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The effect of vibroacoustic therapy on the structural integrity of erythrocytes and platelets in patients with acute exogenous poisoning

M.S. Makarov✉[1], Yu.S. Goldfarb[1,2], A.V. Badalyan[1,2],
A.Yu. Simonova[1,2,3], M.M. Potskhveriya[1,2]

[1]N.V. Sklifosovsky Research Institute for Emergency Medicine,
3 Bolshaya Sukharevskaya Sq., Moscow 129090 Russia;
[2]Russian Medical Academy of Continuous Professional Education,
2/1 Bldg. 1 Barrikadnaya St., Moscow 125993 Russia;
[3]Lopukhin Federal Research and Clinical Center of Physical-Chemical Medicine of Federal Medical Biological Agency,
1A Malaya Pirogovskaya St., Moscow 119435 Russia

✉Corresponding author: Maksim S. Makarov, Dr. Sci. (Biol.), Senior Researcher, Scientific Department of Biotechnologies and Transfusiology, N.V. Sklifosovsky Research Institute for Emergency Medicine, makarovms@sklif.mos.ru

Abstract

Background. *Vibroacoustic therapy is used as a non-drug method of correcting respiratory disorders in various diseases, including acute poisoning. The effect of vibroacoustic therapy on blood cells currently remains unexplored.*

Objective. *To evaluate the impact of vibroacoustic therapy on the morphofunctional rate of erythrocytes and platelets in patients with acute poisoning in patients with acute poisoning.*

Material and methods. *Thirty eight patients with complicated acute poisoning transferred to the Toxicology Department of the N.V. Sklifosovsky Research Institute for Emergency Medicine were*

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examined. In 19 patients, along with the standard therapy, a vibroacoustic therapy was performed using a VibroLUNG device (the main study group); the other 19 patients received only standard therapy (the comparison group). Vibroacoustic therapy began on the 2nd day after the patient admission to the Toxicology Department. The course of vibroacoustic therapy consisted of 2–9 procedures. Morphofunctional analysis of erythrocytes and platelets in all cases was performed before the start of the vibroacoustic therapy (before treatment) and before discharge from the hospital (1–2 days after completing the vibroacoustic therapy course).

Results. *In both groups, before treatment, we noted normal morphofunctional rate of erythrocytes and normal level of platelets with granules in the circulating blood. The level of severely damaged or altered platelets was only slightly higher than normal and did not differ between the groups. Meanwhile, in 50% of patients, platelets had a tendency to spontaneous activation and hyperactivation. Before discharge, the morph functional parameters of erythrocytes and platelets did not significantly change in both groups, while treatment with vibroacoustic therapy allowed to eliminate or reduce spontaneous platelet activation in 7 of 9 patients in the main study group. In the comparison group spontaneous platelet activation was absent in only 3 of 10 patients. In parallel, the time till pneumonia resolution turned statistically significantly reduced, by 1.5 times.*

Conclusions. *In acute exogenous poisoning with complicated course, the risk of spontaneous platelet activation and hyperactivation increases. Vibroacoustic therapy does not violate the structural integrity of circulating erythrocytes and platelets. Vibroacoustic therapy, using the VibroLUNG device, reduces the tendency of platelets to spontaneous activation and hyperactivation, reduces the time for resolving pneumonia.*

Keywords: acute poisoning, vibroacoustic therapy, erythrocytes, platelets, morphofunctional rate, adhesion on glass, spontaneous activation

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MFPR, Morphofunctional platelet rate
pCS, poisoning with corrosive substances
PGR, platelets with granules
PMD, platelets with membrane damage
SSP, spindle-shaped platelets
VAT, vibroacoustic therapy

Background

Currently, vibroacoustic therapy (VAT) is used as a non-drug method for correcting respiratory disorders in various diseases. Pulmonary functional disorders, especially pneumonia, are common complications, including complications from acute exogenous poisoning [1, 2]. The therapeutic effect of VAT is aimed at improving bronchial drainage, recruiting alveoli and improving ventilation-perfusion ratios in the lungs [3]. Moreover, during VAT, the frequency of the influencing signal constantly changes over a wide range, which can have a varying effect on the body's systems, including the circulating blood. Patients with acute exogenous poisoning have an increased risk of damage to blood cells, primarily platelets and erythrocytes [4, 5]. Meanwhile, exposure to various physical factors can cause changes in the structural and functional organization of platelets and erythrocytes. In particular, the impact of vibroacoustic waves on blood cells remains unstudied at present.

The objective was to evaluate the effect of vibroacoustic therapy on the morphofunctional erythrocyte and platelet rates in patients with acute poisoning.

Material and methods

The work examined 38 patients aged from 18 to 80 years (25 men, 13 women, the mean age 44±13 years) with a complicated course of acute poisoning, 36 of whom were transferred from the Intensive Care Unit to the Toxicology Department of the N.V. Sklifosovsky Research Institute for Emergency Medicine. There was poisoning with psychopharmacological agents in 14 patients, with neurotoxicants (drugs of the opium group, psychodysleptics, ethanol) in 12, with corrosive substances (CASs) in 2. The course of disease was complicated by the development of either unilateral or bilateral pneumonia in all the patients. Examination and treatment of patients with acute poisoning was performed during the rehabilitation period i.e. after the end of the Life Support, emergency detoxification measures, and intensive therapy. The hospital length of stay made from 4–27 days; the outcome of poisoning in all cases was favorable. All patients received conservative (baseline) therapy, including enhancement of natural detoxification (gastric lavage, bowel cleansing, forced diuresis), restoration of effective hemocirculation, vitamin therapy, nootropic, symptomatic therapy, administration of histamine H_2 receptor blockers, antispasmodics, hormones, antibiotics, taking antacids (for pCS), sedatives, if indicated.

In addition to drug therapy, we used VAT using the VibroLUNG device to treat pneumonia. The patients were allocated into two groups: the main study group consisting of 19 people (12 men, 7 women), in whom VAT was used along with baseline therapy, and the comparison group consisting of 19 people (13 men, 6 women), who received only the

baseline therapy. The groups were comparable in terms of gender and age characteristics, and the severity of the disease. Vibroacoustic therapy was initiated on the 2nd day after the patients had been admitted at the Toxicology Department. One VAT procedure was performed daily. During the procedure, two signal emitting devices of the "VibroLUNG" machine were used, which were tightly applied to the surface of the chest, approximately in the projection of the inflammatory infiltrate (infiltrates) area in the lungs, so that the sonic waves propagated into the lungs, causing vibrations in the structures of the pulmonary parenchyma. The frequency of the influencing signal was constantly changing, which provided a number of effects, including the effect of resonance [1, 3]. The procedure duration was 5 minutes, the course included 2–9 procedures. VAT was discontinued after the inflammatory process in the lungs had resolved, positive dynamics of laboratory parameters and improvement in the general condition of the patients achieved.

To assess the changes in platelets and erythrocytes in patients with acute poisoning, the quality of platelets and erythrocytes was also assessed in 20 donors of blood components (13 men, 7 women, the mean age 39±11 years). In donors, the morphofunctional analysis of cells was performed 1–2 hours after donation of blood components; in patients, the analysis was performed before the initiation of VAT (before treatment) and before the discharge from hospital (1–2 days after the VAT termination). For the study, venous blood was sampled from donors and patients into standard tubes with ethylenediaminetetraacetate used as a preservative. The erythrocytes and platelets were studied using vital fluorochrome dyes, followed by analysis of the cells in a fluorescent microscope. To stain erythrocytes, a mixture of trypaflavin and rhodamine C was used. When stained with trypaflavin-rhodamine C, structurally complete erythrocytes (disc-shaped cells) do not have

luminescence or have a very narrow luminescent area along the edge of the cytoplasm. In erythrocytes of altered shape, the peripheral luminescence of the cytoplasm intensifies; in severely damaged erythrocytes, the entire cytoplasm is diffusely stained. When examining erythrocytes in the blood, the relative contents of the main morphological types of these cells were assessed: disc-shaped erythrocytes (norm, 85–92%), erythrocytes with an uneven edge (norm, 4–6%), echinocytes (norm, 4–6%), and deformed erythrocytes (norm, 0-3%). In addition, the presence of “shadows” of erythrocytes in blood (erythrocytes with a very low hemoglobin content and marked damage to the plasma membrane) was assessed [6]. For platelet analysis, a dye based on trypaflavin and acridine orange was used [7]. Staining with trypaflavin-acridine orange allows one to assess the structural integrity of the platelet, the presence and number of granules in platelets, the integrity of platelet membranes, the adhesive activity of platelets and their morphofunctional rate. During the study, we assessed the proportion of platelets with granules (PGR) (biologically complete platelets), (norm, 35–75%), the morphofunctional platelet rate (MFPR) (norm, 75–130 points) the content of platelets with severe membrane damage (PMB) (norm, 1–3%), as well as the intensity of platelet adhesion to glass. Normally, the duration of adhesion of one platelet is 10–30 minutes from the moment the platelet suspension is applied on the glass. During this period, the shape of the platelet changes and platelet granules are released (degranulation). In addition, spindle platelet (SSP) content (%) was assessed. SSPs are absent in the circulating blood of healthy people and can be detected in various pathologies.

During statistical data processing, the median (Me), 1st and 3rd quartiles (Q1;Q3) were calculated, the Mann–Whitney test was used to assess differences in results between groups, the Wilcoxon test was used to assess differences between the values of related parameters, and

Fisher's exact test was used to assess the significance of differences in frequencies. Differences were considered statistically significant at a significance level of more than 95% ($p<0.05$).

Results

All examined patients had normal erythrocyte quality before treatment and before discharge from hospital. The content of the main morphological types of erythrocytes in all cases corresponded to the norm and did not differ from similar values in the blood of donors (Table 1); there were no “shadows” of erythrocytes in the circulating blood of patients. It is worth noting that before treatment in both groups, almost all patients had small erythrocyte sludges in their blood, i.e. columns of cells containing 4–7 red blood cells. After the treatment, erythrocyte sludges were also detected in the same patients.

Table 1. Morphofunctional parameters of erythrocytes in donors and patients with acute exogenous poisoning

Blood component donors (n=20)				
Assessed parameters	**Discoid red blood cells**	**Jagged-edged red blood cells**	**Echinocytes**	**Deformed red blood cells**
	90 (88;91)	5 (4;5)	4 (4;5)	1 (1;2)
Patients with vibroacoustic therapy (n=19)				
Stage of investigation	**discoid red blood cells**	**red blood cells with a jagged edge**	**echinocytes**	**deformed red blood cells**
Before treatment	89 (87;90)	5 (4;6)	4 (4;5)	2 (2;3)
Before discharge	89 (87;91)	5 (4;6)	4 (3;4)	2 (1;3)
Patients without vibroacoustic therapy (n=19)				
Stage of investigation	**Discoid red blood cells**	**Jagged-edged red blood cells**	**Echinocytes**	**Deformed red blood cells**
Before treatment	88 (86;90)	6 (4;6)	4 (4;5)	2 (2;3)
Before discharge	89 (88;90)	5 (4;5)	4 (3;5)	2 (1;3)

It is seen from Table 1 that no perceptible changes in the assessed parameters during the treatment process.

Before treatment, the morphofunctional parameters of platelets in did not differ statistically significantly between two groups (Table 2).

Table 2. Morphofunctional parameters of platelets in donors and patients with acute exogenous poisoning

Blood component donors (n=20)				
Assessed parameters	**PGR, % Me(Q1;Q3)**	**MFPR, scores Me(Q1;Q3)**	**PMD, % Me(Q1;Q3)**	**SSP, % Me(Q1;Q3)**
	50 (43;60)	92 (78;106)	2 (2;3)	0 (0;0)
Patients with vibroacoustic therapy (n=19)				
Stage of investigation	**PGR, % Me(Q1;Q3)**	**MFPR, scores Me(Q1;Q3)**	**PMD, % Me(Q1;Q3)**	**SSP, % Me(Q1;Q3)**
Before treatment	48 (42;56)	89 (76;103)	5 (3;6)*	1 (0;4)*
Before discharge	49 (42;54)	85 (75;100)	4 (3; 7) *	1 (0;4) *
Patients without vibroacoustic therapy (n=19)				
Stage of investigation	**PGR, % Me(Q1;Q3)**	**MFPR, scores Me (Q1;Q3)**	**PMD, % Me (Q1;Q3)**	**SSP, % Me (Q1;Q3)**
Before treatment	48 (35;57)	90 (63;106)	5 (4;8)*	1 (0;3) *
Before discharge	45 (34;60)	86 (61;108)	4 (4;10)*	1 (0;3) *

Note: * $p<0.05$ compared to values in donors

Patients in both groups had normal values of PGR and MFST, the PMD level was only slightly higher than normal, the SSP level was low and did not exceed 1–2% in most patients. The number of microscopically distinguishable granules in all SSPs was noticeably lower than in normal disc-shaped platelets; most of the granules in were bound to the cell membrane, indicating their readiness for exocytosis (release). In both groups, SSPs did not form contacts with other platelets and did not affect their activity during the adhesion of individual platelets to glass. Meanwhile, in 9 patients of the main study group and 10 patients from the comparison group, the platelets with granules had a pronounced tendency to spontaneous activation and hyperactivation; upon contact

with glass, the platelets of patients began to adhere within 1–2 minutes, frequently forming flattened platelet aggregates with a diameter of up to 20 μm, the rate of granule release by adhesive platelets was also increased and amounted to 3–10 minutes from the onset of adhesion. There could be identified SSPs along the periphery of such aggregates. In 3 patients of the main study group and in 4 patients from the comparison group, the platelet hyperactivation was accompanied by the presence of platelet conglomerates with a diameter of up to 10 microns in the circulating blood. In the group with VAT treatment, the platelet hyperactivation was observed in 3 cases in patients under 40 years of age, in 4 cases in patients from 40 to 60 years of age, and in 2 cases in patients over 60 years of age; in the comparison group, the number of platelet hyperactivation cases in these groups was 3, 4 and 3, respectively. In patients without hyperactivation, no platelet conglomerates were detected in blood of patients in both groups before treatment. In the group where VAT was used, among the parameters of patients with platelet hyperactivation and without hyperactivation, a statistically significant difference was detected only in the SSP level amounting to 4 (1;5)% and 0.5 (0;1)%, respectively ($p<0.05$). This difference was absent in patients in the comparison group. The remaining morphofunctional parameters of platelets in both groups did not differ statistically significantly, comparing to the values before treatment.

Before discharge from hospital (after VAT), the morphofunctional parameters of platelets in both groups did not undergo statistically significant changes ($p>0.05$). However, in the group where VAT was performed, spontaneous activation and hyperactivation was noted only in 2 of 9 patients. In 5 patients who had platelets prone to hyperactivation before treatment, hyperactivation was completely absent after VAT; in other 2 patients it was less pronounced than before treatment: the rate of

platelet adhesion decreased to 7–10 minutes and the size of the aggregates formed on the glass did not exceed 10 μm. On the other hand, patients in the main study group showed heterogeneous PMD and SSP dynamics: these parameters could either decrease or increase and changes in PMD and SSP did not correlate with the presence or absence of platelet hyperactivation before VAT treatment. In the comparison group, spontaneous activation and hyperactivation of platelets persisted in 7 of 10 patients, and the PMD and SSP levels in all patients did not change statistically significantly compared to the values before treatment.

Analysis of clinical results showed that the use of VAT allows a statistically significant, 1.5-fold reduction in the treatment time for pneumonia (Table 3). Compared with the data of patients in whom VAT was not used, there was also a reduction in the length of hospital treatment (on average 1.3 times) in the main group, but this difference was not statistically significant.

Table 3. Clinical efficacy of complex treatment for psychopharmacological agent poisoning at the rehabilitation stage

Parameter (days)	Group of patients		p
	Comparison group (without VAT Me (Q1;Q3)	Main study group (with VAT) Me (Q1;Q3)	
Duration of pneumonia (according to X-ray data)	6.0 (5.0;7.5)	4.0* (3.0;6.0)	0.024
Treatment duration	13.0 (9.5;15.5)	10.0 (7.0;13.0)	>0.05

Note: *p<0.05 compared to the result in the comparison group

Discussion

According to the literature, VAT stimulates blood and lymph flow, reduces tissue swelling and bleeding [2, 3], therefore, it could be assumed that the VAT effect will not cause disturbances in the structural and functional organization of erythrocytes and platelets. The study showed

that all patients maintained normal morphofunctional erythrocyte rate after VAT. On the other hand, exposure to VAT did not affect the formation of erythrocytes sludges. Adhesion of erythrocyte membranes occurs under conditions of their damage or as a result of the adsorption of large volumes of protein and other components, including drugs [4, 6]. It is possible that the presence of erythrocyte sludges in patients after VAT can be caused by drug therapy, and also can be a consequence of the underlying disease course.

Human platelets exhibit high sensitivity to many forms of chemical and physical exposure [7–12]. The structural and functional organization of platelets undergoes changes under the influence of factors such as extremely high frequency radiation, membrane oxygenation, and cardiopulmonary bypass [8–10]. The analysis showed that patients suffering acute exogenous poisoning with neurotoxic substances had a normal level of platelets with granules (biologically complete platelets) before treatment, and the number of platelets with pronounced defects was slightly increased. Thus, in case of poisoning with neurotoxic substances, there is no sudden destruction of platelets. On the other hand, amid poisoning, the platelets of many patients showed a tendency to spontaneous activation and hyperactivation, which increases the risk of thrombotic complications. The conducted study showed that the level of platelets with granules and the level of platelets with membrane damage were not statistically significantly changed by VAT, and thus VAT was not associated with significant changes in the platelet population. Meantime, the use of VAT made it possible to reduce the tendency of platelets to spontaneous activation and hyperactivation in vitro in the patients whose platelets exhibited increased rates of adhesion to glass and hyperactivation prior to VAT. After VAT, in some patients, along with a decrease in platelet hyperactivity, the proportion of spindle-shaped

platelets decreased. According to the literature, spindle-shaped platelets in vitro are formed under the impact of certain physical and chemical factors (high blood pressure, organic acids, impaired gas exchange) [11]. In acute exogenous poisoning, the oxygen saturation of tissues is impaired, circulating blood cells experience an oxidative stress, which creates a significant risk of damage to the membranes and cytoskeleton of platelets [12, 13]. These factors can lead to the SSP formation, which, as can be seen from our material, can be more pronounced with a tendency of platelets to hyperactivation and spontaneous activation. In patients of the main study group, whose platelets had a tendency to hyperactivation, the SSP level before exposure to VAT was higher than in patients without platelet hyperactivation, while the number of microscopically distinguishable granules in SSPs was noticeably lower than in normal disc-shaped platelets. It can be assumed that, against the pathology, SSP were partially degranulated, which increased the risk of their irreversible activation even without exposure to a standard inducer. It is believed that platelets of elderly people have an increased tendency to spontaneous activation, increasing the risk of thrombotic complications in pathological conditions [14, 15]. In our study, the platelet hyperactivation was observed both in individuals over 60 years and under 40 years of age, indicating that characteristic features of platelets were not associated with gender and age characteristics, but were determined by individual characteristics of the course of the disease.

Identification of the risks of spontaneous platelet activation is currently very urgent [16–19]. There are instrumental approaches to solving this problem, while known methods often do not allow characterizing the morphofunctional platelet rate. Therefore, the assessment of platelet hyperactivity using morphofunctional techniques seems very relevant.

Conclusion

In case of a complicated course of acute exogenous poisoning, the risk of spontaneous activation and hyperactivation of platelets increases. Vibroacoustic effects do not break the structural integrity of circulating erythrocytes and platelets. Vibroacoustic therapy using the VibroLUNG device acting on the platelet hemostasis link, reduces the tendency of platelets to spontaneous activation and hyperactivation, which can have a sanogenetic effect in the pathology under study.

Based on the conducted study we made the following conclusions:

1. In patients with acute poisoning with psychopharmacological agents, neurotoxicants and corrosive substances, before treatment, the normal morphofunctional erythrocyte rate and the level of platelets with granules were noted in the circulating blood. Levels of severely damaged or altered platelets were only slightly higher than normal and did not differ between groups. At the same time, in 50% of patients in both groups, platelets had a tendency to spontaneous activation and hyperactivation.

2. At the stage before discharge from hospital, the morphofunctional parameters of erythrocytes and platelets did not change statistically significantly in the main study group (treatment with vibroacoustic therapy) and in the comparison group (treatment without vibroacoustic therapy). The changes over time in the levels of platelets with membrane damage and spindle-shaped platelets in the circulating blood in the main study group were heterogeneous.

3. The treatment using vibroacoustic therapy eliminated or reduced the tendency of platelets to spontaneous activation in 7 of 9 patients (77.8%) in the main study group, while in the comparison group, the tendency of platelets to spontaneous activation before discharge from

hospital was absent in only 3 of 10 patients (30%) (the difference in results when assessed using Fisher's exact method was statistically significant, p=0.02).

4. The use of vibroacoustic therapy makes it possible to statistically significantly reduce the treatment time for pneumonia by 1.5 times ($p<0.05$) and the duration of hospital treatment by 1.3 times.

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Information about the authors

Maksim S. Makarov, Dr. Sci. (Biol.), Senior Researcher, Scientific Department of Biotechnologies and Transfusiology, N.V. Sklifosovsky

Research Institute for Emergency Medicine, https://orcid.org/0000-0002-2184-2982, makarovms@sklif.mos.ru

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Yuriy S. Goldfarb, Prof., Dr. Sci. (Med.), Head of the Department of External Scientific Relations, Researcher, Department of Acute Poisoning and Somatopsychiatric Disorders, N.V. Sklifosovsky Research Institute for Emergency Medicine; Honorary Head of the Department, Professor of the Department of Clinical Toxicology, Russian Medical Academy of Continuous Professional Education, https://orcid.org/0000-0002-0485-2353, goldfarbjs@sklif.mos.ru

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Amayak V. Badalyan, Dr. Sci. (Med.), Head of the Department of Acute Poisonings for psychic patients, Leading Researcher, Department of Acute Poisonings and Somatopsychiatric Disorders, N.V. Sklifosovsky Research Institute for Emergency Medicine; Associate Professor of the Department of Clinical Toxicology, Russian Medical Academy of Continuous Professional Education, https://orcid.org//0000-0003-4429-2503, badalyanav@sklif.mos.ru

20%, the development of the study design and the study arrangement, analysis and interpretation of the study results, revision of the text of the article

Anastasiya Yu. Simonova, Cand. Sci. (Med.), Leading Researcher, Department of Acute Poisonings and Somatopsychiatric Disorders, N.V. Sklifosovsky Research Institute for Emergency Medicine; Head of the Department of Clinical Toxicology, Russian Medical Academy of

Continuous Professional Education; Senior Researcher, Information and Advisory Department, Lopukhin Federal Research and Clinical Center of Physical-Chemical Medicine of Federal Medical Biological Agency, https://orcid.org/0000-0003-4736-1068, simonovaau@sklif.mos.ru

15%, data analysis and interpretation

Mikhail M. Potskhveriya, Cand. Sci. (Med.), Chief of the Scientific Department of Acute Poisonings and Somatopsychiatric Disorders, N.V. Sklifosovsky Research Institute for Emergency Medicine; Professor of the Department of Clinical Toxicology, Russian Medical Academy of Continuous Professional Education, https://orcid.org/0000-0003-0117-8663, potskhveriyamm@sklif.mos.ru

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