CYLINDER OF THE DISPOSABLE MASS EXCHANGE DEVICE FOR HEMOSORPTION

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BACKGROUND Hemocarboperfusion, previously widely used in our country, can universally pass out of use due to the lack of industrial production of disposable mass exchange devices.

MATERIAl AND METHODS Physicochemical properties of materials and design features of the body samples elements of various sizes have been studied.

RESULTS The elements and materials properties of the hemosorption mass exchanger cylinder have been studied. Hydrodynamic parameters of manipulation using the developed cylinders at different perfusion rates have been studied in bench experiments.

CONCLUSION The original cylinder of the disposable mass exchange device for hemosorption, which meets the current clinical needs, has been developed.

keywords: hemocarboperfusion, hemosorption, hemosorbent, cylinder of the mass exchange device, mass exchange device.

INTRODUCTION

It has been over 40 years since a group of enthusiasts from the Soviet Union headed by Y.M. Lopukhin (member of the Academy of Sciences) initiated studies on the nature of the therapeutic action of hemocarboperfusion — blood perfusion through the uncoated carbon hemosorbents [1]. But despite the encouraging results obtained with the inclusion of this technique into the complex therapy for patients with the syndrome of endogenous intoxication, it has not become widely adopted due to frequent complications. The development and establishment of industrial production of uncoated carbon hemosorbents with good hemocompatibility, athrombogenic nature, and high sorption capacity ensured sharp reduction in the frequency and severity of postsorption and intraoperative complications. This circumstance determined the common practice of hemocarboperfusion in the USSR in treatment of a wide range of diseases and conditions involving endogenous intoxication syndrome [2]. The gap of economic ties among the former Soviet republics such as the abandonment of SKN-type hemosorbents which were the "gold standard" for uncoated carbon hemosorbents, led to significant reduction in the use of hemocarboperfusion in practical public health.

Russian scientists were the first to show that the main effect of therapeutic action of hemocarboperfusion is extraction of hydrophobic compounds from the surface of transport proteins and cytoplasmic membranes [3, 4]. Given this fact, a number of foreign companies have developed devices for extracting not only

* This article is the first part of the research conducted by the authors. In the second part, which is also expected to be published in our journal, we will present the results of clinical application of the device for hemosorption.

hydrophilic substances from the body but hydrophobic substances as well. However, the principle of operation of this equipment does not provide deligandization of the formed elements and does not positively affect microcirculation, as in case of hemocarboperfusion. Devices for artificial liver support such as *Mars* and *Prometheus* show complexity in operation. They are produced and sold with expensive set of consumables, which limits their extensive and widespread use even in European countries [5-8].

The main part of the extracorporeal circuit is a mass exchange device that consists of a cylinder and hemosorbent. The nature of the distribution of blood flow in the cylinder, the presence of zones of stagnation, thrombus formation and turbulence largely determine the efficiency of pathogenetically important substances removal from the blood. Mass exchange device design should provide a uniform distribution of blood flow throughout the cross-section of the device. One postulate of hemocoagulology indicates that the thrombosis is initiated in a zone of turbulence, slowing or stopping the blood flow. It is known that the average velocity of blood perfusion through the mass exchanger of this type ranges from 50 to 150 ml per min. In those cases when the ratio of length to width of the cylinder is 2:1 or even 3:1, the maximum blood perfusion is performed along the column axis, which is termed as "centralization" of the blood flow. Here, the stagnation zones are formed in the near-wall layer of the hemosorbent charge mixture with subsequent running of coagulation processes and as a result, preterm onset of thrombosis of hemosorbent charge. It should be noted that the vast majority of currently produced mass exchangers does not meet modern requirements. These disadvantages affect not only their structures, but the materials they are made of [9]. To design and build the cylinder of the mass exchange devices for hemosorption which meet all modern requirements, taking into account technical features of hemocarboperfusion and devoid of the drawbacks of known prototypes, you must perform a number of conditions:

1. The surface of the material of the mass exchange device cylinder must have good hemocompatibility to be hydrophobic, must not cause adhesion of blood cells and lead to the activation of clotting factors.
2. The design of the mass exchange devices should have no areas of stagnation, turbulence, centralization of blood flow, and hydrophobic materials of the device must prevent aggregation of heterogeneous surface of thrombocytes and prevent the launch of the coagulation system in the extracorporeal circuit.
3. Conduction of hemoperfusion through a device within the given parameters should not lead to excessive resistance to blood flow.
4. The cylinder must be a sealed container, eliminating blood loss.
5. For the patient's safety, the device must only be used once.

Thus, the objective of our research was to create a disposable cylinder of a device for hemocarboperfusion, which overcomes the disadvantages of devices currently in use.

MATERIAL AND METHODS

We have chosen samples made of polycarbonate in six sizes, with the inner chamber which is a sealed cylinder of proper forms to be filled with hemosorbent (Fig. 1). Study of hydrophobic properties of the device components was conducted by the method of determining the wetting of the materials in contact with blood. During the experiment, cylinders and lids made of polycarbonate as well as caps, filters-dividers made of polyurethane and silicone O-rings were completely immersed into a container with a solution of sodium chloride for 2, 12 and 24 hours. Thereafter, the elements were removed from the investigated vessel and weighed after free flow of fluid for 10 min.

The tightness of the universal cylinder was checked by feeding medical gas (oxygen) into the device at a pressure of 4.9 Atmospheres from the centralized supply valve. The device was then completely immersed into a container of liquid with a temperature of 20±1° *C*. Presence or absence of leakage was monitored visually by release of air bubbles.

The perfusion resistance of the mass exchange device was examined by comparing the fluid pressure at the inlet and outlet of the device without hemosorbent at different perfusion rates (Fig. 2). It was determined by the pressure gradient at the inlet and outlet of the mass exchange device and was measured in mm Hg. The solution of sodium chloride from the thermostatted tank (37±1) ° *C* was used as perfusate. The lids were screwed onto the cylinder with a torque wrench with an operating torque of 20 Nm (6 kg) with the arm length of 33 cm. The device was installed in a vertical position and unions were connected to the inlet and outlet blood tubing with gauges attached to them. The mass exchanging device was filled with the sodium chloride by a perfusion pump.

In order to optimize the processes of distribution of blood flow within the cylinder of the device, it was decided to use elements, which we called "filter-dividers" as filters. Filter-dividers are circular plates with a thickness of not more than 0.5 mm, in which about 10,000 polysulfone capillaries of 0.1 ± 0.05 diameter are filled with polymeric compound (polyol and isocyanate) (Fig. 3).

To study the distribution pattern of fluid flow as it passes through the filters we have developed original bench apparatus and original method of bench experiments (Fig. 4).

RESULTS AND DISCUSSION

In order to create a model of the cylinder for the mass exchange device it was necessary to examine the possibility of using elements of various sizes. The material meeting the requirements of a good hemocompatibility and most suitable for the manufacture of the device cylinder, was polycarbonate. This synthetic material is biologically stable and does not degrade upon contact with blood. According to statistics, the volume of industrial production of materials with similar properties is about 0.1% of the global total of all types of biopolymers [10]. Confirmation of the highest possible hemocompatibility of polysulfone is the fact that it is used for the manufacture of artificial heart valves and elements of the artificial heart. During the research, the mass exchanger design was proposed, which was a cylindrical column where the ratio length/diameter depending on its volume might vary from 5:1 to 10:1, allowing to change the amount of hemosorbent in the device and, accordingly, adjust its sorption capacity. At the ends of the cylinder the lids were tightly screwed, under which there were the input and output filters-dividers of blood flow made of polysulfone. To ensure the best possible seal between the lids and filter-dividers, silicone O-rings were placed.

Fig. 1. General view of the mass exchange devices

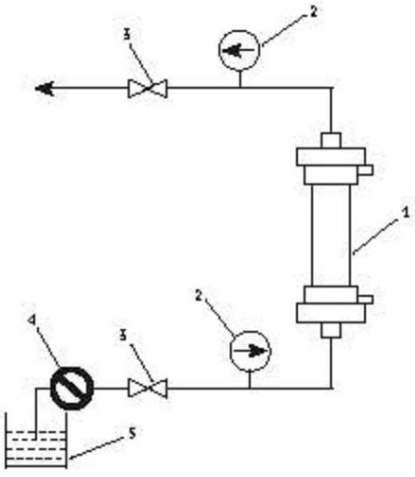

Fig. 2. Diagram of perfusion resistance control. 1 - the cylinder; 2 - pressure gauges; 3 - clips; 4 - a blood pump; 5 – tank with a thermostatted liquid

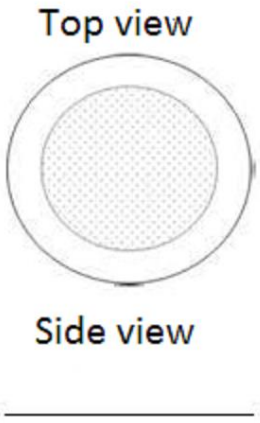

Fig 3. Filter- divider of the blood flow

Designed sample of the cylinder of the mass exchange devices has universal properties; it can be filled with any hemosorbent (or activated carbon, such as biospecific sorbent). This constructive solution is most effective in terms of mass exchange and prevention of thrombus formation in stagnant zones. Mass exchange device can be highly adaptively switched into the circuit of hemosorption with blood lines in short terms.

Cylinders of mass exchange devices have six sizes with the volume of the inner chamber from130 to 450 ml and a ratio of length to diameter of the device ranging from 10:1 to 5:1. A wide range of length to diameter ratio is explained by the fact that in urgent clinical practice different methods of hemosorption are used. Thus, to achieve the therapeutic effect in the biospecific hemosorption it is sufficient to use relatively small amounts of hemosorbent (70 to 150 cm^3) at perfusion rate in the range of 60±20 ml / min. In this situation, mass exchanger with the ratio length/ diameter of 10:1 ensures better prevention of formation of dead zones, so they can be used in supervision of patients with low weight or in pediatric practice. When we should use hemosorbents of 400-500 cm^3 and perfusion rate of 120±20 ml / min in order to achieve a sufficient therapeutic effect of hemosorption, the ratio may be 5:1. This constructive solution is most effective in terms of both mass exchange and prevention of thrombus formation in stagnant zones. This range of cylinder sizes, the universal nature of its filling and commutation significantly extends the capabilities of acute care by emergency detoxification service. At the same time, there is a choice of sizes of mass exchange devices based on height and weight of patients, the severity of their condition and the nature of the disease [9].

Study of hydrophobic features of materials of the cylinder, and the degree of its surface wetting with liquid, showed no statistically significant change in their weights after exposure to the liquid. This confirms the data in the literature on the hydrophobic properties of the materials used to manufacture the cylinder's parts. This fact ensures the absence of thrombocytes adhesion on the heterogeneous surface of mass exchanger parts and a high degree of athrombogenic property and hemocompatibility of the device. Study of the sealing of the mass exchanger by the above method showed no release of gas bubbles which indicates tightness inside the cylinder, it is sufficiently reliability, and hence the impossibility of leakage from the device.

The study of the perfusion pressure gradient according to the pressure gauges (Fig. 2) showed that it did not exceed 6±1 mm Hg in the inlet and outlet of the device (Table. 1). As can be seen, the change in perfusion rate from 10 to 200 ml / min does not result in a statistically significant increase in the gradient of the perfusion resistance.

Table 1

The pressure gradient of the inlet and outlet

Perfusion rate, ml / min	10	50	100	150	200
Perfusion resistance, mmHg	X	X + 1	X + 3	X + 4	X + 5

The study of the distribution of the liquid through filters-dividers of the blood flow was performed by the original method developed (Fig. 4). To do this, the filter surface was divided arbitrarily into two sectors: central and peripheral. The central sector, located in the center of the filter, had an area circumscribed by a half radius from the center and peripheral had the rest of the filter area. More than 50 bench perfusions of 0.9% sodium chloride solution, stained with methylene blue, were performed through various sizes of mass transfer devices cylinders when the perfusion rate changed from 10 to 200 ml / min. As can be seen on Fig. 4, along the entire length of the cylinder perpendicularly to the input filter -divider and with one profile close to it, the sections were placed in polyvinyl chloride tube of a 5-mm diameter. Fifty of these tubes were placed in the cylinder with a 40 mm diameter. Other free ends of the tubes located in the central and peripheral portion of the filter were placed in the measuring tube. Using a peristaltic pump, perfusate was pumped into the suction tube at different speeds. The distribution of fluid flow through the filter at different speeds divider is shown in Table 2. In a filter diameter of 40 mm, the area of the central sector was 3.1 cm^2 and peripheral area was 9.4 cm^2.

When pumping fluid at a rate of 40 ml per minute through the filter, the volume of perfusion through 1 cm^2 of its surface in the central zone was 3.9±0.1 ml, which was almost 1.5 times higher than the rate in the peripheral zone. As the figure increased to 100 ml per minute, the fluid flow in the central and peripheral sector equalized. With further increase in flow rate of fluid to 160 and 200 ml / min, this tendency persisted.

After many experiments it was visually confirmed that the filter-divider distributed blood flow throughout the cross sectional area of the cylinder in a plug flow way. Such filling of the inner chamber of the cylinder prevented the formation of zones of turbulence, vorticity and thus thrombosis. The rate of blood perfusion can vary from minimal of 10-20 ml / min to 150 ml / min or higher.

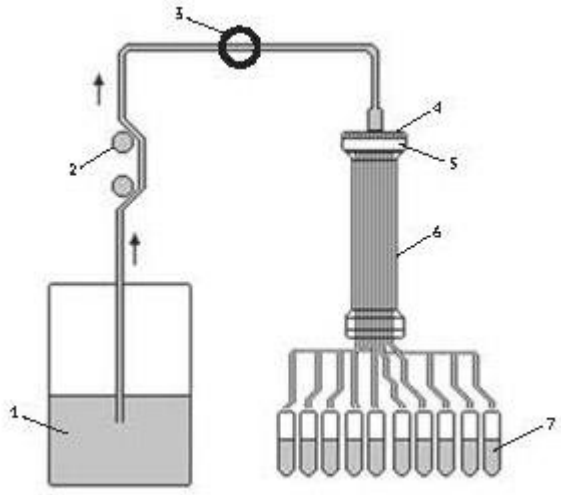

Fig 4. The diagram of on the bench experiment on features of the mass exchange device cylinder 1 - vessel with solution; 2 - peristaltic pump; 3 - pressure gauge; 4 - a lid of the cylinder; 5 – filter-divider; 6 – cylinder of the mass exchange device; 7 – test tubes

Thus, the presence of inlet and outlet filters-dividers in a mass exchange apparatus with a diameter of 4 cm, evenly distributes liquid across the cross sectional area of the cylinder in the most frequently used in the clinic perfusion modes. Design features of the filter-divider promote uniform filling of the inner chamber of the mass exchanger cylinder from the center to the periphery, which prevents current and near-wall slowing and stasis of blood, prevent hemosorbent from leaking of the device and sorbent particles from getting into the blood of the patient, provide efficient and safe hemosorption. Transparent polycarbonate cylinder provides visual control over the hemoperfusion with the direct passage of blood through hemosorbent in the device. Due to the hydrophobic properties, the polycarbonate cylinder of the developed device has a high hemocompatibility. This material has impact resistance, thermal stability, biological inertness and lack of toxicity. There is no adhesive activity of the inner surface materials of the unit with respect to the blood corpuscles. In addition, to ensure the tightness of the cylinder we found an original solution to eliminate the space between the cylinder and lids by pouring polyurethane (utility model patent of the Republic of Belarus "cylinder of the disposable mass exchange device for hemosorption ", № 800). [11] Due to the physico-chemical properties of the materials, as well as the fact that commercial production of the parts for the mass exchange device is performed at a high technological level, these products are easy to use and require minimal preparation time for emergency extracorporeal procedures. The completion of the tests of elements for relatively inexpensive and effective cylinder of the disposable mass exchange device allowed it to be recommended for hemosorption.

Table 2

Changes in the distribution pattern of fluid flow through the filter-diveder at different speeds of perfusion

	Flow rate							
	40		100		160		200	
	central	peripherial	central	preripherial	central	pperipherial	central	pperipherial
Volume of fluid passing through central and peripheral zones, ml/min	12 ± 3	27 ± 7	25 ± 4	74 ± 6	41 ± 5	118 ± 5	49 ± 6	150 ± 4
Volume of fluid passing through 1 cm^2 of the filter area	3.9 ± 0.4	2.9 ± 0.1	8.1 ± 0.2	7.9 ± 0.3	13.3 ± 0.2	12.6 ± 0.4	16.2 ± 0.3	16.3 ± 0.2

CONCLUSION

Thus, our research allowed for the first time to prove and develop the basic component of the mass exchange device for hemoperfusion – a universal cylinder, manufactured with the use of modern high-quality materials, in 6 sizes of various volumes. Connectors of the device require the ability to connect to disposable lines for hemosorption and hemoperfusion on the equipment, including foreign products for an extended replacement therapy like *Multifiltrat*, *Prometheus* and others. The inner chamber of the cylinder is 100% ready for various types of hemosorbents.

Designs are made using high-tech, have no analogues in the Republic of Belarus and other CIS countries and have a number of significant advantages in comparison with foreign protorypes.

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