The Turkish Journal of Pediatrics 36: 43-47, 1994

LONG – TERM USE OF ANTI – D IN CHRONIC IDIOPATHIC THROMBOCYTOPENIC PURPURA*

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SUMMARY: Yaprak I, Çağlayan S, Kansoy S, Özdoğru E, Bakiler AR, Aydınlıoğlu H. (Department of Pediatrics, SSK Tepecik Teaching Hospital, Yenişehir, İzmir, Turkey). Long-term use of anti-D in chronic idiopathic thrombocytopenic purpura. Turk J Pediatr 1994; 36: 43-47.

Chronic idiopathic thrombocytopenic purpura is an autoimmune disease characterized by antibody-mediated destruction of platelets. To maintain the platelets above the symptomatic level, we administered anti-D (100 µg for 5 consecutive days) in 19 children with idiopathic thrombocytopenic purpura (ITP). Four patients did not respond to treatment. Fifteen responded with an increase in the average platelet number to 76,000 / µL on the 7th postinjection day. Within 45 days, however, platelets dropped to 27,000 / µL. Three months after this study, two patients from the study group were re-administered anti-D in daily injections for 5 consecutive days, as was done previously. Monthly administration of anti-D in two patients maintained platelets above 30,000 / µL for periods of five and six months.

We concluded that monthly administration of anti-D after five consecutive daily injections can maintain platelet levels above the symptomatic level and may provide a corticosteroid-free safe interval of nearly five months. *Key words: chronic idiopathic thrombocytopenic purpura, anti-D.*

Childhood immune thrombocytopenic purpura (ITP) is an autoimmune disorder resulting from the formation of autoantibodies to platelets, and leading to platelet destruction in the accessory cell system[1]. Rapid decrease of platelets to levels below 20,000 / µL may result in mucosal, skin and, less frequently, central nervous system bleeding. For the emergency treatment of these situations, either platelet transfusion or some other treatment modalities such as intravenous immunoglobulin (IVIg), intravenous methyl prednisolone and splenectomy have been advised. To achieve a long-term complete remission (platelets consistently greater than 100,000 / µL) or partial remission (platelets between 30,000 and 100,000 / µL) without clinical symptoms, other therapeutic protocols have been proposed. Corticosteroids have been the drugs of choice for long-term therapy for

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many years. High-dose methyl prednisolone[2,3], cytostatics[4,5], IVIg[6,7], danazol[8] colchicine[9] and ascorbic acid[10] have also been used.

Anti-D is an alternative drug for chronic ITP. It has been used in varying doses and in varying protocols[11-13]. In this report we present our results of long-term use of anti-D in chronic ITP and discuss the potential benefit of its use in reducing the steroid requirement to maintain the platelets above the critical level.

Material and Methods

Nineteen children, age 15 or less, with chronic ITP and platelet levels lower than 30,000 / μL, (coulter counter, coulter electronics) were enrolled in the study. All patients had been treated previously with oral corticosteroids, and some had also been given either high-dose intravenous methyl prednisolone or intravenous immunoglobin (Table I). The occurrence of thrombocytopenia resistant to other therapeutic modalities for more than six months was accepted as the criterion for ITP chronicity. Antiplatelet antibodies were not measured. All patients were injected with 100 μg of anti-D using a 25-gauge disposable needle for five consecutive days, and were then followed until the platelet level dropped to 30,000 / μL or less.

Table I: Therapeutic Regimens Previously Used in Patients

Regimen	Patients*
Prednisolone (Oral)	19
IVIg**	4
HDMP	16
Anti-D	19

* All of the patients were given at least two treatment protocols.

** IVIg, intravenous immunoglobulin. HDMP, high-dose methyl prednisolone.

Two of the 19 patients were then enrolled in another study protocol after an interval of three months after the above-mentioned anti-D therapy. Both patients were given the some dose of anti-D for five days, followed by repeat injections on days 15, 30 and every 30 days thereafter until their platelet levels dropped below 30,000 / μL. In both studies, hemoglobin (Hb), reticulocyte and lactic dehydrogenase (LDH) levels and direct Coombs tests were checked at regular intervals, but haptoglobulin levels were not determined.

Results

Of the 19 patients, four were male and 15 female (M / F ratio 1 / 4). Four patients (2M, 2F) did not respond to therapy at all, and their platelet levels did not rise above 30,000 / µL during the therapy. Injections caused no bleeding problems in patients. Table II displays the changes in platelet levels in the 15 responding patients. The average initial platelet level of 18,000 / µL increased to 50,000 on the 3rd and to 76,000 on the 7th day. On day 15, the average level was 63,000, then dropping to 35,000 on the 30th, and to 27,000 on the 45th day.

Table II: Average Platelet Values of 15 Responsive Patients

	Postinjection Days				
	3	7	15	30	45
Platelets (10^3 / µL)	50	72	63	35	27

During monthly administration of anti-D to two patients, the platelet levels remained above 30,000 / µL for five and six months, although a gradual decrease in platelet levels was observed after two months of therapy (Fig. 1). Changes in LDH and Hb values were not significant. Direct Coombs tests became weakly positive in some patients, still with no changes in Hb values.

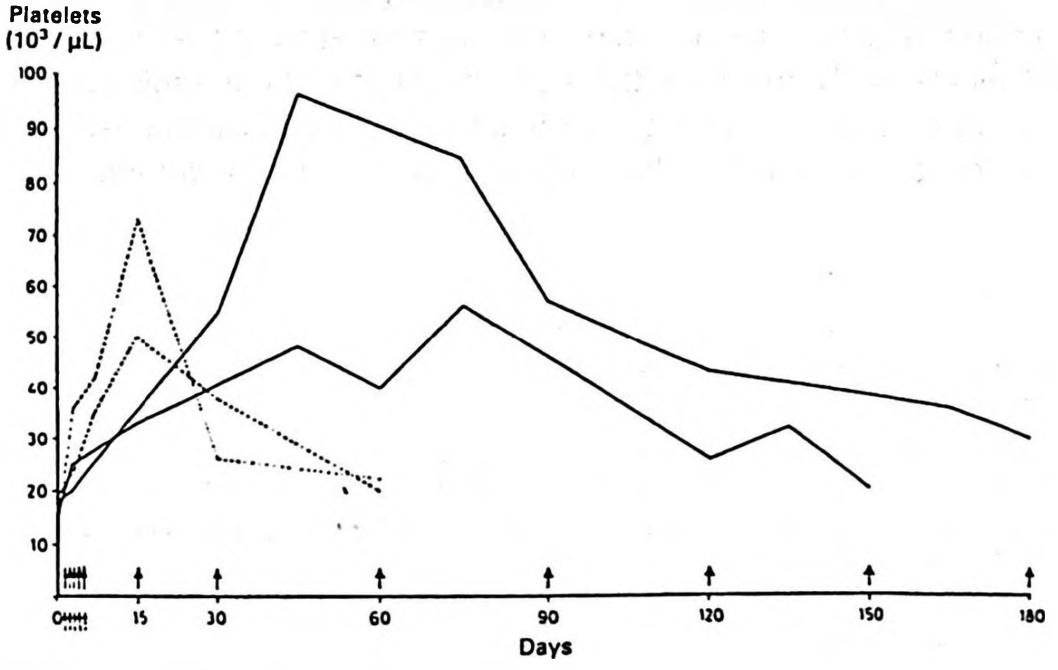

Fig. 1: Platelet levels of two patients after two different anti-D administration. Broken lines: Platelet levels after five days of anti-D. Solid lines: Platelet levels after repetitive use of anti-D.

Discussion

For the treatment of chronic ITP, several treatment modalities have been suggested. In addition to classical oral prednisolone therapy, high-dose methyl prednisolone[2,3], IVIg[6,7], antineoplastic agents[4,5] and recently anti-D[11-13] have been found to be useful with varying success. Anti-D was found to be effective in increasing the platelet counts in 79% of our patients. The highest platelet level of 76,000 / μL was reached between 10 and 15 days after anti-D, then dropping to 35,000 on the 30th postinjection day.

The platelet counts of two patients who were given repeated anti-D were maintained above 30,000 / μL for five and six months. This is an important point, because the platelets of the same patients had dropped below 30,000 within 30 days of the previous anti-D protocol (100 μg for five consecutive days). In accordance with a previous report[14], we could not find any direct relationship between the clearance of red blood cells and direct antiglobulin test positivity, because there was no significant change in Hb and LDH values despite weak antiglobulin test positivity and a slight increase in the reticulocyte count.

A suggested mechanism of action of anti-D is that IgG-coated red blood cells induce a diminution of the Fc-dependent clearing capacity of the accessory cell system. Whatever the mechanism of action, anti-D may be a viable alternative to corticosteroids, because long-term use of corticosteroids is usually limited, due either to resistance or to side effects. In these situations, repeated anti-D injections can provide a safe platelet level for at least five months. After this period, corticosteroids or another alternative drug can be reused.

In summary, anti-D can be an alternative agent in the treatment of chronic ITP. It can maintain the platelet level within safe limits for at least five months if used in repeated injections. To minimize the side effects of corticosteroids and to reduce unresponsiveness to either corticosteroids or to anti-D, rotational use of both drugs can be considered for the long-term treatment of chronic ITP.

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