Management of Primary Immune Thrombocytopenia, 2012: A Survey of Oklahoma Hematologists-Oncologists

Kaelyn H. Lu, BS, James N. George, MD, Sara K. Vesely, PhD and Deirdra R. Terrell, PhD

Abstract: *Background:* Management options for patients with primary immune thrombocytopenia (ITP) have increased, and treatment of patients with ITP has changed during the past 10 years. *Methods:* To document current practice and to determine how current practice is related to recommendations of 2 recent practice guidelines for ITP, an International Consensus report and an American Society of Hematology (ASH) guideline, the authors surveyed practicing hematologists-oncologists in Oklahoma. Surveys were specific for children or adults. Each survey had 3 questions describing patients with a new diagnosis and patients who had not achieved remission with initial treatment. Questions were adapted from the clinical scenarios of the ASH guideline. *Results:* Twelve (92%) Oklahoma pediatric hematologists-oncologists responded; 82 (81%) Oklahoma adult hematologists-oncologists responded. For a child with a new diagnosis of ITP, a platelet count of 8000/μL and minor bleeding, 5 (42%) hematologists-oncologists selected observation without drug treatment (recommended by both guidelines). For an adult with a platelet count of 9000/μL who had failed to respond to initial treatment with corticosteroids and IVIg, 32 (39%) selected splenectomy (recommended by the ASH guideline); 30 (37%) selected rituximab and 13 (16%) selected thrombopoietin-receptor agonists (both recommended by the International Consensus report). Hematologists-oncologists who had more years in practice were more likely to select splenectomy ($P = 0.047$). *Conclusions:* In a time of changing management for patients with ITP, these data document reported current management in Oklahoma and provide a basis for serial comparisons across time and for comparisons with other regions and comparison of management with patient outcomes.

Key Indexing Terms: Immune thrombocytopenic purpura; ITP; Practice guidelines; Splenectomy; Thrombopoietin-receptor agonists. **[Am J Med Sci 2014;347(3):190–194.]**

With the availability of multiple new agents, management of patients with primary immune thrombocytopenia (ITP) has changed substantially since the initial practice guideline for ITP was developed by American Society of Hematology (ASH), 1994 to 1995.[1] Anti-(Rh)D was approved by the FDA for treatment of ITP in 1995 and has become a common initial treatment for children with ITP.[2] Rituximab was first used for ITP in 1999[3] and is now frequently used for patients who do not respond to initial treatment,[4,5] although it has never been approved by the FDA for treatment of ITP. Two thrombopoietin (TPO)-receptor agonists, romiplostim and eltrombopag, were approved by the FDA for treatment of ITP in 2008; they have been extensively studied in randomized clinical trials, actively marketed and increasingly used.[5–7] Two recently published clinical practice guidelines, an International Consensus report (ICR) published in 2010[8] and an updated practice guideline developed by ASH published in 2011,[9] have made recommendations for management of ITP in children and adults. To document reported current clinical management and to determine how reported current management is related to the recommendations of these guidelines, we surveyed practicing hematologists-oncologists in Oklahoma.

METHODS

Surveys

The ASH clinical practice guideline for ITP[9] based its systematic literature review and recommendations on focused clinical questions to describe management issues for children and adults. We used these clinical questions as the basis for our survey questions, to better compare physician responses with guideline recommendations. Although the ICR[8] did not use the format of focused clinical questions, the clinical indications for its recommendations were similar.

Separate surveys were developed for children and adults. Each survey had 3 clinical scenarios; each clinical scenario had 5 to 7 management choices (see complete surveys, Supplemental Digital Contents 1 and 2, http://links.lww.com/MAJ/A24 and http://links.lww.com/MAJ/A25). Hematologists-oncologists were instructed to select only 1 management choice. Data were collected from each respondent for (1) their number of years in practice; (2) the site of their practice, described as University of Oklahoma Medical Center (OUMC) or community; and (3) the estimated number of patients with ITP they see each year. In addition, whether community hematologists-oncologists had trained at OUMC and whether the hematologists-oncologists practicing at OUMC were faculty or fellows in training were determined from records of the OUMC Hematology-Oncology Divisions. There is no fellowship training program in pediatric hematology-oncology program at OUMC.

To determine if the clinical scenarios and management choices were clear and appropriate, the surveys were pilot tested by 5 pediatric hematologists-oncologists (Carolyn Bennett, Atlanta, GA; George Buchanan, Dallas, TX; Alan Cohen, Philadelphia, PA; Shelley Crary, Little Rock, AR; Cindy Neunert, Augusta, GA) and 6 adult hematologist-oncologists (Mark Crowther, Hamilton, Ontario, Canada; Mehrdad Jafari and Kiarash Kojouri, Mt. Vernon, WA; Mujahid Rizvi, Medford, OR; Lawrence Solberg Jr, Jacksonville, FL). Their comments were incorporated into the final version of the surveys. The surveys were approved by the Institutional Review Board of the University of Oklahoma Health Sciences Center.

From the Department of Biostatistics and Epidemiology, College of Public Health, Department of Medicine, College of Medicine, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma.

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Correspondence: Deirdra R. Terrell, PhD, The University of Oklahoma Health Sciences Center, Hematology-Oncology Section, Room CHB-237, P.O. Box 26901, Oklahoma City, OK 73126-0901 (E-mail: deirdra-terrell@ouhsc.edu).

Identification of Hematologists-Oncologists

Hematologists-oncologists were identified by searching the Oklahoma Board of Medical Licensure and the Oklahoma Osteopathic Association Web sites for all physicians certified in hematology/oncology, hematology, oncology or pediatric hematology/oncology. Hematologists-oncologists were included if they had an active Oklahoma license and were currently treating hematology-oncology patients in Oklahoma as of December 31, 2011. Current practice was determined by contacting the hematologists-oncologists' offices. Exclusion criteria included physicians who were radiation oncologists, gynecologic oncologists, surgical oncologists and pathologists, whose careers were devoted to full-time research or administration, who did not have an active Oklahoma license or who were not currently treating hematology-oncology patients in Oklahoma. In addition, hematologists-oncologists had to report seeing at least 1 ITP patient per year on the survey.

Data Collection

Surveys were initially sent to each physician by e-mail or fax on January 30, 2012. If there was no response within 2 weeks, then the hematologist-oncologist or the office nurse was contacted to remind them. To achieve the maximum response, some hematologists-oncologists were contacted multiple times by one of the authors (J.N.G.). The last surveys were returned on March 15, 2012.

Statistical Analysis

Descriptive statistics were used to describe the characteristics of the respondents and their responses, stratified by pediatric and adult hematologists-oncologists. Because of the small number of pediatric hematologists-oncologists, no comparison of their responses to their characteristics (years in practice, site of practice and number of patients seen each year) was performed. For the adult hematologists-oncologists, comparison of the number of years in practice with the responses was selected *a priori* because it was hypothesized that hematologists-oncologists with fewer years in practice may more readily accept newer treatments whereas hematologists-oncologists with more years in practice may prefer more traditional management. Chi-square or Fisher's exact test were used to determine if treatment responses differed by number of years in practice. SAS version 9.2 was used; alpha was set at 0.05.

Only the stronger grades of recommendations by the ICR and ASH guidelines were used for comparison with the hematologists-oncologists' responses. For the ICR, grade A (based on evidence from randomized clinical trials) or grade B (based on well-designed clinical studies) recommendations were used (not grade C).[8] For the ASH guideline, grade 1 recommendations were used (not grade 2).[9]

RESULTS

Pediatric Hematologists' Treatment of ITP in Children

All 13 pediatric hematologists-oncologists returned their surveys. One survey was not eligible because there was no response to the question of how many ITP patients were seen each year. Characteristics of the respondents included 8 OUMC faculty and 4 community pediatric hematologists-oncologists. None of the 4 community pediatric hematologists-oncologists had trained at OUMC. Two (17%) hematologists-oncologists had been in practice for less than 5 years, 6 (50%) for 5 to 20 years, and 4 (33%) for more than 20 years. Three (25%) reported seeing 1 to 5 ITP patients per year and 9 (75%) more than 5 per year.

TABLE 1. A child with a new diagnosis of ITP and minor bleeding symptoms

Management choice	Responses
Anti-D (Win-Rho)	2
Corticosteroids	3
IVIg	2
Observation with no drug treatment (watchful waiting)[a,b]	5
Thrombopoietin-receptor agonists (Nplate [romiplostim], Promacta [eltrombopag]) (if approved and available for use in children)	0
Other (describe): _____	0

Survey question 1: A 3-year-old boy presents with a 24-hour history of bruising and petechiae. He has a few areas of scattered petechiae and several small bruises on his arms and legs. His platelet count is 8000/μL. His complete blood count and smear review are otherwise normal, and his blood group is A+. What is your management choice?

[a] Management recommended by the ICR: grade B.[8]

[b] Management recommended by the ASH guideline: grade 1B.[9]

For a 3-year-old boy with a new diagnosis of ITP, a platelet count of 8000/μL and only minor bleeding, 5 (42%) pediatric hematologists-oncologists selected observation without drug treatment (watchful waiting); all 5 report seeing more than 5 ITP patients per year (Table 1). This was the management option recommended by both the ICR and ASH guidelines.

For a 3-year-old boy with a new diagnosis of ITP, a platelet count of 8000/μL and active bleeding, 6 (50%) pediatric hematologists-oncologists selected treatment with corticosteroids or IVIg (Table 2). These treatments were recommended by both guidelines. The ICR guideline also recommended treatment with anti-D, which was selected by 5 (42%) pediatric hematologists-oncologists.

For a 6-year-old girl with chronic symptomatic ITP for 12 months and a platelet count of 8000/μL, 7 (58%) pediatric hematologists-oncologists selected treatment with rituximab; 1 selected splenectomy (Table 3). The ICR guideline recommended

TABLE 2. A child with a new diagnosis of ITP and more severe bleeding symptoms

Management choice	Responses
Anti-D (Win-Rho)[a]	5
Corticosteroids[a,b]	1
IVIg[a,b]	5
Observation with no drug treatment (watchful waiting)	1
Thrombopoietin-receptor agonists (Nplate [romiplostim], Promacta [eltrombopag]) (if approved and available for use in children)	0
Other (describe): _____	0

Survey question 2. A 3-year-old boy presents with a 24-hour history of bruising and petechiae. He has a few areas of scattered petechiae and several small bruises on his arms and legs. When in your office, he develops epistaxis that lasts about 15 minutes. His platelet count is 8000/μL. His complete blood count and smear review are otherwise normal, and his blood group is A+. What is your management choice?

[a] Management recommended by the ICR: grade A.[8]

[b] Management recommended by the ASH guideline: grade 1B.[9]