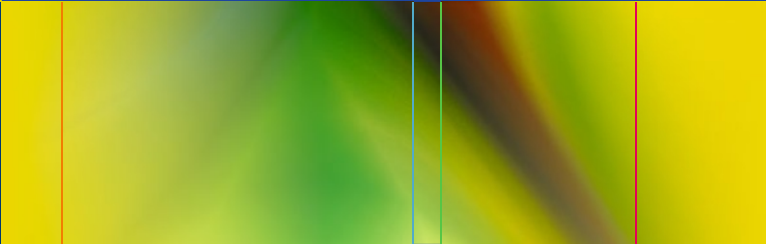


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The Concise Manual of Apheresis Therapy



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Chapter 9

Plasma Diafiltration

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Main Points

- Plasma diafiltration (PDF) is a blood-purification therapy in which simple plasma exchange (PE) is performed using a selective membrane plasma separator (sieving coefficient for albumin, 0.3), while the dialysate flows outside the plasma separator.
- PDF can remove both water-soluble and albumin-bound substances.
- Coagulation factors are preserved because this membrane has a sieving coefficient of 0 for fibrinogen and immunoglobulin M.
- PDF is useful for patients with acute liver failure, severe sepsis, acute pancreatitis, or intoxication.

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9.1 Introduction

Acute liver failure can cause various toxins to circulate in the bloodstream. To remove these toxins, several kinds of artificial liver support systems (ALSSs) can be used, such as plasma exchange (PE), high-flow hemodialysis (HD), high-volume hemofiltration (HF), high-flow volume hemodiafiltration (HDF), and albumin dialysis therapies. Plasma diafiltration (PDF) is a blood-purification therapy in which simple PE is performed using a selective membrane plasma separator while the dialysate flows outside the hollow fibers of the plasma separator [1–4]. This method is a useful ALSS for the removal of both water-soluble and albumin-bound toxins, and has a reasonable cost.

9.2 PDF Procedures

9.2.1 *Flow*

Simple PE is performed with a membrane plasma separator [Evacure EC-2A plasma separator (Kawasumi Laboratories Inc., Tokyo, Japan)] while the dialysate flows outside the plasma separator; HDF is performed simultaneously. A blood flow rate of 80–100 mL/min is used. Dialysate is circulated through the plasma separator at a flow rate of 1,500 mL/h, and additional replacement volume is provided to the patient at a flow rate of 690 mL/h. Fluid removal is performed by reducing the replacement flow rate to 450 mL/h at most. In addition, a 1,200 mL volume of normal fresh frozen plasma (FFP) and 50 mL of 25 % albumin solution is intravenously infused over an 8-h period (Fig. 9.1).

9.2.2 *Features*

The Evacure EC-2A plasma separator has a pore size of 0.01 mm, which is much smaller than that of conventional

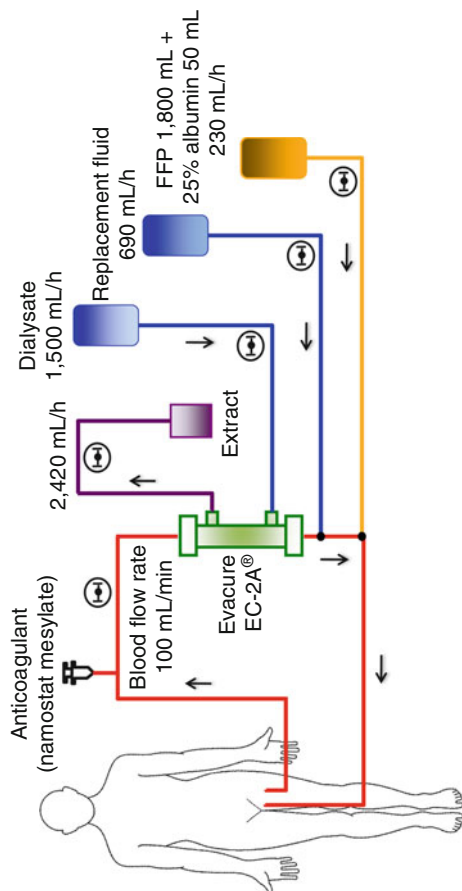


FIGURE 9.1 Schematic representation of PDF. PDF is performed for 8 h once a day as a single session or for 24 h continuously in three sessions, according to the patient's condition. PDF is a simpler modality than plasma exchange with continuous hemodiafiltration (CHDF) and uses only one plasma separator. *FFP* fresh frozen plasma

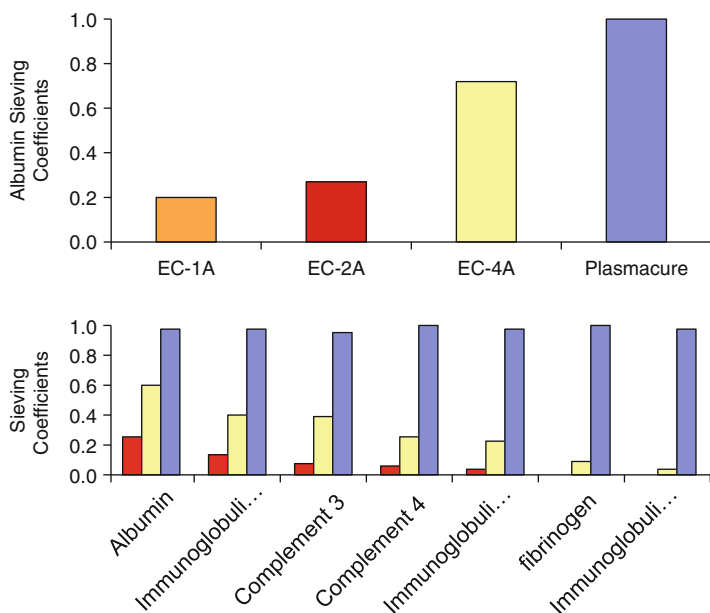


FIGURE 9.2 Features of PDF. The Evacure EC-2A plasma separator used for PDF has a pore size of 0.01 mm, which is much smaller than that of standard plasma-separation membranes. This membrane can selectively remove low and intermediate molecular weight albumin-bound substances while retaining high molecular weight proteins such as fibrinogen and immunoglobulin M

plasma separation membranes (0.2–0.4 mm). This ethylene-vinyl alcohol copolymer membrane has a sieving coefficient of 0.3 for albumin and can thus selectively remove low and intermediate molecular weight albumin-bound substances. In addition, coagulation factors are preserved because this membrane has a sieving coefficient of 0 for fibrinogen and immunoglobulin M (Fig. 9.2). During PE, it is difficult to completely control increases in citrate concentrations by administering FFP. In PDF, the increase in citrate concentration is inhibited more effectively because smaller amounts of FFP are required and because HDF is performed simultaneously. Furthermore, the use of smaller amounts of FFP reduces medical costs

TABLE 9.1 Problems of plasma exchange

Requires large amounts of FFP	Large citrate transfusion • Hyponatremia, hypocalcemia, metabolic alkalosis • Citrate intoxication, nausea, vomiting, convulsion, liver dysfunction Anaphylactic reaction, hypersensitivity Decreased osmotic pressure of plasma colloids • Pulmonary edema, brain edema
Removal of high molecular weight proteins	Loss of essential substances such as clotting factors, a number of hormones
<i>FFP</i> fresh frozen plasma	

TABLE 9.2 Comparisons among PDF, PE+CHDF, and MARS®

Variable	PDF	PE+CHDF	MARS®
Circuit	Simple	Complicated	More complicated
FFP (mL/day)	1,800	3,200–4,000	None
Citrate increase	Slight	Moderate	None
Bilirubin removal	Moderate	Good	Moderate
Fibrinogen retention	Good	Poor	Good
Material cost (/procedure)	Low	Middle	High

PDF plasma diafiltration, *PE* plasma exchange, *CHDF* continuous hemodiafiltration, *MARS* molecular adsorbent recirculating system, *FFP* fresh frozen plasma

(Tables 9.1 and 9.2). Excessive amounts of both water-soluble and albumin-bound substances, such as cystatin C, bilirubin, interleukin (IL)-6, and IL-18 can be reduced by PDF [3, 4]. The clearance rate for creatinine and blood urea nitrogen (BUN) is 20 mL/min, and that for cytokines, such as IL-6 and IL-8, is 18 mL/min. Thus, the cytokine sieving coefficient is 0.8–0.9. The concept behind PDF is that dialysis is also performed during this type of selective plasma filtration (Fig. 9.3).

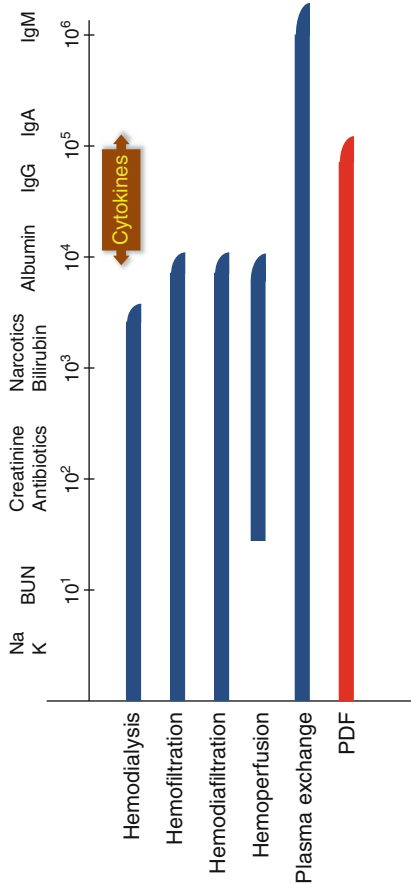


FIGURE 9.3 PDF compared with other blood-purification therapies. Excessive amounts of both water-soluble and albumin-bound substances, such as potassium, bilirubin, and cytokines can be reduced by PDF. *Na* sodium, *K* potassium, *BUN* blood urea nitrogen, *Ig* immunoglobulin

9.2.3 *Priming*

The blood circuit is flushed with 1,000 mL of heparinized saline.

9.2.4 *Anticoagulation*

Nafamostat mesylate is administered at an initial dose of 30 mg/h and the concentration is adjusted to maintain an activated coagulation time of 150–180 s.

9.2.5 *PDF Session*

PDF is performed for 8 h once a day as a single session. Albumin levels did not change significantly on performing PDF for previous studies, but nevertheless, 50 mL of 25 % albumin solution is added at the end of the PDF, to adjust for the loss of albumin by diffusion.

9.3 Options for PDF

9.3.1 *Hepatorenal Syndrome*

Continuous HD is performed using a PDF circuit. The dialysate flow rate is set to 600 mL/h; 50 mL of 25 % albumin solution is also infused every 8 h, to account for the loss of albumin by diffusion.

9.3.2 *Severe Liver Failure*

PDF can be performed for 24 h continuously, according to the patient's condition.

9.3.3 *Sepsis and Severe Acute Pancreatitis*

A patient without disseminated intravascular coagulation (DIC) or bleeding tendency does not need clotting factor-replacement therapy. In such situations, PDF can be performed with a 5 % albumin solution instead of FFP.

9.3.4 *Acute Intoxication*

Almost all intoxicating substances bind to proteins. PDF is performed to remove the intoxicating substances that have high albumin-binding rates [5].

Note: Outcome from PDF/the MELD Score

According to prospective and multicenter studies examining the use of PDF in patients with acute liver failure, no remarkable differences in prognosis were observed compared to the outcomes from studies using albumin dialysis [6–9]. MARS® and Prometheus® have been considered as bridge therapies for liver transplantation in previous studies. However, PDF was intended to be a direct treatment for acute liver failure, considering the scarcity of donor organs in Japan. Therefore, the number of severe cases, with model for endstage liver disease (MELD) scores of ≥ 40 , was larger in the PDF studies than in the MARS® studies.

The MELD score is predictive of survival and is used to prioritize patients with chronic liver disease for orthotopic liver transplantation [10]. This score is also considered to reflect the prognosis for fulminant hepatic failure [11]. The survival rate at a MELD score of ≤ 9 is more than 90 %. The mortality rate at MELD scores of ≥ 40 is 380 %, but is not considered to be indicative of the need for liver transplantation. In Japan, PDF is recommended for patients with a MELD score of 19, which is indicative of the need for liver transplantation.

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