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Acute respiratory distress syndrome

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Abstract
The article provides data proving the toxic nature of the respiratory parenchyma lesions of the lungs during acute respiratory distress syndrome development. They determine the severity of the disease until death, which can't be prevented by drug therapy or various methods of mechanical ventilation, up to extracorporeal membrane oxygenation. The accumulation of large molecular toxic products unable to be excreted by the kidneys is the indication for extracorporeal detoxification. Moreover, using hemosorption, it is possible to remove not only toxic substances but pathogens as well. Subsequent plasma exchange in addition to detoxification leads to the body's immune defense restoration due to the removed plasma replacement with freshly frozen donor plasma. The experience of treating 153 patients with varying ARDS severity stages confirms the need to use extracorporeal detoxification and immunocorrection methods in its treatment.

Keywords: acute respiratory distress syndrome, endotoxemia, immunosuppression, surfactants, extracorporeal detoxification, hemosorption, plasma exchange

Introduction

Acute respiratory distress syndrome (ARDS) is a life-threatening form of respiratory failure that affects approximately 200,000 patients each year in the United States, resulting in nearly 75,000 deaths annually. Globally, ARDS accounts for 10% of intensive care unit admissions, representing more than 3 million patients with ARDS annually [1].

Acute lesions of the lungs respiratory parenchyma are a frequent and severe complication of a number of diseases. First of all, it is a viral and bacterial pneumonia, which sometimes takes a malignant course and is accompanied by a massive, sometimes total, bilateral lesion of the respiratory parenchyma with poorly controlled respiratory failure, which can lead to death in a few days or sometimes hours.

Given the difficulties of treating this complication, accompanied by high mortality rate (from 10 to 90%, depending on the severity of the lesion), this problem seems extremely urgent [2].

Pathogenesis of acute respiratory distress syndrome

Given different etiology of this complication, the pathogenetic mechanisms are common in all types of ARDS. They consist in development of toxic interstitial, and then alveolar pulmonary edema due to impaired permeability of the cell membranes caused by endotoxemia [3, 4].

To verify this, we conducted studies of blood toxicity in patients with acute pneumonia, using a protozoa survival test [5]. The latter were tetrachimenes. If in the blood of healthy people (as well as in animals) the survival is about 20 minutes, then, depending on the severity of the patients' condition, having acute pneumonia, this time reduced down to 10, 5, and even 2 minutes. However, such an increase in blood toxicity could be just one of the acute pneumonia consequences and doesn't have an independent significance in the further development of the lung lesions, which could occur simply due to progression of the main pathological process in the same organ.

In clinical conditions, the local pathological process and the accompanying intoxication are inseparable; therefore, it is impossible to distinguish those changes in the lungs that are a direct consequence of the local pathological process, and those that develop as a result of exposure to toxic products circulating in the blood. On one hand, the process may go in the direction of the alveoli epithelium - interstitium - vascular endothelium, on the other hand - in the opposite direction, that is, from the blood. Only an experimental research can shed light on this question.

Even our first experiments on rabbits with intratracheal administration of pathogenic (isolated from real patients) pneumococci culture gave quite surprising results: in 10-15 minutes this pathogen began to show in the blood and internal organs such as liver, kidneys, and spleen, and the blood toxicity increased to the same level as in patients with acute pneumonia [5]. The same bacteremia seems to occur in patients as well, and it is an early start of antibiotic therapy that prevents to detect this phenomenon in most of the patients; it is found only in about 30% of them.

A microscopic examination of the lungs of these animals revealed a picture of interstitial and alveolar edema associated with inflammation that is expansion of the interalveolar septa with interstitial infiltration by lymphoid cells; in the alveoli there was a liquid rich in protein. The lungs weight then increased by 32%. When reproducing the similar level of endotoxemia by intravenous administration of pneumococci live or killed culture, pulmonary edema was also observed, similar to that described

above, but on a slightly smaller scale. The lungs weight increased by 25%.

It is interesting that both in intratracheal and intravenous administration of the pathogen, edema and extravascular fluid volume increase were also observed in the liver, kidneys, and spleen [6].

The experiments showed that it is not the spread of the primary pathological process along the airways but endotoxemia that plays the key role in the development of the lung respiratory parenchyma lesions that occur on the background of acute pneumonia. It is due to the release of both living microbes and inflammation products into the circulation, leading to endothelial cell membranes permeability disorder associated with both liquid and even protein outflow into the interstitium. This was proved by significant hypoproteinemia with development of endotoxemia - the total protein in experimental animals decreased in an hour from 67.0 to 51.9 g/l, mainly due to albumin (albumin-globulin coefficient decreased from 1.3 to 0.7). These observations confirm that the hypoproteinemia observed in patients, reaching a protein level of 40 g/l, is also due to the outflow of proteins into the interstitium through the more porous membranes of the capillary endothelium. This correlates with the increase in lymph protein concentration, also approaching the level of 40 g/l, instead of the normal 20 g/l.

Thus, in patients with acute pneumonia, a double type of lung lesion develops such as the primary, depending on the spread of pathogens through the respiratory tract, and the secondary, resulting from the penetration of microbes and inflammatory products from the primary focus into the bloodstream associated with toxemia development. Moreover, the danger to the pulmonary parenchyma is no longer from the respiratory tract epithelium, but from the blood through the vascular endothelium [7, 8].

All types of these toxic substances increase the cell membranes permeability, and not only of the lungs, but also of almost all other internal organs and tissue structures associated with disorder of their functional state and development of multiple organ failure syndrome. And although this condition is most often characterized as ARDS according to the most manifested signs of respiratory failure and radiologically detected changes, and the remaining organs disorders are not so obvious, it is difficult to imagine an isolated ARDS with normal function of the other organs.

Moreover, a number of vicious circles appear when toxic pulmonary edema and hypoxemia stimulate hypoxic involvement of membrane permeability; damage to the kidneys contributes to an additional fluid retention in the body – thus, edema is stimulated as well as retention of toxins when toxemia is increasing; damage to the liver associated with suppression of its detoxification function also increases toxemia; toxic myocardiopathy exacerbates organ microcirculation disorders; toxic encephalopathy also leads to the brain disorders, and the released neuropeptides stimulate neurogenic pulmonary edema. It is this summation of lesions in multiple organ failure that determines the extremely high mortality rate - up to 80% [9]. This multiple organ failure syndrome reflects a biological catastrophe, a type of biological suicide that occurs in a wide range of clinical situations.

Interstitial and alveolar toxic pulmonary edema blocks the gas exchange at the alveolar level due to expansion of the blood-air barrier (alveolar-capillary membrane). This leads to severe and poorly treated parenchymal respiratory failure, which is the leading factor in thanatogenesis.

Toxic products circulating in the blood affect not only the vascular wall endothelium, but also the ingredients of the blood itself, mainly its cells. In particular, the activation of platelets contributes to their adhesion, the emergence of microaggregates, which become like nuclei for the subsequent formation of DIC reactions cascade, stimulating microvascular thrombosis and bleeding.

Thus, ARDS is a secondary toxic lesion of the respiratory parenchyma that occurs not only in the lungs diseases, but also in a number of other pathological conditions having common pathogenetic mechanisms. The main one is the toxic disorder of the cell membranes permeability.

Clinical findings and diagnostics of acute respiratory distress syndrome

One of the most characteristic and early manifestations of ARDS is shortness of breath, cyanosis, and tachycardia. On auscultation in the early stages harsh breathing is noted, and then bronchial one due to the increased sound transmission of the pulmonary stroma in interstitial edema. In the later stages, breathing may be impaired and not even transmitted at all (“dumb” or “silent lung”), especially in the posterior regions. Wheezing is not plentiful, often dry, although crepitant rale can be heard. Sputum is scarce or absent, in contrast to hemodynamic ("cardiac") pulmonary edema, which is characterized by a plentiful amount of foamy sputum.

In the blood gases analysis the very first sign is hypocapnia, then hypoxemia appears and increases, and only in the terminal phase hypercapnia does increase. Metabolic alkalosis is characteristic.

The X-ray reflects the main stages of ARDS development. At the initial stage, signs of interstitial pulmonary edema are characteristic: a general increase in the pulmonary pattern over all compartments due to perivascular and peribronchial fluid accumulation. As ARDS progresses and the alveolar phase of the edema develops, first there are small (so called blizzard symptom) and then larger focal and confluent shadings, mainly in the posterior lower regions of the lungs.

Approaching the terminal phase is characterized by intense homogeneous shading of the lung tissue in the lower and middle sections, merging with the shadows of the heart and liver. Only the apices of the lungs keep airiness.

As noted above, ARDS is accompanied by severe hypoproteinemia, which leads to decrease of oncotic pressure and hypovolemia with blood clotting, which exacerbates microcirculation disorders and impairs hemodynamics. Disorders of the latter and the direct effect of toxic substances on the kidneys are accompanied by decreased diuresis and positive water balance in general; impaired liver function reflects a moderate increase in bilirubin and transaminases concentration.

Moderate leukocytosis is possible, but often the total number of leukocytes is not increased, with a slight shift to the left and a relative decrease in the number of lymphocytes. The phagocytic activity of leukocytes also decreases. Toxic granularity of neutrophils is noted.

One of the few methods of objectification and quantitative

assessment of the intoxication level is the determination of the average molecular oligopeptides blood concentration (medium molecules level). Normally, the level of medium molecules is kept within 220-250 Units. In moderate intoxication this indicator increases up to 350-400 Units; in severe - up to 500-600 Units with maximum increase of up to 900-1200 Units, which indicates an incurable condition [8 Voinov V.A., 2016]. In recent years, to diagnose the condition severity in septic complications, procalcitonin level determination is used.

The more accurate criteria to diagnose ARDS are various methods to determine the extravascular lung water (EVLW) [10]. In vivo, including in dynamics, various colorful, radionuclide methods and thermal dilution can be used. At the same time, it is noted that even a twofold increase in the volume of EVLW may still not be accompanied by changes determined clinically, radiologically, or by laboratory tests (blood gases). When we observe the first signs of ARDS, it means that the pathological process has already become advanced.

Given the data above, one can doubt the true rate of this complication. It can be assumed that the ARDS phenomenon is an almost constant companion of many pathological conditions. It is not about the ARDS rate, but about the rate of severity degree in ARDS. Although it is an extreme point of view, it is nevertheless closer to the essence of the problem than its complete denial in a number of diseases, since, having diagnosed ARDS we can timely raise the question of pathogenetic therapy.

Acute Respiratory Distress Syndrome Treatment

Traditional treatment approaches are largely determined by inadequate assessment of the causes of this complication. If only the inflammatory component of pathogenesis is considered the cause, efforts are directed towards providing antibiotic therapy, and to search new more powerful antibiotics of super-wide range action. The process progression is believed to be associated only with the low sensitivity of pathogens to antibiotics.

Naturally, it would be unreasonable to reject the use of antibiotics in cases where the microbial flora is the main etiological factor. The same applies to the viral nature of ARDS. It is also necessary to increase the body's resistance by taking vitamins, immunostimulating drugs, cardiotonics, membrane stabilizers, antioxidants, and antiplatelet agents.

However, even the most effective antibiotics, killing microbes, are not able to eliminate their toxins. Even the microbial bodies themselves require a special elimination system, and considering the reduced phagocytic activity, they are retained in the body and continue their harmful effects. The fact of microbial infection activation already indicates the weakening of the body's defense system, its inability to cope with the pathological condition on its own. Respiratory viral infection contributes even more to immunosuppression, especially in patients weakened by chronic diseases, and intoxications.

Since there are no specific treatment methods for ARDS found yet, one can only rely on mechanical ventilation [1, 11]. Oxygen therapy does not cause any doubts and objections, since the alveolar-capillary membrane expansion in edema dramatically slows the diffusion of oxygen through it. For carbon dioxide, being more soluble still retains the ability to eliminate adequately. However, restoration of the lungs gas exchange function using mechanical ventilation seems rather illusory. The mechanical ventilation is really able to correct ventilation respiratory failure, but alveoli diffusion disorders make it unsuccessful in case of parenchymal respiratory failure. In Europe and America they still hope to adjust some special ventilation parameters, in particular, to increase pressure in the airways in the end of expiration (PEEP).

It is true that maintaining such a pressure at the level of 5-10 cmH_2O for some time can improve the gas exchange due to the alveoli over-inflation that are not yet completely filled with effusion [12]. However, at the same time as special physiological studies showed the EVLW volume neither decreases, nor increases due to the greater porosity of the overstretched alveolocapillary membrane, the increased filtration area. Besides, in increased intrathoracic pressure the lymph outflow from the pulmonary parenchyma slows down. It is known that prolonged mechanical ventilation even in case of ventilation disorders can itself stimulate fluid retention in the lungs, inhibit diuresis, and promote pulmonary barotrauma [13].

In addition, pneumonia and sepsis, which develop not only in the result of microbial insemination of the respiratory tract, but also as a systemic inflammatory response syndrome (septic shock) develops associated with the release of cytokines such as interleukins 6 and 8 (IL-6, IL-8), as well as tumor necrosis factor α (TNF-α). It was noted that an increase in their level occurs 3-4 days before pneumonia occurs [14, 15]. Addition of pneumonia on the background of ARDS is difficult to diagnose, since its signs such as leukocytosis, high fever and radiological changes (lung infiltration) already exist in ARDS and even without infection. On the other hand, endobronchial and pathomorphological studies show the presence of respiratory tract infection on 2–6 days, and signs of pneumonia on 5–12 days of ARDS course.

Due to development of synthetic or semi-synthetic surfactants production methods, their use in treatment of ARDS has become of great interest. However, many studies show only a short-term effect of exogenous surfactant introduction [16, 20].

Our early studies show that surfactant is destroyed due to penetration of toxic products circulating in the bloodstream into the alveoli. Therefore, no matter how much surfactant is added to the lungs, but if toxic substances are not removed from the blood, a newly introduced surfactant will be destroyed just as well as its own [21].

Back in the seventies of the XX century these facts made researchers apply extracorporeal gas exchange, using membrane oxygenators. In animal experiments, it was possible and safe to maintain gas exchange for up to three weeks using membrane oxygenators. This justified their use for auxiliary extracorporeal membrane oxygenation (ECMO) in acute parenchymal respiratory failure.

The first results of ARDS treatment using ECMO were quite encouraging. Indeed, immediately after the connection of membrane oxygenators, gas exchange was restored, and the condition of patients was stabilized. However, there was no significant inverse dynamics of pathological changes in the lungs. After the procedure, the inflammatory and destructive processes were going on. In recent years, the effectiveness of ECMO has increased to 47-60% [22, 24].

Obtaining positive results require up to 16 and even 120 days of ECMO [25, 26]. During this period, one should transfuse significant amounts of donated plasma, platelet concentrates, provide

parenteral nutrition, day and night monitoring and maintenance by highly qualified specialists, which costs for over $100,000. Given such difficulties and the ECMO operations complexity, they are not widely used. However, it has taken a certain place among the ARDS treatments.

Nevertheless, the conservative intensive care methods with various options for mechanical ventilation are still most often used [27].

The presented analysis shows both the complexity of ARDS treatment and the lack of a pathogenetic approach to its therapy, which is due to ignoring the fact of the endotoxic nature of the lungs and other organs damage. As a result, detoxification methods are not used.

Our own initial attempts to use ECMO in ARDS did not give the expected results due to the inability to suspend the progression of pathological processes in the lungs and multiple organ failure, despite the correction of the impaired gas exchange during the operation.

These failures, on one hand, and the results of experimental studies that showed the toxic nature of lesions of the lungs and other organs, on the other hand, convinced us to use detoxification methods. Under these conditions, only direct blood detoxification methods can stop the process progression, and break many existing vicious circles.

Detoxification methods in acute respiratory distress syndrome

During hemosorption (hemocarboperfusion) when up to 3-4 circulating blood volume (CBV) is passed through a column with carbon sorbents, there is quite a complete elimination of many pathological products and even the live bacteria being retained and fixed. For example, in case of infection caused by Pseudomonas aeruginosa on the background of the inadequate antibiotic therapy hemosorption was the only truly effective treatment. There was a decrease of the level of medium size molecules, blood toxicity as a whole (according to the protozoa survival), and the general condition improved. The changes in the lungs shown on the X-ray examination were reversed [8].

Nevertheless, in advanced stages of ARDS associated with severe parenchymal respiratory failure, requiring mechanical ventilation, only ECMO at a rate of 25-30% of the minute volume of the blood flow and lasting up to two days made it possible to gain time, i.e., to maintain gas exchange at the minimal adequate level and during this time to provide more active detoxification. Only such a combination of massive detoxification (up to three hemosorption procedures a day) on the background of ECMO made it possible to reverse organ lesions on extremely severe stages of ARDS. We managed to save seven of ten patients in such an extremely severe condition [7].

It should be noted that it usually takes 2-3 weeks to treat ARDS with ECMO, while in our cases it takes only 15 to 44 hours to stop the ARDS of the same extremely severe degree. And there is only one difference in the treatment tactics: we conducted intensive detoxification using hemosorption during ECMO, which is still ignored.

Here we present a treatment review of 153 patients with ARDS treated in the period from 1998-2013, among whom 67 patients have undergone traditional drug therapy and 86 patients with comparable severity of ARDS have been detoxified by hemosorption or plasmapheresis.

Hemosorption was carried out passing 1-2 CBV through the columns. Membrane plasmapheresis was carried out using Russian plasma filters PFM-800 or PFM-01-TT "Rosa" on devices "Hemofenix" in the plasma exchange mode with removal of 1.2-2.5 l or 0.5 -1.0 CBV and replacement with fresh frozen donor plasma. At the same time, laser irradiation of the blood was performed. In the extremely severe cases of ARDS, ECMO was performed by veno-venous perfusion at a speed of 1.0–1.5 l/min during 15-44 hours, simultaneously with hemosorption every 6-10 hours.

All patients received traditional drug therapy, and as the respiratory failure progressed mechanical ventilation was used, in severe cases with positive pressure at the end of expiration (PEEP).

Three stages of ARDS are distinguished: moderate, severe and extremely severe, according to the level of hypoxemia, medium molecular oligopeptides ("medium molecules") and to the area and intensity of the lung shading shown in X-ray examination (Table 1).

Table 1: Clinical and biochemical signs of ARDS

ARDS severity stage	Middle wight molecules	PaO_2	X-ray lung shading	Respiration
Moderate	350.0±22.5	68.2±1.8 (FiO_2 0.4)	Low zone	Spontaneous
Severe	444.2±45.3	60.3±0.8 (FiO_2 0.7)	Low end middle zones	CPPB
Extremely severe	680.1±52.6	44.7±0.9 (FiO_2 1.0)	Total hepatization	PEEP ECMO

Distribution of patients according to the severity of ARDS is presented in Table 2.

Table 2: Distribution of patients by severity of ARDS and treatment methods

ARDS severity stage		Treatment methods		
		Conventional treatment	Detoxification	
I	Moderate	52	47	99
II	Severe	15	29	44
III	Extremely severe		10	10
		67	86	153

There were no fatal outcomes among patients with a moderate degree of ARDS; however, the duration of treatment using detoxification methods was significantly shorter - 28.0 ± 1.5 versus 40.3 ± 3.3 days in the control group ($p < 0.05$). The

mortality rate in severe and extremely severe stages of ARDS is presented in Table 3.

Table 3: Mortality rate in different ARDS severity stages depending on treatment methods

ARDS severity stage		Treatment methods		
		Conventional treatment	Detoxification (hemosorption or plasma exchange)	Detoxification + ECMO
I	Moderate	0	0	
II	Severe	73.7%	30.8%	
III	Extremely severe			30.0%

It should be noted that a subgroup of patients with an extremely severe stage of ARDS treated only with conventional methods is not considered separately, since mortality in such cases is 100%. As can be seen from the tables, even in moderate stage of ARDS detoxification made it possible to quickly and reliably stop acute lung lesions progression. But in severe stages using detoxification enabled to prevent fatal outcome. It should be noted that the earlier detoxification is used, the more pronounced is its effectiveness. In this case, as a rule, only one hemosorption or plasma exchange procedure, using laser blood irradiation is sufficient to dramatically change the course of the disease and enable the body to cope with the complications, having lower level of drug support. In severe stage of ARDS, it is often required to repeat another two or three detoxification procedures to achieve stabilization and reverse lesions progression. But if detoxification is delayed, not all the patients can be saved.

In extremely severe stage of ARDS with almost total lung damage, there is a severe parenchymal respiratory failure that cannot be stopped by any means of mechanical ventilation. In these cases, ECMO provides faster normalization of the gas exchange, and simultaneous intensive detoxification (up to three procedures a day) contributes to elimination of toxic pulmonary parenchyma edema with restoration of “airiness” of the lungs to some degree shown on X-ray examination even in 7-15 hours. By the time ECMO has been finished it is possible to restore the gas exchange function of the lungs to a completely satisfactory level [7].

Nevertheless, detoxification alone, achieved by hemosorption, is also not enough for a full therapeutic effect, since the body still remains in the state of immunosuppression, which made it possible to develop this serious complication in a certain period of time. A more stable result is obtained by plasma exchange with replacement of the patient’s removed plasma, containing "incompetent" antibodies, immunoglobulins, complement, and opsonins, with freshly frozen donor plasma. Then the above mentioned plasma immune components immediately begin to fight pathogens and other pathological products.

At the same time it should be noted that this approach normalizes not only humoral, but also cellular immunity, since without complementation there is no opsonization of macrophage receptors, without which the capture and subsequent destruction of pathogens is impossible. This provides a more reliable and stable result, especially when replaced plasma is in the volume almost equal with the patient's CPV. Thus, it should be emphasized that it is actually not so much about plasmapheresis, but about plasma exchange. Indeed, in hypoproteinemia it is impossible to remove even a small volume of plasma without immediate replacement with donor plasma in a ratio of 1:1. Photo hemotherapy also helps to restore the level of the immune defense. And in recent years, we have almost completely switched to such tactics.

The following clinical observation gives an example of such an effect of endotoxemia and immunosuppression on occurrence and development of life-threatening ARDS condition and demonstrates the effectiveness of detoxification tactics.

> *A 40-year-old patient S. with sarcoidosis, having been taking hormonal drugs for a long time, developed a total lung lesion with severe multiple organ failure. Gradually increasing immunosuppression determined the scale and speed of viral respiratory infection progression. By the beginning of the apheresis therapy, the patient was in an extremely severe condition. Mechanical ventilation with PEEP did not correct parenchymal respiratory failure and hypoxic coma. The X-ray examination revealed intense and almost total shading (“hepatization”) of the lungs. Hepatic-renal failure was manifested by significant fluid retention in the body associated with increase of creatinine, bilirubin and transaminases. Central hemodynamics was supported by sympathomimetics and there were frequent group polytopic ventricular extrasystoles.*
>
> *On the first stage of apheresis therapy for detoxification hemosorption with laser blood irradiation was performed. The very next day, the condition somewhat stabilized. There was 500 ml of urine received. The X-ray examination showed signs of airiness in the upper parts of the lungs. The normal rhythm with isolated extrasystoles was practically restored and sympathomimetics were canceled.*
>
> *On this background, a repeated procedure of therapeutic apheresis was carried out. It was membrane plasmapheresis with the exchange of 2,000 ml of donor freshly frozen plasma also performed with laser blood irradiation. The next day, there was a restoration of consciousness and independent breathing, followed by a more rapid restoration of the functional state of the lungs and other vital organs followed by complete recovery.*

Massive plasma exchange leads to a more rapid normalization of homeostasis. To compare with hemosorption there is not only a more reliable and complete removal of all pathological products regardless of their electrochemical activity, but also a more complete restoration of all plasma components such as proteins. It is followed by normalization of oncotic pressure and volemic balance, hormonal-enzymatic activity with restoration of autoregulation mechanisms. All this enables to completely prevent the dramatic scenario of ARDS (i.e. toxic pulmonary

edema) development and provides a faster and more complete reverse restoration of other organ disorders as well, a more complete restoration of their functions and, finally, their recovery [8].

Thus, given the insufficient results of surfactant treatment much better results are achieved, using detoxification methods in ARDS. It suggests that the true cause of the surfactant activity decrease is in its inhibition by toxic substances that penetrate the alveoli during toxic deterioration of the vascular permeability. In this case, the administered exogenous surfactant as well as the natural one are affected by these toxic substances and cease its activity.

Detoxification promotes elimination of vascular porosity that is a pathogenetically more justified method of ARDS treatment, since after the toxic substances cease to penetrate into the alveoli and reproduction of the natural surfactant is restored in the coming hours, which eliminates the need of its exogenous preparations.

For a more complete restoration of the immune mechanisms, it is also advisable to combine both hemosorption and plasma exchange with methods of photohemotherapy.

The above mentioned more detailed example, revealing the ARDS pathogenesis and the rationale to use apheresis therapy methods in case of this complication development, also demonstrates the essence of a number of other clinical situations arising from severe burns and injuries, acute inflammatory diseases of the abdominal organs, etc. Active detoxification therapy such as hemosorption or plasma exchange seems more reasonable. And indeed, almost always after the removal of the "toxic burden" from the kidneys, their excretory function is restored. The very next day, diuresis is at least 500-700 ml. At the same time, the functional state of the other vital organs such as the lungs, liver, heart, and brain is improved [28].

With addition of acute liver failure, there is an increase in the level of transaminases - AlAT and AsAT. And the removal of the "toxic burden" from the hepatocytes quickly normalizes the liver function. With an extreme degree of hypoxia, damage occurs to the brain structures up to a deep hypoxic coma. Disorders of both central and peripheral circulation are increasing. But after detoxification their function is also restored.

In an extremely severe course of ARDS associated with multiple organ failure, disorders and hemodynamics occur, which makes it difficult to carry out any extracorporeal detoxification procedures. However, the existing Russian Hemofenix devices make it possible to carry out both plasmapheresis with “Rosa” plasma filters and hemosorption with any available hemosorbents. It can be used even in case of unstable hemodynamics when it is maintained at a relatively satisfactory level only with help of sympathomimetics. This became possible, given the small filling volume of the extracorporeal circuit of this device, not exceeding 65-70 ml, which makes it possible to carry out such a treatment even in infants.

Therefore, the treatment of such patients with ARDS in an extremely serious condition is a rather difficult task. Recently, we have developed treatment tactics that takes into account all the aspects of the ARDS pathogenesis and associated multiple organ failure.

Given the high probability of a number of pathogens circulating in the blood, on the first stage it is advisable to resort to massive hemosorption. In addition to significant detoxification when 1-2 CBV is passed through a sorption column it also provides decontamination that is retention of both living and dead pathogens on the sorbent, considering their growing resistance to antibiotics worldwide. It leads to stabilization of the patients’ condition for the functions of the lungs and all other vital organs are improved.

On the second stage, the very next day, you can start plasma exchange with removal of at least 60-80% of the CPV and replace with an equal volume of fresh frozen donor plasma. Moreover, in addition to detoxification, there is also correction ("prosthetics") of the immune defense system associated with restoration of not only humoral, but also cellular immunity. Very often these hemosorption and plasma exchange procedures are enough for the body to restore its autoregulation systems and recover from a critical state.

It should only be taken into account that a high risk of bleeding requires special tactics for the use of anticoagulants. First of all, heparin is completely eliminated and the prevention of blood clotting in the extracorporeal circuit is provided by sodium citrate solutions (ACD-A) only.

Nevertheless, one should not wait for such extremely severe conditions and conduct adequate treatment on the early stages of ARDS, when the negative dynamics of its development appear evident. In this case, it is necessary to take into account a rather rapid increase in the severity of ARDS in some cases, when literally in a few hours such patients can die.

Conclusion

Thus, both experimental and clinical studies prove the toxic nature of ARDS, which makes it reasonable to carry out various methods of extracorporeal detoxification. On the first stage, it is advisable to carry out sorption detoxification, which allows removing not only pathogens, but also toxic metabolites. Then, during plasma exchange, the removal of toxic products continues followed by replacement with fresh frozen donor plasma and the immunity restoration. Only in this way one can achieve favorable results especially considering the ineffectiveness of drug therapy.

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