Pediatr Blood Cancer 2006;47:665–667

Idiopathic Thrombocytopenic Purpura (ITP) in Children

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Idiopathic thrombocytopenic purpura in children remits spontaneously in the majority of cases but most children require treatment. Between 1995 and 2005, 265 children (0–15 years old) have been consecutively observed and treated: 28 children with high doses of methylprednisolone (HDMP) (15 mg/kg × 4 days), 63 with HDMP (7.5 mg/kg × 4 days), 37 with HD dexamethasone (DXM) pulses, 29 with low doses of MP, and 51 with different doses of intravenous immunoglobulins (IVIG) (0.4 or 0.8 g/kg). Fifty-seven children have not been treated because of a platelet count $\geq 10 \times 10^9$/L and no significant bleeding. Two hundred forty-four (92.1%) children reached a persistent CR, 237 (89.4%) after a first-line treatment or the wait and see strategy. No statistically significant differences in CR related to different treatments have been observed. IVIG and HDMP (7.5 mg/kg for 4 days) are the best treatments to reach quickly safe platelet levels $\geq 30 \times 10^9$/L (3–6 days) and CR (7–11 days). Among non-responding (NR) patients, seven have been splenectomized and three reached stable CR. These results emphasize differences with adult ITP. Pediatr Blood Cancer 2006;47:665–667.

Key words: ITP; platelets; splenectomy; treatment

INTRODUCTION

Acute immune thrombocytopenic purpura (ITP) affects about 2–8 out of 100,000 children per year [1,2,3]. ITP is an immune-mediated disorder related to autoantibodies directed against major platelet membrane antigens, resulting in shortened platelet survival. Spontaneous recovery is reported in about 50% of children. The first-line treatment, when necessary, includes oral or intravenous corticosteroids and/or high doses of IVIG. We report our own center's experience including 265 children with acute ITP observed between 1995 and 2005 at the Children Hospital "Bambino Gesù" of Rome.

MATERIALS AND METHODS

Between January 1995 and December 2005, at the Hematology Division of Children's Hospital "Bambino Gesù", Vatican City, Rome, we observed and treated consecutively 265 children with ITP. Diagnosis was made on well-established criteria, excluding other haematological disorders by bone marrow aspirate showing normal to increased megakaryocytes. In all the children we studied autoimmunity, to exclude systemic autoimmune disorders, and serology for common viral infections (CMV, EBV, HIV). None of the 265 evaluated children had been pre-treated or received any steroid treatment for at least 2 months before the observation.

According to our policy, children with a platelet count $\geq 10 \times 10^9$/L and no significant cutaneous or mucosal bleeding have been observed without any treatment (wait and see). Due to a very early onset of the disease in the absence of symptoms, 4 young children, with platelets between 6 and 10×10^9/L, have only been observed and not treated. According to the protocols in use during these 11 years of our analysis we treated at diagnosis 208 children out of 265. Twenty-nine children younger than 1 year have been treated with low doses of MP (1 mg/kg/day for 2 weeks, tapering thereafter).

We treated 63 children with 4 daily HDMP (7.5 mg/kg/day), 28 with 15 mg/kg/day, 37 with HD-DXM pulses according to GIMEMA Protocol [4], 33 with IVIG 0.8 g/kg and 18 with 0.4 g/kg. Out of 51 children treated with IVIG, 40 received the treatment only once. We considered as CR a persistent platelet count $\geq 100 \times 10^9$/L for at least 3 months without further therapy, as partial remission (PR) a platelet count between 30 and 100×10^9/L for at least 3 months. We treated the children of the "wait and see" group, if disease progressed, identically to those with newly diagnosed ITP. We used chi square test to evaluate the differences in terms of CR between different treatments.

RESULTS

Fifty-three patients out of 57 were not treated (93%) and reached spontaneously CR; one reached CR after MP treatment, one is in PR, one has a chronic disease and another was lost to follow-up (LFU). Twenty-five children (86.2%) out of 29 reached CR after MP; 1 reached CR after 7 months, 2 have chronic disease, and 1 is LFU. Thirty children (81.1%) out of 37 reached CR after HD-DXM pulses; four of them reached CR after MP or continuing HD-DXM for 2–7 months, one has chronic disease although splenectomized and two are LFU. Fifty-seven children (90.5%) out of 63 treated with HDMP (7.5 mg/kg/day) reached CR; two of

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Grant sponsor: Associazione Davide Ciavattini (ONLUS).

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Received 27 June 2006; Accepted 27 June 2006

DOI 10.1002/pbc.20998
Published online 24 August 2006 in Wiley InterScience (www.interscience.wiley.com)

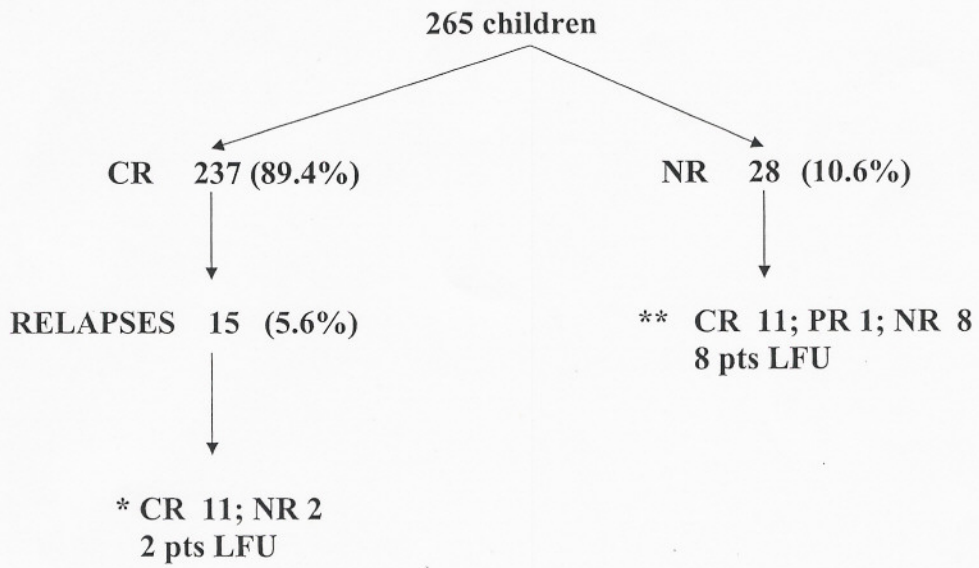

Fig. 1. Children with ITP: clinical follow-up. CR, complete remission; PR, partial remission; NR, non responders; LFU, lost follow-up. *, two after splenectomy; **, one after splenectomy.

them reached CR, respectively, after 9 months and 4 years of very low doses of MP, one has chronic disease and three are LFU. Twenty-four patients (85.7%) out of 28 treated with HDMP (15 mg/kg/day) are in CR; 1 reached CR after 6 months of MP, another one reached CR after MP and splenectomy, and 1 with chronic disease developed lupus erythematosus after splenectomy, the last one is LFU.

Considering the children treated with IVIG, 18/18 with the dose of 0.4 g/kg and 30/33 with the dose of 0.8 g/kg reached CR; in this last group one is now in CR after a subsequent treatment with low-MP doses, one has a chronic disease, another is LFU.

The differences, in terms of CR, between all treatments are not significant. Seven children have been splenectomized (median age 118 months, range 74–216). All children underwent splenectomy after treatments lasting a median time of 36 months after diagnosis (range 8–96); three reached CR, four are living with chronic disease.

Out of 265 children, the final result (Fig. 1) shows that 89.4% of them reached a persistent CR after the first-line treatment; 22 NR or relapsed children reached a new persistent CR after a second-line treatment. Thus, the total percentage of persistent CR is now 92.1% with a median follow-up of 57 months (range 4–132). Considering the high risk of life-threatening bleeding, some of the children that presented extensive bleeding were treated with IVIG (0.4 g/kg) immediately before or at the beginning of steroid treatment. We never observed a significant toxicity, nor adverse events related to the treatment, except transitory hyperglycemia or hypertension in three cases treated with HD steroids. In Table I, we describe the median time to reach 30×10^9/L platelets and CR for each group of patients.

DISCUSSION

The aims of this retrospective unicentric study were to evaluate when to treat and what was the best treatment for children with ITP. Platelet levels $\geq 10 \times 10^9$/L without significant bleeding represent milestones for a wait and see strategy. Indeed, this has been our policy during these 11 years. Based on the used treatments, our experience shows that there are no statistically significant differences in terms of results, even considering that more than 70% of relapses and 39% of NR children can be cured with a second-line treatment. However, the main target of the treatment is to reach safe platelet levels $\geq 30 \times 10^9$/L as soon as possible to avoid life-threatening risks (spontaneous bleeding and trauma for young children) or parent anxiety. IVIG (0.4 mg/kg) and HDMP (7.5 mg/kg/day) for 4 days, seem to be the best options. Furthermore, the low costs of HDMP and its safety need to be considered. Our results do not justify the use of DXM as first-line treatment in children with ITP.

TABLE I. Children With ITP: Response to Treatments

Treatment	Number	CR	Median days to 30×10^9/L	Median days to CR
Wait and see	57	53 (96.3%)	5	14
MP (low doses)	29	25 (86.2%)	16	30
HD-DXM (pulses)	37	30 (81.1%)	15	28
HDMP(7.5 mg/kg × 4)	63	57 (90.5%)	6	11
HDMP(15 mg/kg × 4)	28	24 (85.7%)	9	41
IVIG (0.4 g/kg)[a]	18	18 (100%)	4	7
IVIG (0.8 g/kg)[b]	33	30 (90.9%)	3	7

[a]13/18 = one dose.
[b]27/33= one dose.

In comparison to adults with ITP[5,6,7], in children splenectomy is not a standard therapy and not always a successful procedure. In 11 years we splenectomized only seven children (2.6%) in chronic resistant disease and we obtained three CR. Considering the high percentage of persistent CR (92.1%) after the first- or second-line treatments, the splenectomized children represent a selected high-risk population which needs to be more deeply investigated.

ACKNOWLEDGMENT

This work is partially supported by a grant of "Associazione Davide Ciavattini" (ONLUS). We thank Piero Mancini (Department of Statistics, University "La Sapienza", Rome) for statistical analysis.

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