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Theory and Design

A Wearable Device for Continuous Automated Peritoneal Dialysis with Dialysis–Sorption Regeneration of the Dialysis Fluid

N. A. Bazaev[1,2], V. M. Grinval'd[3]*, B. M. Putrya[3], A. M. Shpikalov[4], Y. V. Tarasov[5], Y. I. Philippov[6], and M. D. Boyarskiy[5]

A technology for dialysis–sorption regeneration of spent peritoneal dialysis fluid and a design concept of wearable artificial kidney for continuous automated peritoneal dialysis are proposed.

Development of modern wearable equipment for long-term detoxification of human body is based on the methods of efferent therapy and uses the following research results:

– fundamental and applied research of Russian and foreign researchers into the problems of development and clinical application of modern methods of artificial purification of biological liquids of human body;

– analysis of design principles of biotechnological systems for artificial purification using intra- and extracorporeal artificial organs;

– theoretical research into the development of equipment for life support in patients with chronic and acute renal and multiorgan failure.

Today, peritoneal dialysis (PD) is successfully used as an intracorporeal method of renal replacement therapy (RRT) in patients with lost renal function requiring long-term life support.

In peritoneal dialysis, elimination of uremic metabolites from the biological liquids of patient's body is carried out in patient's peritoneum. Spent dialysis solution [peritoneal dialysis fluid (PDF)] is several times per day replaced with fresh fluid, patient's peritoneum (peritoneal membrane) being used as a mass-exchange device.

Peritoneal dialysis does not affect considerably the everyday activities and reduces the psychological pressure on the patient, enabling him/her to receive treatment under home conditions instead of being dependent on the availability of dialysis equipment at the hospital. It also allows the safety of treatment to be considerably increased [1].

Currently, manual peritoneal dialysis and automated modifications of chronic peritoneal dialysis are used in clinical practice [2].

Continuous ambulatory peritoneal dialysis (CAPD) is a modification of manual peritoneal dialysis. In CAPD, 2-2.5 L sterile PDF is manually infused into the abdominal cavity through a catheter. The fluid is replaced 4-6 h later with fresh PDF (duration of exposure should be sufficient to provide electrolyte exchange between blood and PDF). The spent PDF is drained. This procedure is repeated 3-5 times per day. Infusion and discharge of the PDF from the abdominal cavity are driven by gravity [2-4]. Presently, CAPD is the most widely used method of peritoneal dialysis.

[1] Zelenograd Innovation Technological Centre, Zelenograd, Moscow, Russia.
[2] Institute of Bionic Technologies and Engineering, I. M. Sechenov First Moscow State Medical University, Moscow, Russia.
[3] Institute of Biomedical Systems, National Research University of Electronic Technology (MIET), Zelenograd, Moscow, Russia; E-mail: vicgrin@gmail.com
[4] Federal Institute of Industrial Property, Moscow, Russia.
[5] Beta-Tech LLC, Moscow, Russia.
[6] Endocrinology Research Centre, Ministry of Health of the Russian Federation, Moscow, Russia.
* To whom correspondence should be addressed.

Automated chronic peritoneal dialysis is performed using special devices (cyclers). It is carried out mainly at night during the patient's sleep. The cycler provides automatic heating, PDF infusion into the peritoneal cavity, evacuation of the spent PDF from the peritoneal cavity, and solution weighing for the purposes of ultrafiltrate control [2, 4].

However, the means of increasing the effectiveness of PD to make it competitive with extracorporeal RRT methods (for example, hemodialysis) are limited. The effectiveness of peritoneal dialysis can be adjusted mainly by changing the PDF volume used by the patient per day. The optimal way to increase the effectiveness of PD is to increase the PDF volume while simultaneously reducing the PDF exposure time in the peritoneal cavity by increasing the frequency of PDF replacement.

Thus, to make peritoneal dialysis effective, patients have to use up to 5-6 disposable containers with PDF per day (total volume, 15-18 L). One-time introduction of 2.5-3 L PDF into patient's abdominal cavity creates discomfort for the patient: backache, feeling of overstretched abdomen, and breathing difficulties. The incidence of hernias and leaks can also increase as the result of an increase in the intraperitoneal pressure [5].

In addition, peritonitis – inflammation of the abdominal cavity caused by microbial contamination – is the disease most commonly associated with the use of PD. The probability of contracting peritonitis is proportional to the frequency of PDF replacement in the abdominal cavity.

Continuous long-term low-flow RRT methods [6, 7] and sorption treatment providing metabolite elimination from body fluids are also successfully used in clinical practice.

Today, the increased interest to low-flow RRT is due to its effectiveness and safety, as well as to insufficient clinical efficacy of conventional dialysis therapy, especially in acute kidney failure [8].

The success of these methods is based on the possibility of continuous long-term application (from 12 h to several days). This allows the metabolite content to be reduced to the optimal level. They also provide more physiological correction of the homeostasis of patient's body as compared to highly effective conventional methods of artificial extracorporeal purification and allow the balance of fluids, electrolytes, and pH to be monitored.

Sorption technologies of extracorporeal artificial purification are based on the processes of adsorption, absorption, and ion exchange. They are widely used in clinical practice for elimination of metabolites from blood (hemosorption), plasma (plasma sorption), and lymph (lymphosorption). Implementation of modern sorption methods of human body detoxification is based on low-flow transport of biological fluids through a sterile disposable sorption column.

The developed method of continuous low-flow automated peritoneal dialysis with continuous regeneration of the spent PDF combines the advantages of automated PD and efficacy of long-term low-flow RRT with sorption purification of physiological fluids.

Theoretical and experimental research into the processes of PDF regeneration and sorption purification [9-11] showed that it is feasible to develop a prototype wearable artificial kidney for elimination of uremic metabolites from sterile PDF to an extracorporeal circuit filled with nonsterile dialysis fluid with further sorption by sorptive materials.

The developed prototype device should provide constant low-flow PD for 24 h. This allows the efficacy of artificial purification to be considerably increased, because transport and purification of the spent PDF are performed in a continuous round-the-clock mode. Thus, the process of metabolite elimination from the patient's body becomes similar to that provided by the excretory function of the kidneys in a healthy subject, while the negative effects of intermittent elimination of metabolic by-products from the patient's body are reduced.

Use of a membrane mass-exchange device provides the following advantages: maintenance of sterility of the PDF circuit in the process of sorption material replacement in the nonsterile extracorporeal circuit; regulation of the volume of ultrafiltrate removed from the peritoneal cavity. A hemodiafilter is used in the prototype as the membrane mass-exchange device. It provides mass transfer of low- and medium-molecular-weight compounds (including protein compounds) from peritoneal solution to dialysate. It also allows the ultrafiltration rate to be controlled at low levels of vacuum-gage pressure in the cavity.

607C, WTD 816 and KAUSORB-212 activated carbons can be used to increase the efficiency of sorption of such metabolites as bilirubin, uric acid, and creatinine from the spent dialysate. Excessive potassium is removed using clinoptilolite (zeolite) $Na_6[Al_6Si_{10}O_{32}]\cdot 7H_2O$.

Special selective sorbents were developed and manufactured to provide removal of urea and protein compounds from the spent dialysate.

Proteins are undesirable products of PD. The peritoneal membrane is permeable to protein compounds with the molecular weight up to 30,000-40,000 Da. As the result, a protein layer is deposited on the sorbent surface and reduces the efficiency of sorption.

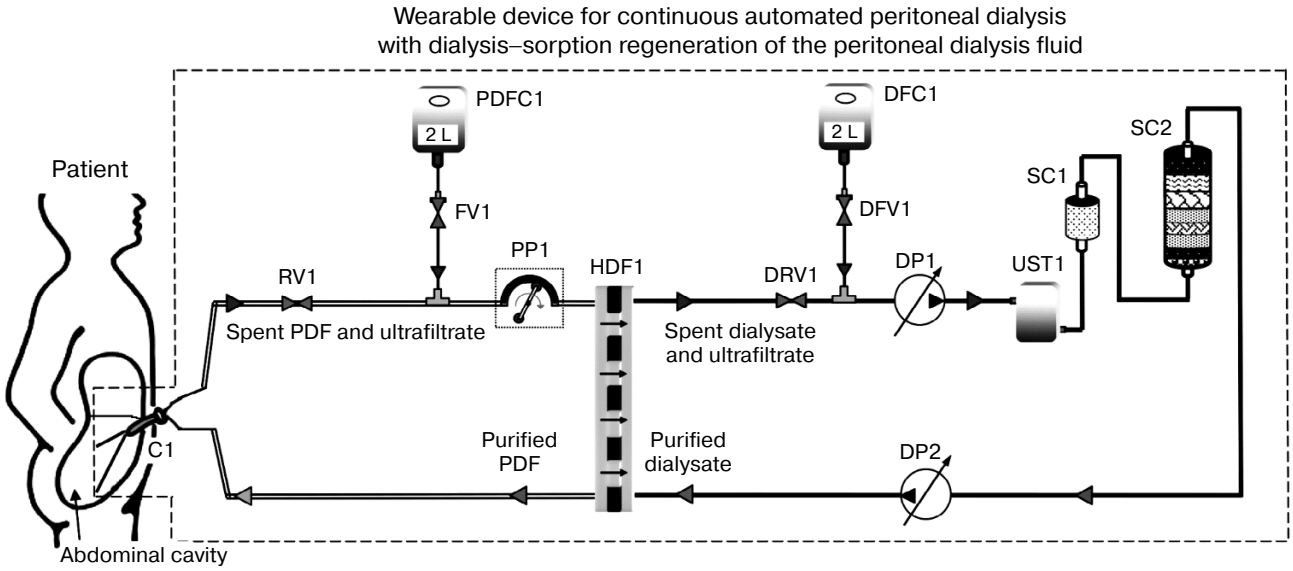

Fig. 1. Biotechnological system for continuous automated peritoneal dialysis with dialysis–sorption regeneration of the peritoneal dialysis fluid: C1 – catheter; FV1 – fill-in valve; RV1 – recirculation valve; PDFC1– PDF container; PP1 – perfusion pump; HDF1 – hemodiafilter; DFV1 – dialysate fill-in valve; DP1, DP2 – dialysate pumps; UST1 – ultrafiltrate storage tank; DRV1 – dialysate recirculation valve; SC1, SC2 – sorption columns.

Experimental research confirmed the efficiency of selective materials for sorption of urea and proteins from physiological solutions suggested in theoretical works. Principles of design of devices for low-flow detoxification of human body with dialysis–sorption regeneration of the spent PDF were formulated. The suggested technology eliminates the need for preliminary decomposition of nitrogen-containing compounds of, for example, urea to ammonia, carbon dioxide, and water, as is typical for urease decomposition of urea.

The structural hydraulic diagram of the wearable artificial kidney for automated low-flow PD with dialysis–sorption regeneration of PDF forming a part of the biotechnological system is shown in Fig. 1.

A dual-lumen catheter C1 is used for infusion of sterile PDF from a PDF container PDFC1 into patient's peritoneal cavity. PDF is pumped into the peritoneal cavity with a perfusion pump PP1 through a fill-in valve FV1 and the PDF cavity of the hemodiafilter HDF1.

Upon filling, the fill-in valve is closed and the recirculation valve RV1 is opened. The PDF starts to recirculate between the peritoneal cavity and the PDF cavity of the hemodiafilter HDF1. The volumetric flow rate of recirculation is 150 mL/min.

The extracorporeal circuit is filled with the dialysis fluid from the dialysis fluid container DFC1 using dialysate pumps DP1 and DP2 through an open dialysate fill-in valve DFV1, an ultrafiltrate storage tank UST1, sorption columns SC1 and SC2 providing, respectively, removal of excessive potassium and uremic metabolites from the spent dialysate, and the dialysate cavity of the hemodiafilter HDF1. Upon filling, the dialysate fill-in valve is closed and the dialysate recirculation valve DRV1 is opened. Dialysate starts to recirculate with the volumetric flow rate of 350 mL/min.

Blood and lymph circulation in the peritoneum provide considerable transmembrane transport of electrolytes, nitrogen-containing metabolites, peptides, plasma proteins, and protein-bound toxins to the PDF [12].

The hemodiafilter HDF1 provides regeneration of the spent PDF by means of diffuse, filtration, or convective transfer of low and medium molecular weight compounds, protein compounds, and liquids through the mass-exchange membrane into the dialysis fluid. The sorption column is used to eliminate uremic metabolites from the spent dialysis fluid. Its composition is shown in Fig. 2.

The sorption column SC2 (Fig. 2) contains the following sorbent components: modified activated carbon U-HHDP, MgO-saturated activated carbon BAU, activated carbon FAS, granulated polycarboxylic acid and triacetate fibers, a composition of cation-exchange resin KU-23 and FAS carbon, magnesium carbonate, and magnesium oxide with activated carbon.

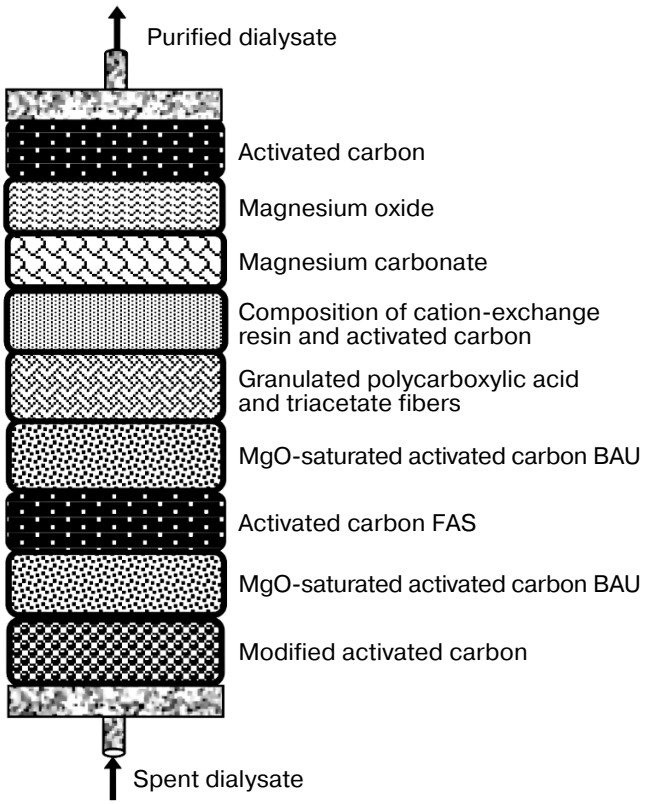

Fig. 2. Composition of the sorption column used for elimination of uremic metabolites from spent dialysis fluid.

The first layer (modified activated carbon) provides elimination of protein compounds from the dialysate. The modified activated carbon for this layer was obtained by introducing virtually water-insoluble hexahydroxydiphenic acid (HHDP) into the structure of the activated carbon BAU. HHDP is a tanning agent that activates coagulation and agglomeration of protein molecules in the process of interaction with water–protein solutions on a highly developed surface structure.

Application of HHDP shifts the solution pH into the acidic range: pH = 4.5-5.0. To maintain the pH value in the range of 7.2-7.4, the second layer is composed of MgO-saturated activated carbon BAU.

The third layer (pharmaceutical activated carbon FAS) provides elimination of creatinine from the spent dialysate. The activated carbon KAUSORB can also be used for this purpose.

Granulated polycarboxylic acid and triacetate fibers are used to eliminate urea from the dialysate. Polycarboxylic acid has the properties of an inner salt. Therefore, to optimize its action on urea, an alkaline environment with pH ~ 8.5-9.0 is required. To reach this level of pH, a second layer of MgO-saturated activated carbon BAU is introduced before the layer composed of granulated polycarboxylic acid and triacetate fibers.

Positive and negative charges in urea interact with those in the polycarboxylic acid, which is an amphoteric compound. Polycarboxylic acid has rather high molecular weight, which leads to a sharp decrease in solubility and urea deposition on the sorbent.

To stabilize the output solution pH in the range of 7.2-7.4, a composition of cation-exchange resin KU-23 (sulfoderivative of polystyrol–vinylstyrene copolymer) and pharmaceutical carbon FAS is used.

Virtually water-insoluble magnesium carbonate is used to eliminate uric acid from the dialysate. It provides a significant decrease in the content of uric acid and free phosphorus in the dialysate. The specific surface of crystalline magnesium carbonate is rather small. To increase its value, magnesium carbonate is deposited on the activated carbon BAU.

Magnesium ureide produced by the reaction between uric acid and magnesium carbonate has low water solubility. However, carbon dioxide is released in the course of this reaction. To remove it, magnesium oxide is used to bind carbon dioxide.

Direct use of magnesium oxide available as fine powder is rather difficult. Although it is water-insoluble, it slowly reacts with water producing magnesium hydroxide, which tends to be washed away and spread all over the sorption column in the absence of fixation. To avoid this, the activated carbon BAU is used to fix the hydroxide on its developed surface.

At the output of the sorption column, purified dialysate passes through a layer of activated carbon to filter out suspended particles.

Excessive potassium is eliminated from dialysate using clinoptilolite contained in the sorption column SC1 (Fig. 1).

The rate of ultrafiltration [liquid removal from the PDF in the peritoneal (intracorporeal) circuit] is regulated by adjusting the transmembrane pressure using the dialysate pumps DP1 and DP2 in the extracorporeal circuit (Fig. 1).

When the service life of the disposable components is over, PDF and dialysate are drained from the system to make their replacement possible.

The prototype wearable artificial kidney can be controlled from a smartphone using special software. The device components are installed on a support placed into a backpack. The operation time from self-contained power supply is approximately 5 h. It is recommended to replace disposable components of the device every 12 h of operation.

Conclusions

A technology for dialysis–sorption regeneration of PDF based on dialysis purification of the spent PDF with subsequent sorption regeneration is proposed.

The novel feature of the suggested technology is the use of a membrane mass-exchange device providing the following advantages:

– the peritoneal cavity circuit filled with sterile PDF is separated from the extracorporeal circuit with nonsterile dialysis fluid;

– expendable nonsterile materials can be used for dialysis fluid regeneration;

– the volume of ultrafiltrate removed from the peritoneal cavity can be regulated.

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