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Biospecific hemosorption

on the device Hemofenix

methodical instructions

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INTRODUCTION

Therapeutic apheresis is increasingly used in clinical practice. Many human diseases are accompanied by disturbances of the internal environment, which largely determine the severity of the disease and even are the main causes of adverse outcomes, despite the use of the most modern medications or surgery. Such problems arise in acute inflammatory diseases of the thoracic and abdominal cavities, severe trauma and burns, poisoning and infectious diseases, when the syndrome of endogenous intoxication is arise. Under these conditions, detoxification with endotoxins and other pathological products removal allows to achieve a breakthrough in the course of the disease.

This primarily relates to acute pancreatitis, which occurs on a background of severe endotoxemia on the basis of a sharp increase in the level of proteolytic enzymes and the resulting increase in the content of an average molecular weight substances, activation of lipid peroxidation with the suppression of the antioxidant defense system. In this case, the liver first takes the brunt of the enzyme eluted into the blood from the pancreas, to a certain point, while maintaining the ability to inactivate them. Then comes the depletion of its detoxifying function, which determines the transition to the decompensated phase of endotoxemia with the increase in the level of transferases, phenol, ammonia, fatty acids and other toxic metabolites.

One of the most effective methods of detoxification is hemosorbtion. This method is based on the ability of certain compounds to bind a variety of substances, including pathogenic, due to surface (adsorption), volume (absorption) or chemical interactions (chemisorption). It should be noted that many of the natural metabolites – protein molecules, lipids, mucopolysaccharides – have "closed" structure of the molecules that are electrically, and therefore – and biologically inert. Therefore, the majority of physiological metabolites contact with sorbents is not terrible, they quietly pass by them and remain in circulation, which minimizes the possible harmful effects of the procedure. By passing through a column of 1-2 BCV occurs fairly complete elimination of many pathological products and even delay and fixation of live bacteria that, for example, when an infection caused by *Pseudomonas aeruginosa*, represent the only truly effective method of treatment because of the low adequacy of antibiotic therapy. Reduced the level of middle molecules, blood toxicity in general (for protozoa survival time), the general condition improves.

Hemosorbtion proved effective at destructive processes also, and even gangrene of the lungs. Naturally subjected ichorization areas lungs could not restore the structure, but decreased perifocal changes and intoxication that allows you to quickly prepare patients for the inevitable surgery, which are easier to carry.

Biospecific hemosorbtion based on the ability of some sorbents, in particular, "Ovosorb" selectively removing the activated forms of serine proteases that accompanies many of the critical state in clinical practice – from allergies to sepsis. Correction proteinase inhibitory imbalance there is allows to interrupt the development of organ disorders, reduce and improve the results of treatment.

Device Hemofenix is designed for not only the membrane plasmapheresis, but hemosorption on one needle method using any hemosorption columns permitted for medical use, including the column "OVOSORB", and a set of lines KMAP-01.

The basis of the device "Hemofenix" is a type of ventricular pump driven by an electromagnet. The device works biphasic. While squeezing the tube pumping blood to the sorption column and then back into the vein. At this point, is carried out the hemosorption process. Upon termination of compression pump tube passively straightened due to its flexibility, which helps blood sampling from the same vein. Translational motion of the blood is promoted by two solenoid valves, each of which is compressed by the three tube line simultaneously. During the phase of the return of blood the right valve is opened – open line of blood flow in the column and the branch of the anticoagulant, which allows to fill a special collapsed bag of the dosing device. In order to reduce the recirculation of blood in the system during hemosorption expedient return line blood **M5** put in the nest of the right valve, designed for line, escaping the plasma (it is not used at hemosorption). During the phase of blood sampling valve left open – open line of blood sampling, the branch supply isotonic sodium chloride solution and branch guide anticoagulant from dosing bag into the pump tube.

STRUCTURE, PRINCIPLES OF DEVICE AND SAFETY

The process of return of blood is controlled by a pressure gauge that measures the pressure of blood in front of the sorption column. Patient safety is ensured by means of ultrasonic and capacitive sensors, stopping the machine with the appearance of air inclusions (bubbles or falling blood level in the filter trap) in the return line of blood.

The main body of the device has special rack-holders on which are mounted filters – air trap, air inclusions ultrasonic transducer, two clamps for mounting the sorption column, vials or packets with the solutions, as well as special slotted dosing device.

Pumping compartment for security is under a removable protective cover.

The control panel consists of a two-line alphanumeric scoreboard indicator, which displays the basic parameters of the device, reports of it condition and of emergency situations that may arise during the operation.

For more information about using the "Hemofenix" is in the instructions for this unit.

Logistical support

- **Portable device for single-needle membrane plasmapheresis "Hemofenix"**
- **Main line single use "KMAP-01"**
- **Biospecific antiproteazny hydrogel hemosorbent "OVOSORB" in the mass exchange module for hemosorption (MMG)**
- **Adapters** (disposable - come with hemosorbent).
- **Sterile styling** with scissors, clamps Billroth, swabs and balls, bottles or bags with isotonic sodium chloride solution and a solution of sodium citrate (ASD-A).

METHODS of HEMOSORPTION

Preparations for hemosorption

1 For the hemosorption necessary to prepare the workplace, are located there, with the laying of sterile (sterile "Plain", scissors, clip Billroth, a glass of alcohol, gauze balls and swabs, bandages), adhesive tape, tonometer.

2. Check the expiration date of the sorption column, tightness of individual containers. Check the expiration date set lines KMAP-01, sealed individual containers. Unpack the package, remove the line and put in the workplace (sorption column and line must be used immediately after opening the package, in violation of its integrity products use is prohibited).

3. Building the system is carried out under aseptic conditions in accordance with the scheme shown in Fig. 1.

4. Lay the lines on the unit Hemofenix, remove the top of protecting cover and place according to the scheme pump element **Н** in its bed, and then cover protection put in place again.

5. Fold the cover of the left fastening device **ЭМК1** and fix in it the line for blood collection **М1** and tubes **М2, М3**, leading to the packages with anticoagulant and isotonic sodium chloride solution, and then re-lock this cover.

6. Soft dosing bag of anticoagulant **МД** inserted into one of the slots of the dosing device **UV** so that the flow direction is upwards.

7. Filter – air trap **ЛВ** set into the appropriate slot of the sensor air of filter holder, and the return line **М5** fix then over the sensor in the air in the direction of line **ДВ2** not from right to left, as in plasmapheresis, and the **left-to-right (!!!)**.

8 Fold the cover right pinch device **ЭМК2** and fix leading line **М4** blood flow to the adsorption column, repeat the branch leading from the metering device to the package with an anticoagulant and blood return line.

9 Remove the protective caps from the connectors leading branch line, transition insert with red nipples **П1**and input (red) fitting sorption columns **КГ** and connect them.

10 Remove the protective caps from the connector outlet branch line, insert transition **П2** with blue fittings and output (blue) fitting sorption columns **КГ** and connect them.

11 **Close all the clips on the line "!".**

12 Branch line that goes to the pressure sensor **ДД** connected to the latest tightly bolted to the union.

13 Remove the protective cap and filter dropper needle **К1** connect with bottle **Е1** with an anticoagulant and install it into the right slot transfusion rack unit. Filter dropper **К1** fill half the volume.

14 Remove the protective cap and filter dropper needle **К2** connected to bottle **Е2** with isotonic sodium chloride solution. Set last in the nest on the left transfusion rack unit. Filter dropper **К2** fill to half volume. Attention is drawn to the desirability of pre-warming the sorption column and solutions used.

15 Do not removing the protective cap from the infusion site **УИ**, immerse it in a sterile empty vial.

16 Open the clamp on the branch blood sampling **Ж1** and clamp **Ж4** on a branch feeding anticoagulant and fill this branch together with a bag-dispenser until the pump tube. Close clamps **Ж1** and **Ж4**.

17 Open the clamp **Ж5** on the branch supplying isotonic sodium chloride solution and clip **Ж1** on branch of drawing blood and fill the latter. Close clamp **Ж1**.

18 Continue filling the pump segment, lifting the right side of the latter in order to completely remove air from it.

19 Turn on the device, which plug the power cord into electric socket mains voltage of 220 V, 50 Hz. At the rear of the device turn on the power switch to «I». Subsequent filling of the extracorporeal circuit should begin in the "pumping" mode.

20 Press "Start" button and continue the displacement of air from the adsorption column by fluid flow from bottom to top, and then fasten the column in the special slot in the position of the fluid flow "top-down". Leave the device working a few more minutes to complete cessation of the air intake from the sorption column into a trap, and then open the clamp **Ж3** Duct air trap and remove air from the latter. Close the clamp **Ж3** on the air vent.

Attention! *Draws attention to the need for the widest possible removal of air from all parts of the extracorporeal circuit. Otherwise, there is excessive recirculation of blood in the device and reducing the actual perfusion rate compared with the rate on the display board. Besides, the sorption column "Ovosorb" is able to be compressed at a negative pressure and over distended at positive. That is why it is connected to the device other than a membrane plasma filter that provides therein a constant positive pressure.*

21 Continue laundering sorption column isotonic sodium chloride solution according
to the instructions attached to the column.

22 After the implementation of the program of the laundering the sorption column stop device (press the "Stop"). Remove the protective cap from the infusion part **УИ**, connect the needle (attached to a set of line) and enter it in a bottle with isotonic sodium chloride solution.

23 In a bottle with isotonic sodium chloride enter 5000 IU of heparin (if there are no contraindications to it), press the "Start" button and start recycling in the extracorporeal circuit of device for sorbent saturation with heparin for 10 minutes (according to the instructions for use of this hemosorbent).

24 Press the "Stop" button. The device is put on "work" regime when involving all security and lock the device in this mode, and at this regime it should work until the end of the procedure.

25 Touchstone alternate clamping jaws **Ж1** and **Ж2** on branchts intake and return blood to check the reliability of the automatic locking and sealing compounds in the system as a whole. Switch off the machine. Again pinch all the clips.

Performing hemosorption

1 Perform venipuncture one of the peripheral or central venous catheter with the insertion of the venous catheter with diameter of 1.1 - 1.4 - 1.7 mm (20-16G). If necessary enter intravenously heparin at a dose to 150-300 U/kg.

2 Remove the needle of infusion part УИ from container with sodium chloride, remove this needle, and this infusion part connected to the venous catheter.

3 Inflate the cuff of tonometer on the arm above the venipuncture to the level of 20-30 mm mercury, open the locks **Ж1** and **Ж2** on the lines of the intake and return of blood and clamp **З4** of anticoagulant line. Press the "START".

Anticoagulant tactics

Anticoagulant tactics determined coagulation parameters, hematocrit, and should provide an adequate rate of blood perfusion through the sorbent recommended by the manufacturer (20-60 ml per min). By taking into account the indications and possible contraindications it is possible to use only heparin or sodium citrate only, or a combination thereof. When performing of hemosorption using only heparin is added to the vial with isotonic sodium chloride solution **K2** and dosed 10-15 drops with each cycle. When using only sodium citrate the dosing bag must initially insert in to the first metering gap (0.9 mL). By increasing duration of the return time this bag must be moved into the second slot, leaving out 1.1 ml anticoagulant. With simultaneous use of heparin and sodium citrate, the latter may be maintained at a level of 5-7 drops per cycle.

Keep in mind that when hypercoagulation dose anticoagulant should be increased, and if hypocoagulation – reduce. *It should be emphasized that at the high risk of internal bleeding (acute ulcers and gastric erosions, abscesses and other lung destruction, excessive blood flow to the drainage from wounds, bed pancreas, uterus, nosebleeds, etc.) heparin is contraindicated and hemosorption may be carried out using as anticoagulant sodium citrate solution (ACD-A) only.*

In cases of thickening and increased blood viscosity is advisable to add to the flow of blood and anticoagulant some more isotonic sodium chloride solution, which was used for priming the extracorporeal circuit. At the same time, to determine the true volume of blood pumped, you must subtract the amount of addition of a solution of the total volume of perfusion.

Completion of the hemosorption

At the end of the hemosorption program should be closed clamp **Ж1** line blood samplingб clamp **Ж4** supply line anticoagulant and fully open the clamp **Ж5** on the supply line isotonic sodium chloride solution. In this case, there is the displacement of blood from the adsorption column and other parts of the extracorporeal circuit in the bloodstream of the patient.

Attention! Although the device provides a dual system of protection against ingress of air inclusions in the blood return line, *but forced out of the extracorporeal circuit device blood and other fluids air is prohibited!*

After completion of the displacement of the blood device must be stopped, closed all the clips on the trunk and removed the catheter from the vein with the imposition of oppressive aseptic dressings. If necessary, continue the infusion therapy infusion part **УИ** disconnected from the venous catheter and connect it to the system of blood transfusion or solutions.

Indications for hemosorption

Resuscitation and critical care indications are:
- Acute pancreatitis, peritonitis;
- Respiratory distress syndrome, massive pneumonia;
- Septic, burns, traumatic shock, poisoning;
- The consequences of serious injuries, the syndrome of "long-term compression" (“crush syndrome”);
- Acute radiation and radionuclide destruction;

- Serious withdrawal symptoms;
- Severe intoxication in infectious diseases.

Chronic diseases:
- Allergies, especially with symptoms of allergic dermatitis or aspirin (prostacyclin) forms of bronchial asthma;
- Psoriasis;
- Toxicosis of pregnant women, genital infections;
- Chronic intoxication (industrial, environmental, radiation, medication);
- Drug addiction, substance abuse, alcoholism.

Contraindications to hemosorption

Absolute contraindications:
- *Irreversible damage* to the brain and other vital organs;
- *Non stopped profuse bleeding*.

Relative contraindications:
- *Increased bleeding or high risk of bleeding* (for example, when "stress" ulcers or erosions of the gastrointestinal tract). For living indications in these situations may by performed hemosorption, but without the use of heparin. If heparin is still used after the termination of the procedure should be introduce intravenously solution of protamine sulfate at a dose 50-150 mg.
- *Unstable hemodynamics:* hemosorbtion possible under the "cover" of dopmin or other symphatomimitics or pacemakers with mandatory monitoring of the performance of the cardiovascular system;
- *Acute respiratory or intestinal infections*: in acute phase hemosorbtion shown in the presence of severe intoxication, or - significant hypercoagulable (required higher doses of heparin), and under the guise of antibiotic therapy.

Advantages of hemosorption on the device "Hemofenix."

1 Single-nature connection, a particularly valuable with limited venous access ("bad" veins of the patient).

2 Translational movement of blood through the sorption column, whereby during the shutdown phase flow within blood collection takes longer its contact with sorbent surface and more efficient capture of the pathological products subject to removal from the body of the patient.

3 Small volume filling the extracorporeal circuit (50 ml capacity without column) allows to perform hemosorption even with hemodynamic instability, as well as in children (using catheters with a diameter up to 1.0 - 0.6 mm).

4 Portable character device "Hemofenix" allows to perform hemosorption in any environment, including on the leaving in the other hospitals and urgent indications in the ambulance and emergency medicine for urgent indications directly to place of catastrophe.

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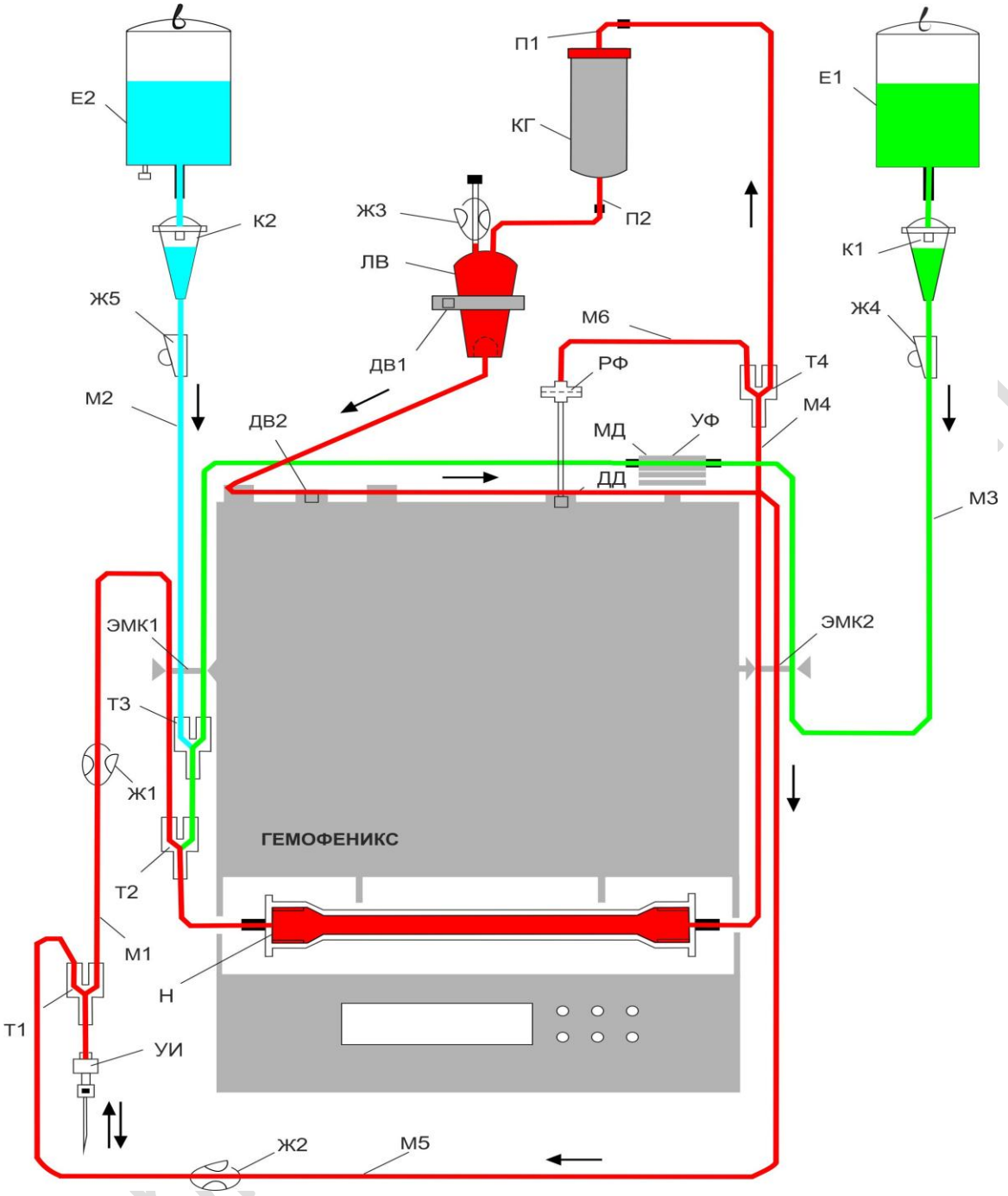

Fig.1. Extracorporeal circuit diagram hemosorption "Hemofenix" device.

Гемофеникс - Hemofenix - Device, ДВ1 and ДВ2 - Sensors air, ДД - pressure sensor, Е1 - a container with an anticoagulant, Е2 - with capacity with saline solution, Ж1 - Ж5 - clamps, К1 and К2 – dropper, КГ - column hemosorption, ЛВ - trap air, М1 - М6 - line tubes, MD - bag dispensing, Н - pump, Р1 and Р2 - adapter, rf - hydrophobic filter , Т1 - Т4 - tees, МД - Infusion part, УФ - fixing unit dosing bag, ЭМК1 and ЭМК2 – electromagneting (solenoid) valves, Н – pumping tube.

Fig. 2 Biospecific anti-proteinase hemosorbent OVOSORB.

Hemosorbent "Ovosorb" is a polyacrylamide hydrogel cross-linked N, N¹ - metilenbisakrilamidom, immobilized it biospecific ligand - ovomucoid, packed in a single used mass transfer module for hemosorption (MTM), filled with isotonic sodium chloride solution, placed in a plastic bag and sterilized. Designed for the selective removal of proteolytic enzymes from blood, plasma and other biological fluids in order to normalize disturbed during the development of the pathological process in the balance of proteinase inhibitors and eliminate the negative pathophysiological effects of hyper-enzyme concentration by selective extraction of the activated forms of serine proteinases.

Hemosorbent "Ovosorb" has no allergic or general toxic effect on the body, the relevant toxicological standards. No side effects were found. Hemosorbent is mass-produced in the mass transfer module for hemosorption (MTM), a single using, of 100 ml capacity, each MTM contains 25-45ml sorbent. It is safe for the patient and staff. The specific capacitance for trypsin at least 0.5 mg / ml of hydrogel.

Biospecific ligand - ovomucoid isolated from duck egg protein is a glycoprotein with a molecular weight of 30,000 D, capable of forming the strong chemical complexes with proteinases. Ovomucoid effectively binds trypsin, chymotrypsin, cathepsin, pancreatic and neutrophil elastase and bacterial proteinases, without changing the concentration of precursors, and inhibitors of these enzymes.

Clinical data indicate a high efficiency anti-proteinaze biospecific hemosorbent "Ovosorb" in the correction of protein metabolism and associated systemic disorders. Selectively removes from circulation active forms inhibitors of proteinases or their complexes with inhibitors. The physico-chemical properties of the polyacrylamide matrix possesses nonspecific adsorption capacity, but it is considerably lower than carbon

sorbents. Because of this, significant sorption of protease inhibitors and other individual plasma proteins does not occur, but reduced the severity of functional disorders of major organs and life support systems, there is a normalization of metabolic processes maintaining homeostasis in general. (Kirkovski V.V., 2012)