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SHORT REPORT

Efficacy of high-dose methylprednisolone as a first-line therapy in adult patients with idiopathic thrombocytopenic purpura

ÖNDER ALPDOĞAN, TÜLIN BUDAK-ALPDOĞAN, SIRET RATIP, TÜLIN FIRATLI-TUĞLULAR, SERPIL TANRIVERDI, SAMI KARTI, MAHMUT BAYIK AND TEVFIK AKOĞLU *Department of Haematology-Immunology, Marmara University, School of Medicine, Istanbul, Turkey*

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Summary. Fifty-seven adult patients with idiopathic thrombocytopenic purpura (ITP) were treated with either conventional-dose prednisolone (CDP) (1 mg/kg/d, 36 patients) or high-dose methylprednisolone (HDP) (30 mg/kg/d, 21 patients), as first-line treatment. Patients in the HDP arm responded more rapidly (4·7 *v* 8·4 d), with a higher response rate (80% *v* 52·7%), and without severe side-effects. One quarter of the patients (3/12) who were non-responsive to CDP achieved complete remission when they were treated with HDP. The findings suggest that HDP may be a more effective first-line treatment than CDP for adult ITP, and it may also be preferred for life-threatening cases of ITP. However, these results must be confirmed by a randomized study prior to any change in the current practice of employing CDP as first-line treatment for adult ITP.

Keywords: idiopathic thrombocytopenic purpura, high-dose methylprednisolone.

Nearly two-thirds of adult patients with idiopathic thrombocytopenic purpura (ITP) who are initially treated with conventional doses of prednisolone (CDP) (1–2 mg/kg/d p.o.) achieve a complete response. However, relapse is common during or following CDP therapy and only one quarter of the patients have a persistent complete response (Berchtold & McMillan, 1989; George *et al*, 1994).

None of the currently available therapeutic options, other than splenectomy, produce a better cure rate. Promising results for high-dose glucocorticoid therapy (HDP) in childhood ITP has been reported (Özsoylu *et al*, 1989, 1993; Barrios *et al*, 1993; George *et al*, 1996). There have been a few small studies of HDP therapy in patients with adult ITP which report a transient but rapid increase of the platelet count (von dem Borne *et al*, 1988; Akoğlu *et al*, 1991). HDP therapy has also been suggested to be effective for resistant patients with adult ITP (Akoğlu *et al*, 1991; Godeau *et al*, 1995). The aim of this study was to compare the efficacy of CDP and HDP as first-line treatment in adult ITP.

PATIENTS AND METHODS

Fifty-seven adult patients with ITP (43 female and 14 male) with a median age of 40 years (15–79) were recruited to this non-randomized study. The diagnosis of ITP was made according to the widely accepted clinical criteria: lack of an infectious aetiology, no history of a bleeding disorder and drug exposure, a normal leucocyte and differential count, a normal bone marrow appearance with normal or increased megakaryocytes, and no alternative explanation for thrombocytopenia (Berchtold & McMillan, 1989). All platelet counts were performed on an automatic cell counter (Coulter Electronics, U.S.A.).

Twenty-one patients who had a platelet count of $<15\times10^9$/l and severe or persistent mucosal or vaginal bleeding were treated with HDP at an initial dose of 30 mg/kg/d by i.v. infusion over 1 h. The dosage was gradually tapered down every 3 d (20, 10, 5 and 3 mg/kg/d, i.v.) to 1 mg/kg/d p.o. All patients in the HDP group were hospitalized and maintained on cardiac monitors for 4 h during HDP infusion.

Thirty-six patients who had more favourable clinical features at presentation were treated with CDP at a dose of 1 mg/kg/d p.o. until a response was obtained. Persistence of the platelet count $<20\times10^9$/l for 2 weeks, or 50×10^9/l for 4 weeks, was accepted as a treatment failure, and HDP or splenectomy was considered for these patients. The CDP dose was tapered down gradually if a complete response was obtained according to the recommended schedule (Berchtold & McMillan, 1989).

Correspondence: Professor Dr Tevfik Akoğlu, Marmara Tıp Fakültesi Hastanesi, Hematoloji Bilim Dalı, 81190 Altunizade, Istanbul, Turkey.

Table I. Clinical features and results of conventional-dose prednisolone therapy (CDP) versus high-dose methylprednisolone therapy (HDP).

	High-dose prednisolone ($n=21$)	Conventional-dose prednisolone ($n=36$)	P
Age (median, range)	40 (15–76)	34·5 (15–79)	NS
Sex (female/male)	14/7	29/7	NS
Mean platelet count (10^9/l)	10·4 ± 7·0	15·3 ± 8·6	<0·03
Median platelet count (10^9/l) (range)	8·0 (3·0–26·0)	14·5 (3·0–33·0)	
Mean time to response (d)	4·7 ± 1·4	8·4 ± 2·9	<0·0002
Response*	17/21 (80·1%)	19/36 (52·7%)	<0·05
Complete response†	16/21 (76·1%)	17/36 (47·2%)	NS
Complete remission‡	11/21 (52·6%)	17/36 (47·2%)	NS
Persistent complete remission§	7/21 (33%)	9/36 (25%)	NS
Relapse rate	2/9 (22·2%)	7/16 (43·7%)	NS
Mean follow-up (months) (range)	26·0 (3–90)	21·8 (3–76)	NS

*Response: achievement of either a complete or a partial response.
†Complete response: a rise in platelet count to $>100\times10^9$/l.
‡Complete remission: maintenance of the complete response for 2 months or more off medication.
§Persistent complete remission: a lasting complete remission at the final follow-up (at least 6 months duration).

A rise in platelet count to $>100\times10^9$/l or 50×10^9/l was defined as a complete response or a partial response respectively. Any patient who had either a complete or a partial response was defined to have a response. Complete remission was defined as the maintenance of platelet count at $>100\times10^9$/l for 2 months or more without taking any medication. If complete remission persisted until the last follow-up (at least 6 months), it was then accepted as persistent complete remission.

Data was reported as the mean ±SD or the median and range. Student's *t*-test, Chi-square and Fisher's exact tests were employed.

RESULTS

Although the mean platelet count was significantly lower in the HDP group compared with the CDP group ($10·4 \pm 7·0\times10^9$/l and $15·3\pm 8·6\times19^9$/l, respectively, $P<0·03$), HDP appeared to be significantly more effective than CDP in terms of response rate (80%:95% CI 63–97 *v* 53%:95% CI 38–69), and time taken for the response (4·7 ± 1·4 d *v* 8·4 ± 2·9 d) (Table I). However, treatment modalities were similar with respect to the complete remission and persistent remission rates.

Twelve out of 17 CDP unresponsive patients were treated with HDP as a second-line treatment and one quarter (3/12) of these patients achieved a complete remission.

Side-effects of HDP and CDP therapies, such as cushingoid appearance, myopathy, gastrointestinal bleeding and infectious complications were similar. However, secondary amenorrhoea which resolved within 6 months of therapy, was observed more commonly in the HDP group ($P<0·03$) (Table II). No mortality was encountered in this study.

DISCUSSION

Oral or intravenous HDP therapy in symptomatic childhood ITP patients has been suggested as an appropriate first-line

Table II. Side-effects of HDP and CDP therapy.

Side-effect	Total (%) ($n=57$)	HDP (%) ($n=21$)	95% CI	CDP (%) ($n=36$)	95% CI	P
Cushingoid appearance	14 (25)	4 (19)	2·3–35·7	10 (27)	12·5–41·5	NS
Upper GI bleeding	3 (5)	2 (9·5)	0–22	1 (3)	0–8·5	NS
Infection	2 (4)	2 (9·5)	0–22	–	–	NS
Osteoporosis	4 (7)	1 (5)	0–14·3	3 (8)	0–16·8	NS
Myopathy	7 (13)	1 (5)	0–14·3	6 (15)	3·4–26·6	NS
Sinusal tachycardia	2 (4)	2 (9·5)	0–22	–	–	NS
Hyperglycaemia	2 (4)	2 (9·5)	0–22	–	–	NS
Depression	1 (2)	–	–	1 (3)	0–8·5	NS
Secondary amenorrhoea	3/43 (7)	3/14 (21)	3·6–38·4	–	–	0·03

therapy (Özsoylu *et al*, 1989, 1993; Barrios *et al*, 1993; George *et al*, 1996). The experience with adult patients has been limited by the small number of the patients (von dem Borne *et al*, 1988; Akoğlu *et al*, 1991; Godeau *et al*, 1995).

The results of this non-randomized study suggest that HDP therapy may be more effective than CDP as a first-line treatment. This study is currently the largest, to our knowledge, on the effectiveness of HDP in adult patients with ITP. The response was prompt, and the response rate was higher than in patients treated with CDP. The HDP treatment was well tolerated. Therefore HDP treatment could be considered as an alternative for severe ITP cases or CDP-resistant patients prior to splenectomy. Intravenous immunoglobulin (IVIg) is commonly employed as an emergency treatment and in corticosteroid-resistant cases (George *et al*, 1996). However, it is more expensive in comparison with high-dose corticosteroid therapy.

A number of short reports of patients with renal disease suggested that HDP therapy may have serious cadiac side-effects such as arrhythmias and sudden death (Bocenegra *et al*, 1981; Moses *et al*, 1981; Fujimoto *et al*, 1990). All patients in this study were observed with a cardiac monitor and no side-effects were detected.

In conclusion, HDP may be more effective than CDP as a first-line treatment of adult ITP, and a rapid increase in platelet count can be expected. HDP therapy may be considered as an alternative first-line treatment in severe adult ITP, emergency situations and in CDP-resistant patients prior to splenectomy. The results of this report must be confirmed by a randomized study prior to changing the currently accepted clinical practice of using CDP as the first-line treatment for adult ITP.

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