Short-course High-dose Dexamethasone Therapy for Chronic Idiopathic Thrombocytopenic Purpura in Children

by Dinesh Yadav, Jagdish Chandra, Sunita Sharma, and Varinder Singh

Division of Pediatric Hematology, Department of Pediatrics, Kalawati Saran Children’s Hospital, New Delhi 110001, India

Department of Pathology, Lady Hardinge Medical College, New Delhi 110001, India

Correspondence: Dinesh Yadav, Room No. 02, New Registrar’s Block, Lady Hardinge Medical College, New Delhi 110001, India. Tel.: +9868493930; E-mail <dineshmamc@gmail.com>.

Summary

First-line therapies of acute and chronic idiopathic thrombocytopenic purpura (ITP) include intravenous immunoglobulin, IV anti-D and corticosteroids. A short-course high-dose dexamethasone (HDD-SC) therapy has recently been reported to be efficacious in acute ITP. The present study was conducted to assess the efficacy of HDD-SC in children with chronic ITP. Over a period of 10 months, 13 patients with chronic ITP were given HDD-SC (20 mg m⁻² IV daily for 4 days, four cycles repeated every 15 days). Of the 12 patients who could be evaluated, complete response was observed in 8 (66.6%) and moderate response in 2 (17%) patients, whereas 2 (17%) patients had no response. HDD-SC appears to be a safe and effective therapy in childhood ITP.

Key words: ITP, dexamethasone.

Introduction

Over the past two decades, most significant advancements in childhood idiopathic thrombocytopenic purpura (ITP) have occurred as a result of a better understanding of its natural history and absence of significant bleeding manifestations even with severe thrombocytopenia (platelet count <20,000 mm⁻³) [1–3]. This has led to wider acceptance of ‘observation only’ approach. However, platelet-enhancing drug therapy is required for management of children with acute and chronic ITP, either because of moderate to severe bleeding symptoms or for very low platelet counts. Intravenous immunoglobulin (IVIgG), IV anti-D and corticosteroids form the first-line therapy for ITP.

High-dose dexamethasone (HDD, 40 mg daily for 4 days, every month for 6 months) for ITP was first used by Andersen [3] who reported good response in all patients. However, subsequent studies using similar protocol showed only moderate success [4–7].

A shorter version of HDD [short-course high-dose dexamethasone (HDD-SC)] has recently been used in patients with acute ITP and has shown long-lasting response in 85.6% patients (GIMEMA study) [8]. We report here our observations on HDD-SC in children with chronic ITP.

Patients and Methods

Children under 18 years of age having chronic ITP (disease duration >6 months) were the subjects of this prospective study. They had received one or more forms of therapy earlier when they had very severe thrombocytopenia (platelet count <10 × 10³ mm⁻³) or moderate to severe bleeding manifestations. Based on these two criteria, if the need for further therapy had arisen, they were enrolled for HDD-SC. All patients underwent serological tests including HIV, hepatitis B and C, Coombs test and lupus erythematosus (LE) cell phenomenon. Dexamethasone was administered at a dose of 20 mg m⁻² IV daily for 4 days. These cycles were repeated every 15 days for four cycles. Platelet counts were performed daily for 5 days and then at the beginning of the next cycle.

Response was defined as follows: complete response (CR) if the platelet count increased to >150 × 10³ mm⁻³; moderate response (MoR) if platelet counts were between 50 × 10³ and 150 × 10³ mm⁻³; minimal response if platelet counts were between 20 × 10³ and 50 × 10³ mm⁻³; and no response (NR) if platelet count did not increase or increased but still was <20 × 10³ mm⁻³. Decrease and/or subsidence of bleeding manifestations were
recorded. Patients were monitored for side effects like hypertension, hyperglycemia, infections and weight gain.

Results

Over a period of 10 months, 13 patients (age 3–16 years, median 8 years) with chronic ITP received HDD-SC. All cases were hepatitis B, C and HIV negative. Coombs test and LE cell phenomenon were negative in all cases; however, one child had positive test for antinuclear antibody, although his double stranded DNA was negative.

Three patients had received IVIgG, two IV anti-D, eight methyl-prednisolone, six long-term prednisolone and six HDD (>6 months). None of the patients was splenectomized. Twelve of the 13 patients had only cutaneous bleeds at presentation, while 4, 2 and 1 had gastrointestinal, gum and vaginal bleeding, respectively. Initial platelet count was between $1 \times 10^3 \text{mm}^{-3}$ and $37 \times 10^3 \text{mm}^{-3}$ (median $7 \times 10^3 \text{mm}^{-3}$). Platelet count was <$10 \times 10^3 \text{mm}^{-3}$ in 10 patients and they were started on HDD-SC for this very severe thrombocytopenia, remaining 3 patients received HDD-SC on account of significant mucosal bleeding.

One patient was lost to follow-up after the first cycle. Of the 12 patients who could be evaluated, CR was observed in 8 (66.6%) and MoR in 2 (17%) patients, whereas 2 (17%) patients had NR (one of the responders had thrombocytosis—platelet count >500 $\times 10^3 \text{mm}^{-3}$—after third cycle and was not given subsequent therapy). Four patients had response after second cycle, two after third cycle and remaining four responders had response after fourth cycle. Median duration of response (calculated as time when any platelet-enhancing therapy was required after initial time of response) was 5 months (range 3–11 months). Bleeding manifestations subsided in all patients as their platelet count improved.

Therapy was well tolerated by most patients except one who developed hypertension, requiring antihypertensive therapy. No other adverse effects of steroid therapy were observed.

Discussion

In a recent Italian study, response rate of 89.2% and relapse-free survival of 90% at 15 months was reported using HDD in 4-day pulses every 28 days for six cycles in acute ITP. However, they observed high rate of discontinuation of therapy due to medical decision or poor compliance with a long-lasting treatment [8]. Based on this observation of poor compliance and encouraging response observed by Cheng et al. [6] using a single 4-day course of oral HDD in initial treatment of adults with ITP, the Italian group used four cycles at 2 weeks interval. This treatment schedule has shown a high initial response rate (86%) and a high CR rate (64.5%). Besides this, they observed good tolerance and better quality of response (CR vs partial response) in patients younger than 18 years of age [8]. However, these results should be viewed in light of the fact that the patients included in this study had acute ITP, many of whom were likely to achieve spontaneous remission.

We used this shortened version in children with chronic ITP and observed good response rate (83%) and high CR rate (66.6%). Median relapse-free duration was 5 months. GIMEMA study did not observe any increase in response rate after third cycle, whereas we observed continued increase in response rate till fourth cycle.

HDD-SC appears safe and effective therapy in chronic ITP as response rates are similar to response rates observed with methyl prednisolone, IVIgG and IV anti-D [2, 9]. Besides this, dexamethasone therapy is much more cost-effective [10].

References