SHORT COMMUNICATION

# Efficacy and Safety of Anti-D for Immune Thrombocytopenic Purpura in Children

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*Received: June 25, 2008;*
*Initial review: September 5, 2008;*
*Accepted: June 9, 2009.*

This study was conducted in 20 children (16 males) (mean age 9.2 ± 4.34y) with immune thrombocytopenic purpura (ITP) to assess the response to anti-D immunoglobulin. Six patients had newly diagnosed ITP, 6 had persistent ITP and 8 had chronic ITP. The overall response rate was 70% (14/20). The median time to response was 3 days (1-13 days). Response to anti-D was not related to age, sex, severity of bleeding, platelet counts at presentation, ABO blood group, or prior steroid or IVIG response.

**Key words:** *Anti D, Children, Immune thrombocytopenic purpura.*

***Published online: 2009 September 03. PII: S097475590800401-2***

The decision to treat children with ITP is driven by fear of severe bleeding, especially intracranial hemorrhage(1,2). Randomized clinical trials have demonstrated that therapy with intravenous immune globulin (IVIg) shortens the duration of severe thrombocytopenia faster than oral prednisolone. However, the relative efficacy of these two regimens is unresolved(1). Anti D is an antibody to the D (Rh) antigen(3). This prospective study was planned, as there is no published clinical trial on safety and efficacy of anti-D in ITP in Indian children.

## METHODS

This open label, non-comparative prospective trial was conducted after IRB approval. Inclusion criteria were ITP patients with bleeding symptoms; platelet counts<30,000/mm$^3$, Rh-positive blood group and who were non-splenectomized. Bleeding symptoms were graded as described elsewhere(4).

Patients were classified as: Newly-diagnosed ITP: within 3 months from diagnosis; Persistent ITP: between 3 to 12 months from diagnosis; and, Chronic ITP: lasting for more than 12 months, as per current consensus definitions(5).

Anti D (WinRho, Cangene, Winnipeg, MB) 50 µg/Kg was given intravenously single dose over 5-minute as infusion. Platelet counts were done on days 1, 2, 3 and 7 and then at weekly interval after anti-D infusion. Response was defined as Complete (CR): platelet count ≥100×10$^9$/L; Response (R): platelet count ≥30×10$^9$/L and at least twofold increase from the baseline count; and No response (NR): platelet count <30×10$^9$/L or less than twofold increase of baseline platelet count or bleeding(5). Time to response was calculated as time taken from starting anti-D to achievement of CR or R. Loss of CR or R: platelet count below 100×10$^9$/L or bleeding (from CR) or below 30×109/L or less than twofold increase of baseline platelet count or bleeding (from R).

## RESULTS

There were 16 males and 4 females. The mean age of the study cohort was 9.2 ± 4.3 years. Six patients had newly diagnosed ITP, 6 patients had persistent ITP and 8 had chronic ITP. One patient had no bleeding

but was administered anti-D twice, first for maxillary biopsy, which revealed mucormycosis and subsequent dose for eventration of her left eye. There were 6 children with grade 1 bleeding, 11 children with grade 2 bleeding and 2 patients with grade 4 bleeding.

The median platelet count at the time of administering the anti-D was $8\times10^9$/L ($2\text{-}22\times10^9$/L). Median hemoglobin (Hb) was 12.9 g/dL (10.2-14 g/dL). Eight patients had received prednisolone (1.5-7 months, median 5 months) prior to administration of anti-D. In addition, 2 children had previously received prednisolone but were 4 months and 10 months off steroid at the time of administration of anti-D. One child had received IVIg 21 days prior to administration of anti-D and had again presented with thrombocytopenia and purpuric spots. One child was receiving dapsone since 6 months. Three patients had not received any prior treatment. The overall response rate was 70% (14/20) (***Table* I**).

*Response kinetics*: The median time to response was 3 days (1-13days). Only one patient responded in 24 hours of administration of anti D. Three patients responded in 48 hours. There was no correlation of response with age, sex, severity of bleeding, presenting platelet counts, ABO blood group, or prior steroid or IVIG response. One patient continued to have purpuric spots even after normalization of platelet counts. He had an unclassified platelet function defect. One child went into sustained remission (likely spontaneous remission). Rest all patients had loss of response after a variable period of time. The median duration of response was 21 days (14-53 days).

Some of the patients received repeat administration of anti-D after loss of response. Four patients received 2 doses and one child received 3 doses**.** Of these 5 patients; 1 PR went into CR on second dose, 1 PR again went into PR and 1 patient (PR) did not respond to second dose. One child, who received 3 doses, attained CR with all the doses. One child who failed to respond to first course, failed again with the second dose also.

**TABLE I** RESPONSE RATES IN IMMUNE THROMBOCYTOPENIC PURPURA (ITP) (*N*=20)

| ITP | *n* | Complete response | Response | No response | Overall response |
|---|---|---|---|---|---|
| Newly diagnosed | 6 | 2 | 3 | 1 | 5 (83%) |
| Persistent | 6 | 2 | 3 | 1 | 5 (83%) |
| Chronic | 8 | 1 | 3 | 4 | 4 (50%) |

Intravenous administration was associated with low grade fever in 2 patients. We observed fall in hemoglobin (Hb) in 18 (90%) patients. The average fall in Hb was 1.1 (0.4-2.0) g/dL. Polychromasia and sherocytosis was seen in 13 and 2 patients, respectively. Median reticulocyte count was 2.9% (1-7%). Median bilirubin rise was 0.9 (0.9-1.5) mg/dL. One patient had Hb fall of 2 g/dL but he had bleeding manifestations also. The fall in Hb was transient and recovered in 7-14 days in all cases.

## DISCUSSION

Intravenous anti-D treatment compares favorably with IVIg with a shorter infusion time (minutes), a single infusion, much smaller donor pool size and therefore, less risk of infection transmission and a lower cost compared with IVIg(6).

The presumed mechanism of action of anti-D immunoglobulin in ITP involves extravascular hemolysis of anti-D–sensitized red blood cells (RBCs) by splenic macrophages, which results in decreased splenic sequestration of autoantibody-sensitized platelets and an increased platelet count(3,6). Different trials have reported overall response rates of 67-92%(6-15). One earlier Indian study using intramuscular preparation documented a response of 62.5%(10).

The most frequent drug-related adverse events are chills, pyrexia, fall in Hb, and increase in bilirubin. However, major side effect reported includes prolonged intravascular hemolysis. Thus, utmost care should be taken while using the drug in patients with borderline hemoglobin.

There is evidence that a dose of 75 µg/Kg is more effective than 50 µg/kg(7,8). Larger trials are required to find if this dose would lead to higher response rates in Indian children with ITP.

**WHAT THIS STUDY ADDS?**

- Use of Anti-D immunoglobulin in ITP provided an overall 70% response rate.

*Contributors*: RN, RK and MM planned the study. ST helped in diagnosis of cases. All the authors were involved in the execution of the protocol. RN drafted the script, which was critically analyzed by all the authors.

*Funding*: None.

*Competing interests*: Some children received free Anti-D injections from Cangene Corporation.

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