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Implementation of an IGIV-sparing Treatment Protocol for Immune Thrombocytopenic Purpura (ITP) in a Large Children's Hospital

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Background

Due to limited availability[1] and high cost[2], the use of intravenous immunoglobulin (IGIV) as a therapeutic agent in pediatric patients with immune thrombocytopenic purpura (ITP) was examined. Following an evidence-based review, an IGIV-sparing treatment protocol utilizing Anti-D immune globulin (Anti-D) was proposed. The 2 most common dosing regimens for these therapies are as follows:

- IGIV administered in a 1 g/kg x 2 dosing regimen or a single 800 mg/kg dose[3,4,5]
- Anti-D administered as a single, indicated dose of 50 mcg/kg[6] or an off-label dose of 75 mcg/kg[7]

These 2 agents have similar efficacy and comparable side effect profiles in pediatric ITP[3,7,8] However, significant cost and product availability issues exist for IGIV.[1,2,9] In addition, the need for an adequate supply of IGIV at Childrens Hospital Los Angeles (CHLA) for numerous indicated and off-label uses warranted a review of its use.

Because of these considerations, a treatment protocol (algorithm) for newly diagnosed pediatric ITP has been developed* and implemented at CHLA (Table 1). The goal of the protocol is to promote efficacious and safe ITP therapy that most effectively employs both IGIV and Anti-D.

Objectives

The CHLA protocol was developed recently and is in the early stages of an ongoing implementation process. Therefore, the objective of this study is to provide a "snapshot" of the initial success of the protocol implementation illustrated through a series of recent ITP case-studies and other data from CHLA.

Methods

Medical records for newly diagnosed, nonsplenectomized pediatric ITP patients, who were admitted and treated with either Anti-D or IGIV were examined in a retrospective (2006) review. The following key data were evaluated for the case-studies:

- Demographics
- Physical examination and history
- Rh status
- Rise in platelet count at various intervals post-therapy
- Adverse events (AEs) from intake to discharge
- Information on processing, such as treatment preparation time and "chair-time"

Three pediatric ITP case-studies were selected that illustrate the:

- Successful use of the protocol to select appropriate, individualized initial therapy
- Efficacy and safety of treatment options in the protocol
- Applicability of the protocol to different clinical presentations of ITP
- IGIV-sparing aspect of the protocol

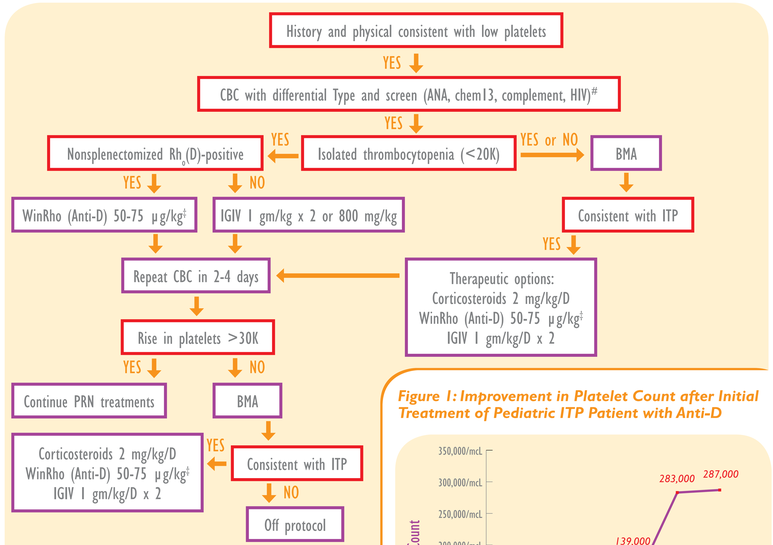
Results

Case Study 1: 2.5-month Remission with Anti-D

- 18-month-old, Rh (+) male
- Pertinent history: 2 days of ecchymoses, petechiae, and mild bleeding; recently treated with antibiotics for pharyngitis
- Initial complete blood count (CBC): Hemoglobin (Hgb) 14.1 g/dL, platelets <5,000/mcL
- No active bleeding upon admittance to CHLA; diagnosed with ITP

After premedication (corticosteroid, acetaminophen, and diphenhydramine) to minimize potential discomfort, the patient received 1 dose of 75 mcg/kg Anti-D.§ He did not exhibit the signs of AEs associated with IV dosing and his thrombocytopenia improved rapidly. The patient was discharged and his platelet counts continued to increase to acceptable levels over time (Fig. 1).

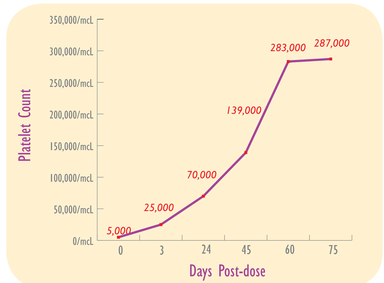
Table 1: CHLA Algorithm for Diagnosis and Initial Treatment of ITP in Children†



† Laboratory tests are indicated on the basis of patient age, history and physical examination.

‡ Hemoglobin levels must be ≥10g/dL prior to treatment.

Figure 1: Improvement in Platelet Count after Initial Treatment of Pediatric ITP Patient with Anti-D



Case Study 2: Same-day Improvement in Platelet Count with Anti-D

- 3-year-old, Rh (+) male
- Pertinent history: 1 month of "easy bruising" and occasional epistaxis subsequent to a viral illness
- Initial CBC: Hgb 11.2 g/dL, platelets 4,000/mcL
- Some petechiae and bruises present upon admittance; diagnosed with ITP

The patient received 1 dose of 75 mcg/kg Anti-D,§ which was well-tolerated. Immediately after therapy, the patient's platelet count rose to 12,000/mcL and Hgb slightly improved (11.6 g/dL). He was discharged and a review of his records indicated that no further treatment was required.

Case Study 3: Effective IGIV Therapy for Anemic Patient

- 3-year-old, Rh (+) female
- Pertinent history: 1 week of petechiae, epistaxis, and bruising
- Initial CBC: Hgb 7.4 g/dL, platelets <5,000/mcL
- Diagnosed with anemia and ITP

Due to the patient's low Hgb levels, she was treated with 2 doses of 1g/kg IGIV given once daily over 2 consecutive days. With premedication, the first dose of IGIV was well-tolerated; however, the patient experienced shaking chills with the second dose. After the first dose of IGIV, platelet counts rose to 15,000/mcL and to 72,000/mcL following the second dose. The patient was discharged after therapy.

Additional Assessments of Protocol Implementation

In the reviewed patient population, differences were identified in the typical time taken to prepare and administer IGIV versus Anti-D:

- Total infusion time for IGIV ranged from 2.5 to 7 hours for each of the 2 IV sessions
- Total infusion time for Anti-D was <1 hour

Anecdotal reports from CHLA nursing staff indicate that fewer AEs were experienced by patients receiving Anti-D versus IGIV-treated patients. Preliminary assessments also indicate that the protocol has positively impacted the processing time and cost associated with treating children with ITP.

Conclusions

Based on initial assessments, the CHLA protocol for the treatment of initial ITP in children has been successful in:

- Rapidly and safely improving platelet counts in nonsplenectomized, Rh (+) ITP patients utilizing Anti-D in place of IGIV
- Decreasing overall healthcare costs due to Anti-D being less expensive than IGIV (ie. less expensive drug cost, no reconstitution time, and shorter infusion time [several minutes versus several hours for IGIV])
- Sparing the use of IGIV for the treatment ITP, while enhancing its availability for the highest-need clinical areas

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Disclosure

The author of this presentation has the following to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation:

Christopher Lomax, PharmD: Speaker's Bureau: INO Therapeutics; Consultant: FFF Enterprises, Inc., Baxter Healthcare Corp., Baxa Corp.; Stockholder: Medco Health Solutions, Inc.

1. O'Day M, Boyle J, Moran TL, Winkelstein J. Availability of immune globulin intravenous for treatment of immune deficient patients: United States, 1997-1998. *MMWR Morb Mortal Wkly Rep.* 1999;48:159-162. **2.** Sandler SG, Novak SC, Roland B. The cost of treating immune thrombocytopenic purpura using intravenous Rh immune globulin versus intravenous immune globulin. *Am J Hematol.* 63:156-158. **3.** Shad AT, Gonzalez CE, Sandler SG. Treatment of immune thrombocytopenic purpura in children. *Pediatr Drugs.* 2005;7:325-336. **4.** Blanchette V, Imbach P, Andrew M, et al. Randomised trial of intravenous immunoglobulin G, intravenous anti-D, and oral prednisone in childhood acute immune thrombocytopenic purpura. *Lancet.* 1994;344:703-707. **5.** Blanchette VS, Luke B, Andrew M, et al. A prospective, randomized trial of high-dose intravenous immune globulin G therapy, oral prednisone therapy, and no therapy in childhood acute immune thrombocytopenic purpura. *J Pediatr.* 1993;123:989-995. **6.** Rh$_0$ (D) Immune Globulin Intravenous (Human). WinRho® SDF. Prescribing Information. Baxter Healthcare Corp., December 2005. **7.** Tarantino MD, Young G, Bertolone SJ, et al. Single dose of anti-D immune globulin at 75 microg/kg is as effective as intravenous immune globulin at rapidly raising the platelet count in newly diagnosed immune thrombocytopenic purpura in children. *J Pediatr.* 2006;148:489-494. **8.** Sandler SG and Tutuncuoglu SO. Immune thrombocytopenic purpura – current management practices. *Expert Opin Pharmacother.* 2004;5:2515-2527. **9.** Kumar M, Vik TA, Johnson CS, Southwood ME, Croop JM. Treatment, outcome, and cost of care in children with immune thrombocytopenic purpura. *Am J Hematol.* 2005;78:181-187.

*This protocol is the subject of American Society of Health-System Pharmacists Midyear Clinical Meeting Poster Presentation 403D. § 75 mcg/kg Anti-D is an unapproved, off-label use; Anti-D is indicated as ITP therapy at a dose of 50 mcg/kg.[6]