Work Group Report of the American Academy of Allergy, Asthma & Immunology

Update on the use of immunoglobulin in human disease: A review of evidence

Elena E. Perez, MD, PhD,[a] Jordan S. Orange, MD, PhD,[b] Francisco Bonilla, MD, PhD,[c] Javier Chinen, MD, PhD,[b] Ivan K. Chinn, MD,[b] Morna Dorsey, MD, MMSc,[d] Yehia El-Gamal, MD, PhD,[e] Terry O. Harville, MD, PhD,[f] Elham Hossny, MD, PhD,[e] Bruce Mazer, MD,[g] Robert Nelson, MD,[h] Elizabeth Secord, MD, PhD,[i] Stanley C. Jordan, MD,[j] E. Richard Stiehm, MD,[k] Ashley A. Vo, PharmD,[l] and Mark Ballow, MD[m] *North Palm Beach and St Petersburg, Fla; Houston, Tex; Boston, Mass; San Francisco and Los Angeles, Calif; Cairo, Egypt; Little Rock, Ark; Montreal, Quebec, Canada; Indianapolis, Ind; and Detroit, Mich*

Human immunoglobulin preparations for intravenous or subcutaneous administration are the cornerstone of treatment in patients with primary immunodeficiency diseases affecting the humoral immune system. Intravenous preparations have a number of important uses in the treatment of other diseases in humans as well, some for which acceptable treatment alternatives do not exist. We provide an update of the evidence-based guideline on immunoglobulin therapy, last published in 2006. Given the potential risks and inherent scarcity of human immunoglobulin, careful consideration of its indications and administration is warranted. (J Allergy Clin Immunol 2017;139:S1-46.)

Key words: *Immune globulin, immunoglobulin, IVIG, SCIG, IGIV, transfusion, adverse events, primary immunodeficiency, immunomodulation, immune modulating, autoimmunity*

Immunoglobulin is increasingly recognized as a treatment of a variety of medical conditions, not only for its ability to fight infection as a replacement therapy but also for its anti-inflammatory and immunomodulating effects. The appropriate use of immunoglobulin can be life-saving. However, its administration can lead to numerous adverse events and potential additional adverse consequences.[1] Due to finite supply, possible adverse events, and the need for further research in some applications of therapeutic immunoglobulin, it is important for clinicians prescribing immunoglobulin to be familiar with current clinical indications and levels of evidence in support of its use in these conditions. This document is intended as an update of the 2006 American Academy of Allergy, Asthma & Immunology guideline[2] and centers on the use of standard immunoglobulin preparations specifically manufactured for intravenous (IV) or subcutaneous (SC) administration. The SC route of administration has become more utilized in the United States, so we include an expanded section to cover practical considerations surrounding the administration of immunoglobulin subcutaneously. Clinical indications for which IV immunoglobulin (IVIG) have been licensed by the US Food and Drug Administration (FDA) include (Table I): (1) treatment of primary immunodeficiencies (PIs); (2) prevention of bacterial infections in patients with hypogammaglobulinemia and recurrent bacterial infection due to B-cell chronic lymphocytic leukemia (CLL); (3) prevention of coronary

From [a]the Allergy Associates of the Palm Beaches, North Palm Beach; [b]the Department of Pediatrics, Section of Immunology Allergy and Rheumatology, Center for Human Immunobiology, Texas Children's Hospital and Baylor College of Medicine, Houston; [c]the Department of Pediatrics, Clinical Immunology Program, Children's Hospital Boston and Harvard Medical School, Boston; [d]the Department of Pediatrics, Allergy, Immunology and BMT Division, Benioff Children's Hospital and University of California, San Francisco; [e]the Department of Pediatrics, Pediatric Allergy and Immunology Unit, Children's Hospital and Ain Shams University, Cairo; [f]the Departments of Pathology and Laboratory Services and Pediatrics, University of Arkansas, Little Rock; [g]the Department of Pediatrics, Allergy and Immunology, Montreal Children's Hospital and McGill University, Montreal; [h]the Department of Medicine and Pediatrics, Division of Hematology and Oncology and Stem Cell Transplantation, Riley Hospital, Indiana University School of Medicine and the IU Melvin and Bren Simon Cancer Center, Indianapolis; [i]the Department of Pediatrics, Wayne State University, Children's Hospital of Michigan, Detroit; [j]Nephrology & Transplant Immunology, Kidney Transplant Program, David Geffen School of Medicine at UCLA and Cedars-Sinai Medical Center, Los Angeles; [k]the Department of Pediatrics, David Geffen School of Medicine at UCLA, Los Angeles; [l]the Transplant Immunotherapy Program, Comprehensive Transplant Center, Kidney Transplant Program, Cedars-Sinai Medical Center, Los Angeles; and [m]the Department of Pediatrics, Division of Allergy & Immunology, University of South Florida, Morsani College of Medicine, Johns Hopkins All Children's Hospital, St Petersburg.

Supported by educational grants from CSL Behring (grant no. 53347), Grifols (grant no. 002308), and Shire (formerly Baxalta BioScience; grant no. BT16-32525).

Disclosures and potential conflicts of interest: M. Ballow has served on the data safety monitoring boards of Prometic and Green Cross; has received consulting fees from Baxalta; has received grant support from CSL Behring and Grifols; and has received lecture honoraria from Baxalta, Grifols, and CSL Behring. I. K. Chinn has received grant support from the Jeffrey Modell Foundation. J. Orange has received consulting fees from Baxalta, CSL Behring, Grifols, Walgreens, ADMA Biologics, and ASD Healthcare; has received grant support from CSL Behring; has received lecture honoraria from Baxalta; and has received royalties from UpToDate. E. Secord has received consulting fees from MDHHS; has received grant support from Wayne State University; and has received lecture honoraria from Hurly Hospital. R. Stiehm has received royalties from UpToDate. E. Perez has received consulting fees from Baxalta, CSL Behring, and Grifols; and has received royalties from UpToDate. T. Harville has received consulting fees from Baxalta. The rest of the authors declare that they have no relevant conflicts of interest.

This Work Group Report, submitted by the Primary Immunodeficiency Diseases Committee, was approved by the AAAAI Board of Directors in November 2015.

Received for publication December 7, 2015; revised September 12, 2016; accepted for publication September 23, 2016.

Available online December 29, 2016.

Corresponding author: Elena E. Perez, MD, PhD, 840 U.S. Highway 1, Suite 235, North Palm Beach, FL 33408. E-mail: eperez@pballergy.com.

The CrossMark symbol notifies online readers when updates have been made to the article such as errata or minor corrections

0091-6749/$36.00

© 2016 American Academy of Allergy, Asthma & Immunology

http://dx.doi.org/10.1016/j.jaci.2016.09.023

Abbreviations used

AD: Atopic dermatitis
APS: Anti–phospholipid antibody syndrome
AT: Ataxia telangiectasia
BMI: Body mass index
CIDP: Chronic inflammatory demyelinating polyneuropathy
CLL: Chronic lymphocytic leukemia
CVID: Common variable immunodeficiency
DSA: Donor-specific HLA antigen
FDA: US Food and Drug Administration
GBS: Guillain-Barré syndrome
GVHD: Graft-versus-host disease
HAART: Highly active antiretroviral treatment
ISR: Infusion site reaction
ITP: Immune thrombocytopenic purpura
IV: Intravenous
IVIG: Intravenous immunoglobulin
JIA: Juvenile idiopathic arthritis
KD: Kawasaki disease
LEMS: Lambert-Eaton myasthenic syndrome
MG: Myasthenia gravis
MM: Multiple myeloma
MMN: Multifocal motor neuropathy
MS: Multiple sclerosis
PAN: Polyarteritis nodosa
PE: Plasma exchange
PI: Primary immunodeficiency
RA: Rheumatoid arthritis
RCT: Randomized controlled trial
RSV: Respiratory syncytial virus
SC: Subcutaneous
SCID: Severe combined immunodeficiency
SCIG: Subcutaneous immunoglobulin
SCORAD: Severity scoring of Alzheimer disease
THI: Transient hypogammaglobulinemia
VOD: Veno-occlusive disease
WAS: Wiskott-Aldrich syndrome
XLA: X-linked agammaglobulinemia

artery aneurysms in Kawasaki disease (KD); (4) prevention of infections, pneumonitis, and acute graft-versus-host disease (GVHD) following bone marrow transplantation; (5) reduction of serious bacterial infection in children infected with HIV; (6) increasing platelet count in idiopathic thrombocytopenic purpura to prevent or control bleeding; and (7) treatment of chronic inflammatory demyelinating polyneuropathy (CIDP) and, more recently, multifocal motor neuropathy (MMN).[3,4] Despite these indications, none of the original immunoglobulin products that were specifically licensed for use in pediatric HIV or post–bone marrow transplantation are still available in the US market. The only licensed indication of SC immunoglobulin (SCIG) to date is PI disease.

This document reviews the basis for the FDA-approved indications and discusses other disease states in which immunoglobulin therapy has been used. Some of these other conditions are extremely rare, making randomized controlled trials (RCTs) difficult. Others, however, are quite common, and rigorous scientific evaluation of immunoglobulin utility has been possible. Immunoglobulin holds great promise as a useful therapeutic agent in some of these diseases, whereas in others it is ineffectual and may actually increase risks to the patient. Thus, the evidence supporting the use of immunoglobulin in these conditions has been reviewed and categorized (Table II). Current recommendations for the appropriate use of immunoglobulin are outlined in this summary. There are relatively few studies looking at SCIG for indications other than PI; however, the SC route is emerging as an alternative for maintenance therapy in patients on IVIG for CIDP as well as other muscle and nerve disorders.[5-7]

This updated summary is current through June 2015 and does not reflect clinical research or reports that have become available since that time. Although prior reviews of evidence were considered to have arrived at the conclusions contained in this document, primary literature for review on each subject was derived from searching the National Center for Biotechnology Information PubMed database using the key words *IGIV, IVIG, intravenous immunoglobulin, intravenous immune globulin, subcutaneous immunoglobulin,* and *subcutaneous immune globulin,* along with key words specific for each disease-related topic. The recommendations for appropriate use stated here were based on this literature review but will most certainly change over time as experience and understanding of these diseases increase.

PRIMARY IMMUNODEFICIENCY

Immunoglobulin replacement therapy via the IV or SC route is required in patients with certain PI diseases characterized by absent or deficient antibody production and, in most cases, recurrent or unusually severe infection (Table III).[8,9]

Replacement therapy for agammaglobulinemia and hypogammaglobulinemia in well-described immunodeficiencies such as X-linked agammaglobulinemia (XLA) or common variable immunodeficiency (CVID) is necessary and life-saving. Other more genetically complex PIs, however, may also involve defects in antibody function that contribute to an increased susceptibility to infections. Over 250 distinct PIs have been described to date, and with the advent of whole-exome sequencing, new PIs continue to be discovered at a rapid pace.[10] The effects of these newly described gene defects on the humoral immune system may not be fully understood or qualified with currently commercially available tests of antibody level and function. Therefore, the indications of immunoglobulin therapy in various clinical presentations of immunodeficiency are likely to broaden as the disorders are better understood, considering that a majority of PI diseases involve antibody deficiency. A recent publication reviewed the controversies surrounding immunoglobulin therapy, including the need for better laboratory assays of functional antibody responses and better clinical and microbiological evaluation and characterization of the recurrent infections seen in antibody-deficient patients.[11] Here, we provide a framework of 6 distinct phenotypes of PI disease for which immunoglobulin replacement is or may be indicated[12]: (1) agammaglobulinemia due to absence of B cells; (2) hypogammaglobulinemia with poor antibody function; (3) normal immunoglobulins with poor antibody function; (4) hypogammaglobulinemia with normal antibody function; (5) isolated IgG subclass deficiency with recurrent infections; and (6) recurrent infections due to a complex immune mechanism related to a genetically defined PI disease. These categories are briefly discussed subsequently (examples are not all-inclusive of the category described).

Agammaglobulinemia due to the absence of B cells

Agammaglobulinemia due to the absence of B cells is the clearest indication of immunoglobulin replacement. Evaluation of IVIG usage in patients lacking immunoglobulin has

Download English Version:

https://daneshyari.com/en/article/5646985

Download Persian Version:

https://daneshyari.com/article/5646985

Daneshyari.com