Comparison of Intravenous Immunoglobulin (IVIG) and Intravenous anti-D for Treatment of Acute Idiopathic Thrombocytopenic Purpura

Zahra Farahmandinia,[1] Ali Naderi,[1] Fatemeh Sabzevari,[2] Saeedeh Parvaresh

[1]Pediatric Hematologist Oncologist, Department of pediatrics, Kerman Medical University, Kerman, Iran.
[2]Pediatrician, Department of pediatrics, Kerman Medical University, Kerman, Iran.

Corresponding author: Dr. Fatemeh Sabzevari
Tel: +989131951947
Fax: +983412234959
E mail: omid.ahangari@yahoo.com

Abstract

Introduction: Acute Idiopathic Thrombocytopenic purpura (ITP) is an autoimmune bleeding disorder of childhood caused by production of auto antibodies against platelets. The aim of the present study was to compare the efficacy of intravenous immunoglobulin (IVIG) and intravenous anti-D(IV anti-D) in ITP treatment.

Methods and materials: In a clinical trial, 43 children with acute ITP referred to Afzalipour Hospital, Kerman/ Iran during 2 years were studied. Children were randomly divided into two treatment groups of IVIG (n=27) and anti-D (n=16). Two groups were compared in regard to the time takes for platelets to increase, platelets count in the 10^{th} post-treatment day and any drug side effects.

Results: Positive response to the treatment was observed in 70.4% (19 patients) of IVIG group and 68% (11 ones) of IV anti-D group. Mean response time was 2.9 days in anti-D and 2.8 days in IVIG groups (p=0.934). Platelets count on the 10^{th} post-treatment day in anti-D and IVIG groups were respectively 202545/µl and 204857/µl (p=0.974). Four patients in IVIG group showed side effects, while the patients in anti-D group had no complication or acute hemoglobin decrease.

Conclusion: In spite of no significant difference between IVIG and anti-D treatment groups in regard to the therapeutic outcomes, IV anti-D is suggested as the first-line treatment in acute ITP because of its lower price, more convenient administration and no need for hospitalization.

Keywords: Acute idiopathic thrombocytopenic purpura (ITP), Intravenous anti-D (IV anti-D), Intravenous immunoglobulin (IVIG).

Introduction

Acute Idiopathic Thrombocytopenic purpura (ITP) is one of the common bleeding disorders of childhood with the prevalence rate of approximately 5 in 100,000 individuals and maximum of 3,500 new cases per year in the United States of America. Acute ITP peak incidence is in the age of 1-4 year old and there is no sex preference. Two thirds of patients have history of viral infection in the last 4 weeks prior to the ITP onset.(1)

ITP is an autoimmune disease characterized by production of anti-platelet autoantibodies. These antibodies are produced against glycoproteines in the platelet membrane and trigger phagocytosis of antibody coated platelets in spleen (through binding Fc receptors of spleen macrophages) or other reticulo-endothelial organs.(1)

The diagnosis is based on ruling out other causes of thrombocytopenia presenting with major signs of petechiae and acute purpura. Asymptomatic cases with platelet count <20000/µl or symptomatic cases with platelet count <50000/µl require therapeutic intervention. Main treatment has been corticosteroids until 1981 followed by intravenous immunoglobulin (IVIG) and in the recent years intravenous anti-D has been proposed for acute ITP treatment.

IVIG blocks Fc receptors through activating FcγRIIB receptors and prevents platelet phagocytosis, but anti-D forms a complex with RBCs. This complex binds Fc receptors of spleen macrophages and inhibits their binding with platelet antibody complex and consequently platelet phagocytosis.(2, 3)

Although acute ITP is the most common bleeding disorder in children, there are either few or controversial studies about treatment selection, the speed of various treatments in cases with risk of severe bleeding and also advantages/disadvantages of different treatments. Anti-D is preferable to IVIG due to route, dose and duration of administration as well as its lower expense and no need for hospitalization.(4, 5) The present study was designed to compare the efficacy of IVIG andIV anti-D in order to validate IVanti-D as the first-line treatment in acute ITP.(6, 7)

Methods and materials

This clinical trial was performed on children with acuteITP referred to Afzalipour Hospital, Kerman, Iran during 2 years. Diagnosis was based on history, physical exam and mean platelet count detected by cell blood count (CBC) test (sysmex K21N instrument) or peripheral blood smear in the case of platelet aggregation. Demographic features, history of viral infections since 4 weeks prior to the disease onset (mild fever, rhinorrhea, coughing, rash), history of drugs consumption, history of allergy, disease symptoms and the results of primary CBC were recorded in a form.

Children with platelet count lower than 20000/µl or lower than 50000/µl accompanied with clinical symptoms (i.e. wet petechia, nose bleed or any hemorrhage) underwent treatment randomly with either IVIG (2gr/kg, 3-5 days) or IVanti-D (50µg/kg, single dose). Inclusion criteria for administration of anti-D were positive Rh, no splenectomy and no hemolytic anemia.

Children were followed up for drug side effects, receiving the other medication due to no response to the first medication, CBC in the first 48 hours, CBC in the second 48 hours if no treatment response and also CBC on the 10^{th} post-treatment day.

Results

In whole, 43 children with acute ITP were enrolled into the study of whom 53.5% were male and 46.5% were female. Mean age of patients was 4.5 years and mean weight was 16kg. From all, 60.5% had history of viral infection in the last month and 62.8% had history of drug consumption (antihistamines, acetaminophen, antibiotics and Ibuprofen respectively). Five children (11.6%) had history of seasonal allergy of whom one child had food allergy too but none of them had drug allergy.

Sixteen children underwent treatment with IVanti-D (group 1) and 27 ones with IVIG (group 2). In IVanti-D group, 11 ones (68.7%) and in IVIG group, 19 ones (70.4%) responded to the treatment and there was no significant difference between the two groups in treatment response (Table- 1). Platelet count increased in 2.9 days in IVanti-D group and in 2.8 days in IVIG group that shows no significant difference (p=0.934) (Table- 2). There was also no significant difference between the two groups in regard to the rate of platelet increase in the 10^{th} post-treatment day (202545/µl in IV anti-D group and 204857µl in IVIG group (p=0.974) (Table- 3).

From 43 patients, 4 ones, who were all in IVIG group, showed drug side effects (chills and fever, nausea, vomiting and hypotension). None of the children in IV anti-D group showed drug side effects.

Discussion

Acute ITP is an idiopathic disorder and 50-60% of the affected cases have history of recent viral infection.(1) In the present study, 60.5% of subjects (26 ones) had history of a viral disease during the last 4 weeks prior to acute ITP occurrence.

In the present study, 68.8% in anti-D group and 59.3% in IVIG group had positive history of drug consumption during the two weeks prior to ITP onset that shows no significant difference between the two groups. Since the most common consumed drugs were acetaminophen, antibiotics and Ibuprofen, it might explain the fact that some drugs such as analgesics, NSAIDs, some antibiotics (like penicillin), ß-blockers disturb platelets function and cause more rapid and severe manifestation of ITP symptoms.(8)

In regard to the history of allergy, 5 children were positive of whom 4 ones had allergic rhinitis and one child in addition to allergic rhinitis had history of asthma and allergy to banana with wheezing and coughing symptoms.

In this study, there was no significant difference between the two groups in regard to the time and rate of platelets count increase. In Son Daw study (2008), IVIG (1gr/kg, daily, for 2 days) or IVanti-D (50µg/kg/d) were administered randomly in acute ITP patients and platelets increase of more than 20000/µl after 3 days was observed in 93% of IVIG group and 92% of IV anti-D group that like our

study shows no significant difference in regard to the time for platelets count to increase.(9) But in Cheung study (2009), IVanti-D treatment caused rapid platelets count increase in 80% of children and 70% of adults affected by acute ITP. He has also asserted that anti-D in higher dose (75µg/kg/d instead of 50µg/kg/d) leads to more rapid treatment response and decreases the rate of future splenectomy.(10) On the other hand, in a randomized study, 146 children with acute ITP and platelet count lower 20000/µl were divided into three treatment groups of IVIG (1gr/kg, for 2 days),IV anti-D (25µg/kg, for 2 days) and prednisolone (4mg/kg/d). Platelets count increase was significantly more rapid in IVIG group as compared toIV anti-D and prednisolone groups and 24% of children inIV anti-D group showed Hg<10gr/dl. The author has mentioned that IVanti-D cannot be suggested as the first-line treatment in those with platelet count lower 20000/µl.(11)

In our study, the rate of platelet count increase was similar in the two treatment groups and no significant hemoglobin decrease was observed in IVanti-D group. The best advantage ofIV anti-D over IVIG is its cost-effectiveness. It has also been found in Gerald Sandler study (2008) thatIV anti-D is an efficient treatment for acuteITP patients with positive Rh who have not underwent splenectomy and while it has less complication, is more cost-effective and can be administered more easily compared to IVIG.(12) In treatment with Anti-D, due to the lower administered volume and consequently shorter time of administration, there is no need for hospitalization and it has been recently emphasized on even subcutaneous administration of anti-D. In a study in Denmark, ITP has been introduced as a benign hemolytic disease in children with the approximate prevalence of 50 cases in year. According to the mentioned study, 25% of patients enter a chronic phase of the disease and while IVIG has been mentioned as the choice treatment, anti-D has been administered subcutaneously and has lead to similar results.(13)

In regard to drug side effects, none of our patients in IV anti-D group showed any complication, while 4 children in IVIG group showed complications such as chills and fever, nausea, hypotension, headache and dizziness. It was noteworthy that from these 4 children, 2 ones had also history of respiratory allergy and allergic rhinitis.

Although IV anti-D group showed higher hemoglobin decrease (mean: 1.1gr/dl) compared to IVIG group (mean: 0.6gr/dl), there was no severe hemoglobin decrease in none of the treatment groups.

Finally, with regard to the similar therapeutic effects of IVIG and intravenous anti-D and observing no treatment complication in anti-D treatment group, in those who have the conditions of receiving intravenous anti-D, it can be used as the first-line treatment. In the case of showing similar effects to other treatments, subcutaneous anti D as a more rapid and convenient treatment, might be substituted other costly and time consuming treatments in future and there may be no need for intravenous treatments in acute ITP patients.

Table- 1. Comparison of response rate in IV anti-D group and IVIG group

Type of treatment	Time				Total
	No response	After 2 days	After 4 days	After 10 days	
Intravenous anti-D	5 (31.3 %)	9 (56.3 %)	1 (6.3%)	1 (6.3%)	16 (100.0%)
Intravenous Immmunoglobulin	8 (29.6 %)	14 (51.9 %)	4 (14.8 %)	1 (3.7%)	27 (100.0%)
Total count (%) within treatment	13 (30.2 %)	23 (53.5 %)	5 (11.6 %)	2 (4.7 %)	43 (100.0%)

Table-2: Mean Duration of Response in two groups.

Treatment	NO.	Mean (days)
IV anti-D	11	2.9091
IVIG	19	2.8421

Table- 3.Number of Platelets in 10th days after treatment

Treatment	NO.	Mean (platelets) Count/µl
IV anti-D	11	202545.45
IVIG	19	204857.14

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