Chapter 21
Avoiding Complications During Apheresis

Tetsushi Yamashita and Hiroko Yamamoto

Main Points

- Complications frequently occur during apheresis and should be detected as early as possible.
- Technicians or operators should fully understand the function and applications of all equipment used and the possible complications of the apheresis procedure.
- It is important that physicians understand the cause of any complications and manage them quickly.

T. Yamashita (✉)
Department of Nephrology & Endocrinology, School of Medicine,
The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8655, Japan
e-mail: teyamashita-tky@umin.ac.jp

H. Yamamoto
Department of Hemodialysis & Apheresis, University Hospital,
The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8655, Japan

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21.1 Introduction

Complications frequently occur during apheresis, but they can be prevented from becoming serious if the technicians or operators understand their causes and how to manage them. We will review the complications associated with the apheresis equipment and those associated with the treatment.

21.2 Complications Associated with Apheresis Equipment

21.2.1 Clotting in the Circuit

Blood takes a longer time to pass through the circuit during apheresis than during hemodialysis due to the lower blood flow rate and higher priming volume of the circuit. Therefore, more extensive anticoagulation should be used during apheresis than during hemodialysis. This is especially true during double filtration plasmapheresis (DFPP), where endogenous anticoagulants are removed, and even more anticoagulation is necessary. It is essential that coagulation is monitored by tests such as activated partial thromboplastin time (APTT) or prothrombin time (PT) during apheresis. When pressure in the circuit becomes elevated, even if adequate anticoagulation has been administered, the problem must be quickly remedied because clots can begin to form. The pressure in the circuit needs to be continuously monitored and it is important to prevent loss of blood in the circuit.

21.2.1.1 Cause

Clotting in the circuit can be caused by a deficiency of anticoagulants, formation of white thrombi through platelet activation, frequent blood removal failure, or other reasons.

21.2.1.2 Management

Management of these complications depends on where the clots form in the circuit (Table 21.1) [1].

21.2.2 Equipment Malfunction

Blood purification equipment must have regular maintenance and inspection, as required by the revised Medical Care Act (Act No. 84 of 2006). The operation of these machines should be tested once a month even if they are rarely used.

21.2.2.1 Management

If the therapy cannot continue due to equipment malfunction, we manually return the blood in the circuit to the body with the hand-powered handle, or through other procedures. If there is a spare apparatus, we continue the therapy with a transfer of the circuit.

21.2.3 Human Errors

It is important that operators become skilled in the procedures and use of blood purification equipment. More than one person should monitor all procedures because a delay in the detection of an error could possibly cause serious harm to the patient. In our hospital, we utilize checklists designed according to the type of therapy and machine. They are used after priming, upon starting the machine, before beginning therapy, and before the initiation of plasma separation.

21.2.3.1 Cause

Problems with the procedure can occur due to technician carelessness, insufficient monitoring lack of knowledge, or an

Table 21.1 Management according to location of clotting within the circuit

Plasma separator	Elevation of the differential pressure	Search the whole circuit for clots after infusion of about 100 mL of normal saline via the extra infusion line. If there are no clots in the venous drip chamber and the differential pressure (the entrance pressure minus the exit pressure) is over 100 mmHg, exchange the plasma separators[a]
	Elevation of the TMP	If the TMP exceeds the 60 mmHg upper limit of the plasma separators, lower the height of the plasma in the outer layer of the separator, lower the separation rate, and continue the therapy if possible. If the TMP continues to rise over 60 mmHg, cease the therapy or exchange the plasma separators[a]
Blood circuit		Search the whole circuit for clots after infusion of about 100 mL of normal saline via the extra infusion line. If it seems that the therapy cannot achieve the goal, the circuit can be partially or wholly exchanged
Adsorption column		Lower the flow rate along the adsorption column and continue the therapy if possible. Discontinue the therapy if the differential pressure rises over 100 mmHg
Plasma fractionator		Lower the fractionation rate and continue the therapy if possible. If the entrance pressure rises over 350 mmHg, interrupt fractionation and only drain plasma temporarily, or backwash the fractionator
		A device that can monitor the TMP of secondary membranes is available

(continued)

Table 21.1 (continued)

Vascular access	Search the whole circuit for clots after infusion of about 100 mL of normal saline via the extra infusion line. If there are no clots in circuit and the venous pressure is elevated, suspect clotting in the access for blood return. If this is present, interrupt the therapy and check whether clots are drawn from the access or whether there is no resistance to saline flushing. Establish a new access if the access is completely occluded. Temporarily return blood to the body via the access for blood removal if establishing another new access will take too much time

TMP transmembrane pressure

[a]There are two ways to exchange plasma separators. One method exchanges only the separators after priming a new separator, the other exchanges all circuits after blood in the circuit is temporarily returned to the body. The safest and most dependable method should be chosen according to technician skill

oversight such as forgetting to lock or unlock Kocher clamp. Problems can also arise from the mistaken entry of air, damage of the circuit, or incorrect setting of the flow rate.

21.2.3.2 Management

The therapy should be interrupted until the patient's safety has been assured. This can involve assessing whether the error has done harm to the patient, sterile conditions have been maintained, and whether an exchange of circuits is necessary, among other considerations. The hospital's risk management plan should be followed.

21.3 Complications Associated with the Apheresis Treatment

Complications affecting the patient's clinical condition should be detected as early as possible thorough monitoring of vital signs and other methods. It is also essential that operators and technicians are trained to manage complications and emergencies that occur during treatment.

21.3.1 Hypotension

Hypotension can occur frequently, and the cause can often be deduced by examining when it occurred. Causes and management of hypotension according to onset time are shown in Table 21.2 [1] (See Chap. 17).

21.3.2 Paresthesias (Citrate Toxicity)

21.3.2.1 Cause

Citrate toxicity results from a temporary reduction in plasma ionized calcium concentration due to exposure to citrate that is contained in anticoagulants used during centrifugal leukocytapheresis or in fresh frozen plasma (FFP) used as replacement fluid in plasma exchange (See 20.2 Calcium).

21.3.2.2 Management

The citrate delivery rate can be lowered (usually along with the blood flow rate) and prophylactic calcium preparations can be infused via the venous return line. The rate of clearance of citrate, which is metabolized by the liver, varies among individuals, and a change of therapy type or combined plasma exchange and dialysis should be considered in patients with both hepatic and renal dysfunction.

Table 21.2 Causes and management of hypotension according to onset time

Initial stage of therapy	Cause		This results from a reduction in plasma oncotic pressure due to an infusion of normal saline for priming (initial drop). Careful attention should be paid to hypotension, especially in patients with low body weight or hypoalbuminemia
	Management		Elevate the patient's legs, lower the blood flow rate, interrupt plasma separation, and administer fluids as soon as possible. If pressure recovers, continue the therapy. Lowering the priming volume (no more than 10 % of the patient's intravascular volume) or using 5 % albumin for priming instead, among other procedures, are preventive measures
Thirty minutes after initiation of therapy	Dangerous	Cause	An allergic reaction to blood products or drugs, or bradykinin shock
		Management	Cease the therapy as soon as possible. Elevate the patient's legs, return blood to the body if possible, and administer fluids. Changing the drugs used and administering glucocorticoids just before the therapy are preventive measures
	Results from a reduction in plasma oncotic pressure	Cause	This results from a removal of a large amount of protein, compared with the volume of replacement with albumin during DFPP
		Management	Adjust the volume of replacement fluid by monitoring the patient's intravascular volume with Crit-Line In-Line Monitor™

(continued)

Table 21.2 (continued)

Regardless of the stage of therapy	Cause	This results from vasovagal reflex. It is caused by sympathoinhibition and vagal efferent activation triggered by emotional or orthostatic stress
	Management	Vasovagal reflex, which frequently happens at venipuncture, may happen during therapy. It is important that we relieve the patient's stress. The therapy can usually continue because the condition resolves quickly. Use atropine when there may be serious hemodynamic instability

DFPP double filtration plasmapheresis

Table 21.3 Complications during apheresis other than hypotension

Hypertension	Cause	Possibly due to the return of blood, a control of the need to urinate or defecate, or sodium loading by using FFP as the replacement fluid in plasma exchange
	Management	Elevate the head and consider administering antihypertensive drugs if no improvement is seen. In plasma exchange, consider combined hemodialysis
Hematoma/ subcutaneous bleeding	Cause	Due to anticoagulants used during the therapy, antiplatelet agents used as medication on a regular basis, or other causes
	Management	Change or reduce anticoagulants and carefully puncture and stanch the vein
Urination/ defecation	Cause	Possibly caused by extra replacement fluids or hypotension
	Management	Interrupt the therapy if possible. Monitor the patient by assessing vital signs
Palpitation/ headache	Cause	Occurs relatively frequently during leukocytapheresis
	Management	Consider a change of devices

FFP fresh frozen plasma

21.3.3 Other Complications

Other characteristic complications are shown in Table 21.3. We should be familiar with the package inserts of each device used because there are different kinds of complications associated with particular devices.

Reference

1. Iwamoto H (2007) Jpn J Apher 26(1):93–100