HIGH DOSE PULSE DEXAMETHASONE THERAPY IN CHRONIC IDIOPATHIC THROMBOCYTOPENIC PURPURA

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ABSTRACT

We studied the response to pulse high dose dexamethasone (DXM) in 12 consecutive patients of symptomatic chronic idiopathic thrombocytopenic purpura (ITP) who had not responded to the standard forms of therapy. All patients had been exhibited to two or more cycles of prednisolone. Besides this 5 patients had also been given danazol and 4 patients had undergone splenectomy. Six cycles of dexamethasone (40 mg per day for 4 sequential days every 4 weeks) were successfully given in all 12 patients. At the end of the sixth cycle there were 7 (58%) complete responders (CR) [platelet count (PLT) $100 \times 10^9/L$], 1 partial responder (PR) [PLT $50-100 \times 10^9/L$] and 4 non responders (NR) [PLT $< 50 \times 10^9/L$]. Follow up at 1 year showed 4 (33.3%) patients each in CR, PR and NR group. Side effects noted were increased appetite in 8 (66.6%) patients, hyperalertness in 6 (50%) patients, abdominal discomfort in 5 (41.6%) patients and nausea with vomiting in 2 (16.6%) patients. We were not able to identify any chemical or laboratory prognostic parameter which would allow prediction of a successful outcome of this treatment.

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KEY WORDS : Dexamethasone, Idiopathic thrombocytopenic purpura.

INTRODUCTION

Chronic idiopathic thrombocytopenic purpura has been a stubborn disease to treat. It is an autoimmune disease where autoantibody coated platelets are removed from the circulation by the monocyte-macrophage system mainly in the spleen and liver [1-5]. It may be a complication of disorders like systemic lupus erythematosus [6] or B-cell lymphomas [7]. The evolution of therapy includes splenectomy in 1926, corticosteroids in 1951 and intravenously administered immunoglobulin (IVIg) in 1981. Other drugs like danazol, colchicine, vincristine, vinblastine, azathioprine, anti-D, dapsone and interferon have been used with variable results [8]. In chronic ITP, the mainstay of therapy has been treatment with prednisolone (1-2 mg/kg body weight/day) or splenectomy. Approximately 70% of patients respond whereas the result is disappointing in the rest [9]. High dose IVIg though effective requires repeated reinfusions and proves very costly [10]. Thus it is not practical in developing countries. Andersen in 1994 reported excellent results with limited side effects of high dose dexamethasone (40 mg/day for 4 sequential days every 4 weeks for 6 cycles) in 10 cases of chronic ITP who were refractory to 2 to 6 previous treatments including splenectomy in 6 cases [11]. However subsequent studies have not reproduced the same results [8,12,13].

The present study evaluated the response of pulsed high dose dexamethasone in patients of symptomatic

refractory chronic ITP who had previously failed to respond to the standard forms of therapy with 2 or more cycles of prednisolone.

Material and Methods

1. Selection of patients

Twelve consecutive patients with a diagnosis of chronic ITP who were symptomatic with bleeding episodes but refractory to conventional treatment modalities were enrolled in the study from May 1994 to July 1997 at Army Hospital (R & R). The diagnosis of ITP was based on a clinical history of mucocutaneous bleeding, absence of splenomegaly and laboratory data of isolated thrombocytopenia with normal or increased bone marrow megakaryocytes: The patient with any infectious disease such as Hepatitis B and C or HIV, hepatic or autoimmune disease, any underlying malignancy, use of any drugs known to cause thrombocytopenia were not included in the study and history of refractory chronic ITP was defined as the failure to respond to repeated (2 or more) cycles of prednisolone therapy and or additional therapy with danazol and splenectomy.

2. Laboratory studies

All patients underwent bone marrow aspiration and biopsy at initial diagnosis. The screening tests carried out at enrollment were: Complete blood counts (CBC), Serology for HIV, HBV and HCV, Anti-nuclear factor (for SLE), Blood sugar levels-fasting and post prandial, chest radiograph, upper gastrointestinal (GI) endoscopy (in patients with history of dyspepsia/GI bleed), liver function tests, renal function tests, Electrolytes (Na^+ and K^+), urine analysis, stool-occult blood.

During each cycle CBC, blood sugar levels, electrolytes (Na^+ and K^+), urinalysis and stool for occult blood was done.

3. Criteria for response

Complete response (CR)	-	PLT $> 100 \times 10^9/L$
Partial response (PR)	-	PLT $= 50 \times 10^9/L$ to $100 \times 10^9/L$

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No response (NR)

PLT < 50 x 10⁹/L

4. Medication

All patients received 40 mg of oral dexamethasone daily for 4 days. Each cycle was of 4 weeks and 6 such cycles were given. Follow up was carried out for a minimum period of 6 months. All patients were hospitalised during the period of therapy and were closely monitored for side effects.

Results

The clinical and demographic characteristics of the 12 patients are summarised in Table-1. Of these 12 patients, 7 (58%) achieved CR, 1 (8%) PR and 4 (34%) NR at the end of the 6th cycle of high dose DXM. Platelet count increased in 7 (58%) patients after 3 cycles of DXM and continued to improve during the subsequent 3 cycles. At the end of 1 year after starting therapy there were 4 patients each in CR, PR and NR group.

Bleeding episodes ceased in all patients except in patients 10 and 12 (Table 1) who were non responders. Patient 8 and 11 who were also non-responders by platelet count criteria (2x10⁹/L) significantly had no bleeding episodes except for occasional gum bleeds on brushing of teeth at one year follow up.

Side effects noticed were limited to increased appetite (8 patients), hyperaltness (6 patients) and nausea with vomiting (2 patients). None of these patients had to discontinue therapy due to these side effects.

Responses were not related to age, sex, duration of disease prior to therapy or to types of pretreatment (example prednisolone, danazol, splenectomy) given to the patients prior to high dose DXM.

DISCUSSION

Chronic ITP is a immune mediated disorder where platelets are destroyed in a setting of normal or accelerated magakaryopoiesis. It is known that approximately 20-30% of these patients are refractory to treatment with corticosteroids with or without splenectomy. It was reported in 1994 that cyclic therapy with oral DXM (40 mg/day for 4 sequential days every 4

weeks for 6 cycles) was effective in the treatment of chronic ITP [11]. However, a few subsequent studies have reported variable responses to this therapy [8,12,13].

Andersen [11] observed an increase in platelet count greater than 100 x 10⁹/L in all cases, with platelet normalization in 8 out of 10 cases. Platelet count remained greater than 100 x 10⁹/L for at least 6 months after the last cycle of treatment and side effects were limited. However, these results were not reproduced in subsequent studies [8,12,13]. Besides, a higher incidence of side effects were also noticed in some studies which necessitated discontinuation of therapy.

We found our results to be intermediate. At the end of the 6th cycle, there were 8 responders (66.6%) (7 CR and 1 PR) and 4 non responders. At 6 month follow-up we documented 4 patients each (33.3%) in CR, PR and NR group. However significantly enough, except 2 of the non responders, all the other patients were free of any bleeding episodes. In chronic ITP the basic aim is to prevent bleeding from any site. This is achieved by lower than normal platelet counts in these patients as many young large platelets are produced due to accelerated magakaryopoiesis. These young platelets are hyperfunctional and help in haemostasis. The median duration at initiation of high dose DXM therapy in our study was 1.5 years. This is shorter than compared to other studies [8,11,12] where the median duration of illness prior to this therapy on an average was 8-12 years. The better response in our study could be because of earlier exhibition of high dose DXM therapy. Though the numbers are small we would rec-

TABLE 1
Characteristics of the 12 patients treated with high-dose dexamethasone

Patient	Age/ Sex	Duration of disease (months)	Prior therapy*	Bleeding symptoms +	Before treatment	Platelet count (10 ⁹ /L)			
						During treatment		After treatment	
						Month 1	Month 3	Month 6#	Month 6
1	28/F	12	P	C,E,M	8	35	76	124 (CR)	65 (PR)
2.	30/F	24	P,S	C,M	17	33	78	118 (CR)	70 (PR)
3.	35/M	14	P	C,F,B	10	110	85	120 (CR)	130 (CR)
4.	25/F	28	P,D	C,B	28	95	55	70 (PR)	60 (PR)
5.	25/F	18	P	C,B,M	26	80	85	140 (CR)	180 (CR)
6.	25/F	32	P	C,B	22	55	68	138 (CR)	80 (PR)
7.	42/F	10	P,D	C,E	35	60	102	140 (CR)	125 (CR)
8.	30/M	30	P,D,S	C,E,B	17	30	28	45 (NR)	40 (NR)
9.	14/M	12	P	C,B	55	110	90	170 (CR)	230 (CR)
10.	56/M	20	P,D,S	C,B	18	25	20	28 (NR)	20 (NR)
11.	39/F	24	P,S	C,B,M	10	18	22	26 (NR)	15 (NR)
12.	18/F	12	P,D	C,B	14	20	28	35 (NR)	18 (NR)

* P: prednisolone; D: danazol; S: splenectomy; #CR: complete response; PR: partial response; NR: no response; +C: cutaneous bleed; E: epistaxis; M: menorrhagia; F: fundal haemorrhage; B: buccal bleed

ommend high dose pulse DXM therapy in all patients who have failed to respond to 2 or more cycles of prednisolone, given in a dose of 1mg/kg body weight for 4 to 6 weeks followed by gradual tapering over 2 weeks in each cycle.

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