Letter to the Editor
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Proposal of the Need for New Korean Guidelines on the Use of Therapeutic Apheresis in Clinical Practice

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Dear Editor,

Therapeutic apheresis is performed for numerous indications in various medicine fields [1-5]. The primary reference on the use of therapeutic apheresis are the evidence-based guidelines issued by the Writing Committee of the American Society for Apheresis (ASFA) [6]. These guidelines provide structured evidence for therapeutic apheresis and are offered for medical consideration worldwide. Recently, new guidelines were issued by the Japanese Society for Apheresis (JSFA) [7]. The main difference between the two guidelines lies in the primary modality used in each country and clinical indications for therapeutic apheresis. The primary apheresis modality used in Japan is the membrane separation method, whereas in the USA, the centrifugal separation method is mainly used. As the target diseases and their backgrounds differ between these countries, there was a need to develop new guidelines in Japan.

The most noticeable difference between the ASFA and JSFA guidelines is that various new techniques are suggested in the latter. New technologies and tools have been developed and applied in clinical apheresis in Japan, including hollow-fiber devices such as double filtration plasmapheresis (DFPP), adsorption devices such as polymyxin B-immobilized endotoxin adsorption columns, and selective plasma exchange devices. In the JSFA guidelines, out of four categories, plasma filtration with dialysis (PDF) for liver failure is classified as category II, implying that therapeutic apheresis can be applied as a second-line therapy, independent of plasma exchange and continuous hemodiafiltration (CHDF) for acute liver failure (category I). In the ASFA guidelines, plasma exchange is the only option suggested for acute liver failure. As for the diseases included in the two guidelines, 39 diseases are included only in the ASFA guidelines and 32 diseases only in the JSFA guidelines (Table 1). This likely reflects the variability in the prevalence of certain diseases according to country and ethnicity. Specifically, babesiosis, malaria, and sickle cell disease are included only in the ASFA guidelines as their prevalence in Asia is extremely low. Extracorporeal photopheresis (ECP) for graft-versus-host disease (GVHD) is classified into category II in the ASFA guidelines, whereas there is no mention of ECP for GVHD in the JSFA guidelines.

Guidelines for therapeutic apheresis have yet to be developed in Korea. At present, medical decisions and national health insurance reimbursements for apheresis are based on the ASFA guidelines. Like in the USA, the main modality used for clinical apheresis in Korea is centrifugal separation. However, the target diseases are closer to those in Japan because of shared ethnic and geographical backgrounds. Due to the language barrier, literature published in Korean was not included in either of the guidelines. There is a need to develop Korean guidelines on thera-

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Table 1. Diseases included in only one of the ASFA and JSFA guidelines and their modalities, indications, categories, and grades

Guidelines	Diseases	Therapeutic apheresis modality	Indication	Category	Grade
ASFA only	Age-related macular degeneration, dry	Rheopheresis	High-risk	II	2B
	Atopic (neuro-)dermatitis (atopic eczema), recalcitrant	ECP		III	2A
		IA		III	2C
		TPE/DFPP		III	2C
	Autoimmune hemolytic anemia, severe	TPE	Severe cold agglutinin disease	II	2C
		TPE	Severe warm autoimmune	III	2C
	Babesiosis	RBC exchange	Severe	II	2C
	Burn shock resuscitation	TPE		III	2B
	Cardiac neonatal lupus	TPE		III	2C
	Catastrophic antiphospholipid syndrome	TPE		III	2C
	Erythropoietic protoporphyria, liver disease	TPE		III	2C
		RBC exchange		III	2C
	Graft-versus-host disease	ECP	Acute	II	1C
		ECP	Chronic	II	1B
	Hemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome	TPE	Postpartum	III	2C
		TPE	Antepartum	IV	2C
	Hemophagocytic lymphohistiocytosis; hemophagocytic syndrome; macrophage activating syndrome	TPE		III	2C
	Heparin-induced thrombocytopenia and thrombosis	TPE	Pre-cardiopulmonary bypass	III	2C
		TPE	Thrombosis	III	2C
	Hereditary hemochromatosis	Erythrocytapheresis		I	1B
	IgA nephropathy (Berger's disease)	TPE	Crescentic	III	2B
		TPE	Chronic progressive	III	2C
	Immune thrombocytopenia	TPE/IA	Refractory	III	2C
	Malaria	RBC exchange	Severe	III	2B
	Myeloma cast nephropathy	TPE		II	2B
	Nephrogenic systemic fibrosis	ECP/TPE		III	2C
	Pemphigus vulgaris	TPE	Severe	III	2B
		ECP/IA	Severe	III	2C
	Peripheral vascular diseases	LA		II	1B
	Post-transfusion purpura	TPE		III	2C
	Pruritus due to hepatobiliary diseases	TPE	Treatment resistant	III	1C
	Scleroderma (systemic sclerosis)	TPE		III	2C
		ECP		III	2A
	Sickle cell disease, acute	RBC exchange	Acute stroke	I	1C
		RBC exchange	Acute chest syndrome, severe	II	1C
		RBC exchange	Other complications	III	2C
	Sickle cell disease, non-acute	RBC exchange	Stroke prophylaxis	I	1A
		RBC exchange	Pregnancy	II	2B
		RBC exchange	Recurrent vaso-occlusive pain crisis	II	2B
		RBC exchange	Pre-operative management	III	2A
	Sudden sensorineural hearing loss	LA/rheopheresis/TPE		III	2A
	Thrombocytosis	Thrombocytapheresis	Symptomatic	II	2C
		Thrombocytapheresis	Prophylactic or secondary	III	2C
	Thrombotic microangiopathy, coagulation mediated	TPE	*THBD, DGKE*, and *PLG* mutations	III	2C

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Table 1. Continued

Guidelines	Diseases	Therapeutic apheresis modality	Indication	Category	Grade
	Thrombotic microangiopathy, drug-associated	TPE	Ticlopidine	I	2B
		TPE	TPE Clopidogrel	III	2B
		TPE	Gemcitabine/quinine	IV	2C
	Thrombotic microangiopathy, transplantation associated	TPE		III	2C
	Thyroid storm	TPE		II	2C
	Transplantation, cardiac	ECP	Cellular/recurrent rejection	II	1B
		ECP	Rejection prophylaxis	II	2A
		TPE	Desensitization	II	1C
		TPE	Antibody-mediated rejection	III	2C
	Transplantation, hematopoietic stem cell, ABO incompatible (ABOi)	TPE	Major ABOi HPC(M) II	II	1B
		TPE	Major ABOi HPC(A) II	II	2B
		RBC	Minor ABOi HPC(A) III	III	2C
		TPE	Major/minor ABOi with pure RBC aplasia	III	2C
	Transplantation, hematopoietic stem cell, human leukocyte antigen desensitization	TPE		III	2C
	Transplantation, liver	TPE	Desensitization, ABOi living donor	I	1C
		TPE	Desensitization, ABOi deceased	III	2C
		ECP	donor/antibody-mediated rejection	III	2C
		ECP	Desensitization, ABOi	III	2B
			Acute rejection/immune suppression withdrawal		
	Transplantation, lung	ECP	Bronchiolitis obliterans syndrome	II	1C
		TPE	Antibody-mediated rejection/ desensitization	III	2C
	Vasculitis, IgA (Henoch–Schönlein purpura)	TPE	Crescentic rapidly progressive	III	2C
		TPE	glomerulonephritis	III	2C
			Severe extrarenal manifestations		
	Vasculitis, other	TPE	Hepatitis B polyarteritis nodosa	II	2C
		TPE	Idiopathic polyarteritis nodosa	IV	1B
		Adsorptive cytapheresis	Adsorptive cytapheresis Behcet's	II	1C
		TPE	disease	III	2C
			Behcet's disease		
	Wilson's disease, fulminant	TPE		I	1C
JSFA only	Acute autonomic sensory neuropathy	TPE		III	2C
	Acute exacerbation of interstitial pneumonia	PMX-DHP		III	2C
	Acute pancreatitis	CHDF, PDF		II	2B
	Acute respiratory distress syndrome	CHDF		III	2C
	Amyopathic dermatomyositis and polymyositis with complications of interstitial pneumonia	PMX-DHP, LCAP		III	2B/3C
	Arteriosclerosis obliterans	LDL-A		II	1C
	Ascites	CART		II	1C
	Autoimmune autonomic ganglionopathy	TPE		III	2C
	Autoimmune encephalitis/cerebellitis LGI1/Caspr2/GABAbR/ AMPAR/GAD/GlyR/NAE	TPE, IAPP, CAP		III	2C
	Bickerstaff brainstem encephalitis	TPE, IAPP		III	2C

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Table 1. Continued

Guidelines	Diseases	Therapeutic apheresis modality	Indication	Category	Grade
	Calciphylaxis	LDL-A, TPE, cryofiltration		III	2C
	Cholesterol crystal embolism	LDL-A		II or III	2C
	Chronic hepatitis C	DFPP		III	2C
	Diabetic nephropathy	LDL-A		III	1C
	Drug-induced lung damage	PMX-DHP		III	2C
	Fisher's syndrome	TPE, DFPP, IAPP		III	2C
	HTLV-1-associated myelopathy	TPE, IAPP, LCAP		III	2C
	Hypertrophic pachymeningitis	LCAP		III	2C
	Isaacs' syndrome	TPE, DFPP		III	2B
	Neuropsychiatric SLE	IAPP, TPE, DFPP		II	2C
	Palmoplantar pustulosis	GMA		III	1C
	Pemphigoid	TPE, DFPP		II	1C
	Psoriatic arthritis	GMA		II	1C
	Pyoderma gangrenosum	GMA		III	2C
	Rapidly progressive interstitial pneumonia associated with anti-MDA5 antibody-positive dermatomyositis	PE		III	2C
	Refractory nephrotic syndrome	PE, DFPP, LDL-A		III/III	–/2C
	Renal failure with unstable hemodynamics	CHDF		I	–
	Severe sepsis and septic shock	CHDF (without AN-69ST)		–	
	Sjögren's syndrome	PE, DFPP		III	2C
	Tumefactive demyelinating disease	PE		III	2C
	Liver failure	PDF		II	1C
	Severe acute pancreatitis	PDF		III	2C

Abbreviations: ASFA, American Society for Apheresis; CART, cell-free and concentrated ascites reinfusion therapy; CHDF, continuous hemodiafiltration; DFPP, double filtration plasmapheresis; ECP, extracorporeal photopheresis; GMA, granulocyte and monocyte adsorption apheresis; HPC, hematopoietic progenitor cell; IA, immunoadsorption; IAPP, immunoadsorption plasmapheresis; JSFA, Japanese Society for Apheresis; LA, lipoprotein apheresis; LCAP, leukocytapheresis; LDL-A, LDL apheresis; PDF, plasma filtration with dialysis; PMX-DHP, polymyxin B-immobilized fiber column direct hemoperfusion; TPE, therapeutic plasma exchange; RBC: red blood cell.

peutic apheresis using both guidelines as a reference, while considering Korea's unique demands. For example, severe fever with thrombocytopenia syndrome (SFTS) is uncommon in the USA and is therefore not included in the ASFA guidelines. Despite there being a few cases of SFTS in Japan, it is not included in the JSFA guidelines either. However, in Korea, the incidence of SFTS is relatively high, at 200–250 cases annually, and the clinical utility of therapeutic plasma exchange (TPE) for the treatment of SFTS has been suggested in case reports [8, 9]. In the guidelines published by the Korea Disease Control and Prevention Agency, TPE has been suggested as a treatment option for removing cytokines in SFTS [10]. New Korean guidelines should be introduced that enable the clinical application of therapeutic apheresis for diseases unique to the Korean population as well as the reimbursement from insurance for apheresis in such cases.

The frequency and modalities used for apheresis in different diseases vary among countries, as does the reimbursement from insurance [5]. Optimal guidelines for clinical apheresis should be established for each country's unique population and could guide physicians in deciding whether to perform apheresis. There should be continuous academic and political efforts to establish clinical apheresis guidelines in Korea.

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CONFLICTS OF INTEREST

The authors have no competing interests to declare.

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