaerobic glycolysis, on physical exertions lactate leaves muscles and is transformed by the liver into pyruvate or metabolized by the bone marrow tissue and heart muscles [13,19,20,22,23]. An intravital increase of the content of lactate in blood is registered in case

of tissue hypoxia owing to a reduced tissue perfusion. At the same time, accumulation of lactate in the muscle tissue (MT) results in metabolic acidosis, its increased activity causing tissue hypoxia, metabolic disorders and acute intoxications [7,10,11,16,18,21]. Requirements of the modern medico-legal assessment are based on the development of reliable and stable criteria that would make it possible to interpret decisively some or other postmortem phenomena, which are observed in the organism, and enable forensic pathologists to approach the real values in determining the prescription of death coming (PDC) as much as possible [1,15]. The current development of medical science and practice of determination of PDC requires from specialists a significant error decrease down to the level of ±1 hour and less, because high-technology abilities exist for it [6,8,9,12,15]. It is for this reason that an interest in studying informative criteria for determining PDC is quite natural [3,4,5]. On the other hand, the activity/level of lactate in MT from the positions of medico-legal investigation for determining PDC during the early postmortem period (PMP) was not studied before.

The aim of the research consisted in studying postmortem regularities of lactate content in different types of MT for improving the accuracy of determination of PDC.

MATERIALS AND METHODS

The content of lactate was determined in homogenates of the myocardial (MMH), oesophageal (OMH), diaphragm (DMH) and intercostal muscles (IMH) within the early PMP (3-13 hours after the coming of death) on 30 human corpses. MT was sampled in conditions of postmortem biopsy with use of special instruments; MT homogenates were prepared following the standard technique [8,9,11,16] with subsequent determination of lactate content in MT homogenates by the enzymatic photometric method using the commercial test system of Vital Development Corporation (Russia) and a Labline-80 biochemical analyzer (Austria) in accordance with their instructions.

The findings were also analyzed statistically with help of variation statistics and assessment of the normality of distribution and reliability of findings [14,17]. Information analysis of the pathometric sign (lactate content) was made by calculation of its comparative informativeness (I, bit) during each time interval as $I=-p*\log_2 p$, where p is the relation between the content of lactate after 3 hours and its content in the relevant postmortem time interval [10,11].Presentation of revealed regularities in changes of lactate content in each type of MT homogenates is provided by building dynamic lines with polynomials of different (2-5) stages and accuracy of reproduction $R^2>0.95$ [2,14]. The tabular nomogram was devised by dynamic extrapolation of polynomial dependencies with an interval of 30 minutes.

The studies were conducted following the basic regulations of *Ethical Principles for Medical Research Involving Human Subjects* approved by the Declaration of Helsinki(1964-2013), ICH GCP (1996), EEU Directive No. 609 (dated November 24, 1986), Orders of the Ministry of Health of Ukraine No. 690 (dated September 23, 2009), 944 (December 14, 2009) and 616 (August 03, 2012).

RESULTS AND DISCUSSION

The analysis of postmortem changes in the content of lactate in MT depending upon PDC revealed that after 3 hours from the moment of death coming its highest content was in intercostal muscles, the least one being in oesophageal MT (respectively, (6.847±0.042) and (3.266±0.031) mmol/g, $p<0.001$; tab. 1).

Changes in the absolute content of lactate in MMH were characterized by their regular steady reduction with time: fluctuations from (6.343±0.050) mmol/g in 3 hours after the coming of death to (4.850±0.054) mmol/g in 13 hours after death coming, reliably ($p<0.001$) differing in different time intervals of the early PMP.

The dynamics of lactate content in DMH were characterized by its progressive ($p<0.01$) increase within the period from 3 to 9 hours after the coming of death, respectively, from (4.699±0.026) mmol/g to (7.122±0.053) mmol/g; then it gradually decreased down to the level of (5.783±0.036) mmol/g in 13 hours after death coming, it being reliably larger than in the beginning of the early PMP ($p<0.01$).

Rather significative were the dynamics of lactate content in IMH, which were characterized by its progressive ($p<0.01$) increase during the period of 9 hours from the coming of death – from (6.847±0.042) mmol/g in 3 hours after death coming to (12.960±0.085) mmol/g in 9 hours; after that it gradually decreased down to the level of (9.088±0.081) mmol/g in 13 hours after the coming of death.

Also, the dynamics of lactate content in OMH within 13 hours from the coming of death was characterized by a nonlinear regularity, as it was demonstrated by its increase within time intervals of 3-5-7 hours after death coming, respectively, from (3.266±0.031) mmol/g to (3.762±0.020) mmol/g and (4.429±0.043) mmol/g; after that (beginning from 9 hours) the content of lactate reliably decreased down to (2.633±0.039) mmol/g without reaching its initial value.On the whole, during 10 hours of the early PMP the level of lactate in OMH was 81.0% of its initial value.

Table 1. Levels of the content and quantitative-analytical regularities in the dynamics of lactate content in different morphological types of the muscle tissue during the early postmortem period depending upon the prescription of death coming
Tabela 1. Poziomy i wartości ilościowo-analityczne w dynamice zawartości mleczanu w różnych typach morfologicznych tkanki mięśniowej we wczesnym okresie pośmiertnym w zależności od zgonu

Content (Y) of lactate and its informativeness	Postmortem time intervals (hours)					
	3	5	7	9	11	13
In homogenates of the myocardial muscles, MMH, mmol/g I_M=1.238bits	6.343±0.050	7.161±0.044	7.865±0.043	7.217±0.039	5.653±0.043	4.850±0.054
	0.000	0.197	0.385	0.212	0.148	0.296
	$Y_M=0.06x^4-0.797x^3+3.193x^2-4.078x+7.964;R^2=0.999$					
In homogenates of the intercostal muscles, IMH, mmol/g I_R =1.088bits	6.847±0.042	10.751±0.075	12.155±0.088	12.960±0.085	10.881±0.111	9.088±0.081
	0.000	0.415	0.157	0.087	0.212	0.217
	$Y_R=0.08x^5-1.378x^4+8.884x^3-27.31x^2+41.84x-15.27;R^2=0.98$					
In homogenates of the diaphragm muscles, DMH, mmol/g I_D =0.772bits	4.699±0.026	5.098±0.053	6.422±0.059	7.122±0.053	6.730±0.068	5.783±0.036
	0.000	0.108	0.264	0.135	0.077	0.188
	$Y_D=0.043x^4-0.689x^3+3.509x^2-5.952x+7.787;R^2=1.00$					
In homogenates of the oesophageal muscles, OMH, mmol/g I_O =0.997bits	3.266±0.031	3.762±0.020	4.429±0.043	3.740±0.028	3.371±0.028	2.633±0.039
	0.000	0.177	0.200	0.206	0.135	0.279
	$Y_O=0.017x^4-0.222x^3+0.753x^2-0.334x+3.03;R^2=0.931$					

Thus, in short form (fig. 1) the level of lactate in different types of MT was characterized by fluctuations with increasing terms of PDC; after all the dynamic lines of lactate content changes, which we obtained (tab. 1), became basic ones in substantiating quantitative temporal dependencies and constructing proper nomograms for forensic diagnosis of PDC by the content of lactate in MT.

The quantitative dependencies between the content of lactate and PDC, that we statistically justified, have the analytical form (polynomial stages 2-5) and their use enabled us to represent the revealed regularities and determine "intermediate" (between time intervals, with an accuracy of at least đ<0.01) values of lactate content, thereby in its turn making it possible to increase the accuracy in diagnosing PDC.

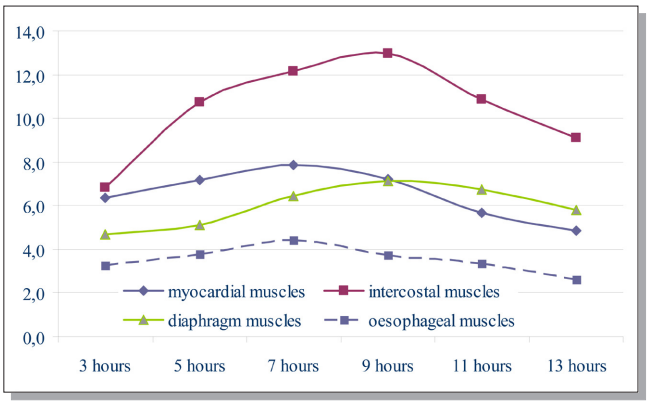

Figure 1. The comparative dynamics of the absolute content (mmol/g) of lactate in different morphological types of the muscle tissue during the early postmortem period depending upon the prescription of death coming
Rycina 1. Porównawcza dynamika bezwzględnej zawartości (mmol/g) mleczanu w różnych typach morfologicznych tkanki mięśniowej we wczesnym okresie pośmiertnym w zależności od zgonu

Besides, using methods of clinical informatics, we calculated informational values for dynamic changes in the content of lactate for each time period and each type of MT. In particular, it was revealed that the total informativeness of determination of lactate for diagnosing PDC by MT of the myocardium was I_M=1.238 bits, by MT of the intercostal muscles I_R =1.088 bits, by MT of the diaphragm I_D=0.772 bits, by MT of the oesophagus I_O = 0.997 bits. It should be noted (tab. 1) that the diagnostic value of determination of lactate content depends upon the type of MT and the term of PDC (time interval of the early PMP). Thus, within the time interval from 3 to 5 hours the most informative was the content of lactate in MT of the intercostal muscles (I=0.415bits), while during the time interval from 5 to 7 hours its content in MT of the myocardium was of the highest diagnostic value (I=0.206 bits). Proceeding from the above, the choice of the criterion "lactate content in MT of the myocardium" is the most reasonable and preferred (a higher total diagnostic value), but in concrete tasks of forensic examination (FE) one can use other criteria (for example, in case where approximate terms of PDC are available).

In order to apply to practice of FE the regularities, revealed by us in the process of this investigation, and to introduce them into the work of medical examiners we constructed a graphic nomogram and made its simplified (traditional), tabular form for determining PDC by the level of lactate in different types of MT. The presented nomograms make it possible to determine PDC by both a single diagnostic criterion and several ones; in order to provide accuracy at a level of p<0.05 it is enough to use one criterion (for example, "lactate content in MT of the myocardium"), but for improving the accuracy (and in conditions of presence of morphological material) it is necessary to use several criteria (tab.2).

In natural conditions of examination of a corpse the following morphological material (in the amount of 100 mg) was isolated by means of postmortem biopsy: MT of the myocardium, MT of the oesophagus, MT of the diaphragm, MT of the intercostal muscles. In conditions of biochemical laboratory the

Table 2. An example of forensic determination of PDC by the value of lactate content in MT
Tabela 2. Tabela 2. Przykład kryminalistycznego oznaczenia PDC na podstawie zawartości mleczanu w MT

Prescription of coming		**Lactat econtentin homogenate of muscles (Y, mmol/g)**							
Minutes	**Hours**	**Myocardium, Y_M**		**Oesophagus, Y_O**		**Diaphragm,Y_D**		**Intercostal, Y_R**	
1	**2**	**3**	$Y=0.06x^4-0.797x^3+3.193x^2-4.078x+7.964;R^2=0.999$	**4**	$Y=0.017x^4-0.222x^3+0.753x^2-0.334x+3.03;R^2=0.931$	**5**	$Y=0.043x^4-0.689x^3+3.509x^2-5.952x+7.787;R^2=1.00$	**6**	$Y=0.080x^5-1.378x^4+8.884x^3-27.31x^2+41.84x-15.27;\ R^2=0.984$
180	**3 hours**	**6.37**		**3.24**				**6.85**	
210	3 h 30 min.	6.48		3.40		4.59		8.59	
240	**4 hours**	**6.69**		**3.56**		**4.65**		**9.66**	
270	4 h 30 min.	6.95		3.72		4.83		10.31	
300	**5 hours**	**7.22**		**3.87**		**5.10**		**10.75**	
330	5 h 30 min.	7.48		4.00		5.41		11.10	
360	**6 hours**	**7.69**		**4.10**		**5.75**		**11.44**	
390	6 h 30 min.	7.84		4.16		6.09		11.79	
420	**7 hours**	**7.90**		**4.19**		**6.39**		**12.15**	
450	7 h 30 min.					6.65		12.49	
480	**8 hours**					**6.85**		**12.76**	
510	8 h 30 min.					6.98		12.90	
540	**9 hours**					**7.04**			
570	9 h 30 min.								
600	10 hours								
630	10 h 30 min.								
660	11 hours								
690	11 h 30 min.								
720	12 hours								
750	12 h 30 min.								
780	13 hours								

above MT fragments (100 mg) were homogenized in the physiological solution in the proportion of 20:1 (100 mg in 2.0 cm^3). After that the samples were centrifuged during 10 minutes at a speed of 3,000 rpm; 2.0 µl of the supernatant fluid were added to 200 µl of the working buffer-enzymatic solution, incubated during 5 minutes at t =37.0°C, and then the optic density was measured at a wavelength of 545 nm. The amount of lactate was calculated by the formula: lactate = C_{st}*(A_s/A_{st})*10 (mmol/g), where C_s is the standard amount of lactate, A_s is the optic density of a sample, A_{st} is the standard optic density, 10 is the conversion factor for 1.0 g of MT. The following values of the content of lactate were obtained: MMH_L = 7.52 mmol/g; OMH_L = 3.94 mmol/g; DMH_L = 4.59 mmol/g; IMH_L = 10.83 mmol/g. Proceeding from results of biochemical determination of lactate activity in MT homogenates and using the nomogram (fig. 1), one can conclude that PDC varies and corresponds to the following terms (See the tabular nomogram): 1) by lactate content in MT of the myocardium – from 5 hours 30 minutes to 6 hours, 2) by lactate content in MT of the oesophagus – also from 5 hours 30 minutes to 6 hours, 3) by lactate content in MT of the diaphragm – from 4 hours to 4 hours 30 minutes, 4) by lactate content in MT of the intercostal muscles – from 5 hours to 5 hours 30 minutes.

Hence, by data of biochemical examination of lactate content in different types of MT, PDC ranged from 4 hours to 5 hours 30 minutes from the moment of sampling of biopsy material. It should be noted that extrinsic factors (factors of the environment, where a corpse is after death), which can affect the dynamics of changes in the content of lactate in different types of MT, were not taken into account; the studies were conducted in usual conditions for preservation of corpses.

Using morphological data from 30 corpses and PDC, which was verified in them before, we carried out inverse approbation of the nomogram technique for determination of PDC and revealed that the accuracy of determination for the term of PDC ranged within ±(1.0÷1.5) hours, with diagnostic inaccuracies of the first (α) and second (β) type being at the level of 10.0-15.0%.

CONCLUSIONS

It was proved that the content of lactate in all MT homogenates changed regularly (and nonlinearly), but the initial and final levels of lactate content differed depending upon the type of MT. Besides, the dynamics in changes of the content of lactate within the time period of 3÷13 hours from the moment of death coming differed upon the type of MT too. The quantitative analytical and graphical dependences of the change in the content of lactate in MT within the early PMP, revealed during the research, made it possible to substantiate relevant nomograms. Limitations for using the nomogram technique are as follows: PDC more than 7 hours, unknown conditions of the stay of a corpse after the coming of death (influence of environmental factors). Advantages of the technique consist in the integrity of biochemical examination of different types of MT and simplicity in interpretation of findings. The application of the nomogram technique for assessing PDC by lactate content in MT makes it possible to improve the accuracy of diagnosis for terms of the coming of death up to 90 minutes.

Prospects of further researches regarding improvement in the accuracy of diagnosis of PDC are related to study of informativeness of other structural-biochemical markers of MT.

REFERENCES

1. Bachinsky VT.: Advanced diagnostic capabilities of the previous prescription of death (problems and prospects). Materials of scientific conference “Achievement in the galuse of marine medicine and problem nutrition during medical and medical examinations at the forensic examination and at the forensic examination of corpses”, Lviv, 2016; 302-304.
2. Bashynska I, Kovalova O, Malovichko O, et al.: Risk Management of Innovative Socially Significant Projects. International Journal of Advanced Research in Engineering and Technology. 2020; 11(4): 294-305.
3. Cherkashyna L, Konoval N, Shklyar A, et al.: Study of structural and biochemical changes in the muscular tissue of the oesophagus for solving the problem of diagnosing the prescription of death coming. Pol Merkur Lekarski, 2020; 48 (283): 42-44.
4. Cherkashyna L, Konoval N, Shklyar A et al.: The dynamics of changes in biochemical markers of the state of tissue in intercostal muscles during the early postmortem period. Pol Merkur Lekarski, 2020; 48 (283): 45-48.
5. Cherkashyna L, Shklyar A, Demikhova N, et al.: Lipofuscin content in the muscle tissue during the early postmortem period: improvement of forensic diagnosis of the prescription of death coming. Polish Medical Journal. 2020; 48 (284): 35-39.
6. Garazdyuk MS, Bachynsky VT, Vanchulyak OY, et al.: Determining the prescription of death by two-dimensional mapping of polarization-heterogeneous images of polycrystalline liquor films. Clin Exp Pathol, 2016; 15 (1): 36-42.
7. Gaiseniuk F, Driianskaia V, Drannik G, et al: Proinflammatory cytokines in patients with pyelonephritis Lik Sprava, 2013; 6: 32-37.
8. Gladkikh DB: Forensic diagnostics of the prescription of the onset of death by the supravital reaction of the pupils. Abstract of the PhD dissertation, Kyiv, 2016;19.
9. Gurov OM, Kozachenko IM, Kutsenko SV, et al.: Determining the prescription of the onset of death in the early post-mortem period by the supravital reaction of the pupils to the action of pilocarpine. Criminal Foren Med.: An Interagency Scientific and Methodological Collection, 2014; 59: 443-451.
10. Konoval NS.: Analysis of archival forensic examinations for determining the limitation period of death. Forensic examination, 2018; 2: 32-35.
11. Konoval NS.: The variability of the criterion of the study of the limitation of the onset of death in the early period. Ukrainian J Med Biol Sport. 2018; 3(5/14): 231-236.
12. Kuzovkov AV, Vavilov AY.: Objectification of diagnostic algorithms for establishing the limitation of human death by the dynamics of tympanic temperature. Modern Probl Sci Educat. 2017; 2: 12.
13. Marushchak M, Krynytska I, Milevska L, et al.: The changes of activity of effector caspase cascade components in case of alimentary obesity in rats. Bangladesh J Med Sci. 2017; 16 (2): 252-258.
14. Moskalenko VM, Voronenko YV.: Social Medicine and Health Organization: textbook, Ternopil, 2002; 50-75.
15. Olkhovsky VO, Golubovich LL.: Determining the prescription of an onset of death: a monograph, Kharkiv: Brovin OV, 2017; 168-173.
16. Olkhovsky VO, Golubovich LL, Khizhnyak VV.: Determining the duration of the post-mortem period in forensic expert practice: current state and prospects. Exp Clin Med. 2016; 4(73): 154-162.
17. Prokopenko O, Holmberg R, Omelyanenko V: Information and communication technologies support for the participation of universities in innovation networks (comparative study). Innovative Marketing. 2018; 14(3): 17-29.
18. Prykhodko O, Gulaya V, Yarmolenko O et al.: Microscopic changes in the organs of rats under conditions of general dehydration of the organism. Azerbaijan Med J. 2016; 4: 95-100.
19. Smiyan OI, Loboda AM, Manko YA et al.: Dynamics of content of some minerals in teenagers with cardiovascular system pathology against the background of chronic tonsillitis. Wiadomosci lekarskie. 2018; 71(4): 861-864.
20. Sopel O, Krynytska I, Marushchak M, et al.: Differential diagnosis of hepatopulmonary syndrome (HPS): Portopulmonary hypertension (PPH) and hereditary hemorrhagic telangiectasia (HHT). Bosnian J Basic Med Sci. 2017; 17(4): 276-285.
21. Teslyk T, Yarmolenko O, Bumeister V, et al.: The remodeling of lungs under the influence of alloxan-induced hyperglycemia. Romanian J Diab Nutr Metab Dis. 2020; 27(1): 45-49.
22. Yarmolenko O, Sikora V, Bumeister V, et al.: Age-dependent cardioprotective action of meldonium on heart remodeling under the experimental hypoosmolar hyperhydration. Bangladesh J Med Sci. 2019; 18(2): 395-401.
23. Zarutskiy Y, Tkachenko A: Surgical treatment of the injured persons for combined cranio-abdominal trauma in an acute period of traumatic disease. Klin Khir. 2015; 11: 5-8.

Disclosure: The authors declare no conflict of interest.

Received: 10.09.2020
Revised: 26.09.2020
Accepted: 20.02.2021

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