

Chronic Idiopathic Thrombocytopenic Purpura Effects of Certain Variables on the Response to Treatment.

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ABSTRACT:

BACKGROUND:

Idiopathic thrombocytopenic purpura is an acquired chronic autoimmune disease .Treatment when indicated is usually by corticosteroids,then splenectomy if no acceptable response,with variable response rate to both types of treatment.

OBJECTIVE:

To look for the effects of certain variables on the type of response to steroid therapy in patients with adult idiopathic thrombocytopenic purpura, and to study the outcome of splenectomy in relation to previous steroid therapy.

METHOD:

A prospective study on 80 patients, presented with bleeding and a platelet count of $\leq 30 \times 10^9 / L$. Initially treated with prednisolone and the response was studied in relation to gender , age , duration of bleeding and platelet count on presentation. Patients who failed to maintain permanent complete remission were advised to have splenectomy.

RESULTS:

Of the 80 patients, 62 (77.5 %) were females and 18 (22.5%) were males. Mean age was 23 ± 10.1 years. Ten (12.5%) patients only had permanent complete remission after steroid therapy. While 70 (87.5%) patients failed. Response to steroid therapy was significantly related to duration of bleeding but not to gender, age and platelet count. Thirty seven (46%) patients underwent splenectomy, permanent complete remission were achieved in 29 (78.2%).

CONCLUSION:

1. Duration of bleeding of ≤ 3 weeks is a good predictor of successful steroid therapy.
2. Results after splenectomy is not related to previous steroid therapy.

KEY WORDS: thrombocytopenia, steroids, splenectomy.

INTRODUCTION:

Chronic idiopathic thrombocytopenia (ITP) is an autoimmune disorder, where platelet surface membrane proteins become antigenic, stimulating the immune system to produce antiplatelet antibodies that induce platelets destruction⁽¹⁾

ITP is a disease characterized by insidious onset, typically affects young and middle age adults predominantly women with a female to male ratio of 3:1⁽²⁾

Patients may present with abrupt fall in platelet count and bleeding, but more often they have prior history of easy bruising or menorrhagia⁽³⁾

The haemorrhagic manifestations of ITP, rather than platelet count should define the indication of active intervention⁽⁴⁾

The goal of treatment is to prevent serious bleeding, and there are two main therapeutic choices which are steroids and splenectomy⁽⁵⁾

The objective of this study were: many previous studies^(5, 6, 7) had reported variable response rates to steroid therapy and splenectomy in patients with ITP. In this study we were prompted to:

1. Find out and compare the response rate to steroid therapy with other similar studies. Moreover we studied the effects of different variables including gender, age, duration of bleeding and platelet count at presentation on the response to treatment with steroids and as a predictor of remission.
2. Find out the type of response to splenectomy in patients who failed to achieve permanent complete remission after steroid therapy.

PATIENTS AND METHODS:

During the period between June 1997 and June 2002, eighty (80) patients with ITP attended Baghdad teaching hospital were included in this study, 62 were females and 18 were males, with a female to male ratio of 3.4 : to 1 , aged 16 - 32 years with a mean of 23 ± 10.1 years.

All patients presented with bleeding (table 1), and documented thrombocytopenia with platelet count

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of less than $30 \times 10^9 / L$. All had bone marrow aspirate examination which showed normal or increase megakaryocytosis.

Patients were excluded from the study if they had:

1. Recently ingested drugs known to be associated with thrombocytopenia.
2. Evidence of sepsis, disseminated intravascular coagulation, or presence of microangiopathy on peripheral blood smear.
3. An established diagnosis associated with thrombocytopenia e.g. systemic lupus erythematosus.

Initial therapy was started with prednisolone 1 mg/kg body weight daily, orally, for 2-4 weeks (8), the dose was gradually reduced after a rise of platelet count to $\geq 150 \times 10^9/L$, these patients were then followed up with weekly platelet count, with gradual reduction of the prednisolone dose to maintain a platelet count $\geq 150 \times 10^9/L$. On the other hand if it didn't reach this level or started to decline, or the dose required to maintain a count more than $30 \times 10^9/L$ was unacceptably high, or no response, prednisolone gradually tapered and stopped, and splenectomy offered to the patient.

Statistical analysis:

All data were collected and tabulated in number and percentage. Associations between variables were measured by using chi-square and fisher's test when it is appropriate. P values of < 0.005 were considered significant.

RESULTS:

The patients characteristics at entry are shown in table (2).

All patients completed the study.

Response to therapy was classified into four categories:

1. Permanent complete remission (PCR): complete clinical and hematological remission (platelet count $\geq 150 \times 10^9/L$).

2. Temporary complete remission (TCR): Relapsing after initial complete clinical and hematological remission.

3. Partial remission (PR): Partial clinical and hematological, (platelet count increase to at least $\geq 30 \times 10^9/L$ while on prednisolone therapy or after splenectomy.

4. No response: No clinical or hematological improvement after prednisolone therapy or splenectomy.

Overall response to steroid therapy is shown in table (3).

Ten (12.5%) patients had PCR with a follow up period of 6-60 months with a mean of 24 ± 12 months, while 60 (75%) had total TCR, 8 (10%) patients had PR, and 2 (2.5%) had no response.

The response to steroid therapy in relation to gender, age, duration of bleeding and platelet count at presentation are shown in tables (4,5,6,7).

There were no significant effects of gender, age and platelet count at presentation on type of response to steroids, while patients with duration of bleeding of 3 weeks or less showed a highly significant response ($P < 0.0002$) in comparison with those having a duration of bleeding of more than 3 weeks.

Seventy patients were advised splenectomy, 37 patients only agreed and underwent surgery, these patients were then followed up, regarding the type of response to splenectomy, and relating this response to their initial response to steroids.

Table (8) depicts the patient's response to splenectomy which showed that 29 (78.3%) patients achieved PCR, while 8 (21.7%) patients had TCR and PR.

There were no significant relation between type of response to splenectomy and the type of response to steroids table (9).

Table 1: Clinical findings at presentation in 80 patients with ITP.

Symptom or Sign	No.	%
Subcut. Bleeding	80	100
Epistaxis	17	21
Gum Bleeding	14	17
Metromenorrhagia	32	40

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Table 2: Patients Characteristics at entry (80 patients)

Variable	No.	%
Gender		
Male	18	22.5
Female	62	77.5
Age (yrs)		
<23	37	46.25
≥23	43	53.75
Duration of bleeding (wks)		
≤3	53	66.25
>3	27	33.75
Platelet count at presentation X 10 ⁹ /L		
≤10	44	55
>10	36	45

Table 3: Overall response to steroid therapy

PCR		TCR		PR		No Response		Total	
No	%	No	%	No	%	No	%	No	%
10	12.5	60	75	8	10	2	2.5	80	100

Table 4: Response to steroid therapy according to gender

Gender	PCR	TCR	PR	No response	Total
Male	2	12	3	1	18
Femal	8	48	5	1	62
Total	10	60	8	2	80

Table 5: Response to steroid therapy according to age

Age(yes)	PCR	TCR	PR	No response	Total
<23	6	25	6	0	37
≥23	4	35	2	2	43
Total	10	60	8	2	80

Table 6: Response to steroid therapy according to duration of bleeding

Duration of Bleeding (wks)	PCR	TCR	PR	No response	Total
≤3	7	40	6	0	53
>3	3	20	2	2	27
Total	10	60	8	2	80

P < 0.0002

Table 7: Response to steroid therapy according to platelet count at presentation

Platelet count at presentation X 10 ⁹ /L	PCR	TCR	PR	No response	Total
≤10	8	32	2	2	44
>10	2	28	6	0	36
Total	10	60	8	2	80

Table 8: Response to splenectomy in 37 patients with ITP.

PCR		TCR		PR		No Response		Total	
No	%	No	%	No	%	No	%	No	%
29	78.3	6	16.3	2	5.4	0	0	37	100

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Table 9: Outcome of splenectomy in 37 patients who failed to response to steroid therapy

Response with Steroid therapy		Type of response after splenectomy					
		PCR		TCR		PR	
Type	No	No	%	No	%	No	%
TCR	30	25	83.3	3	10	2	6.7
PR	6	4	66.7	2	33.3	0	0
No response	1	0	0	1	100	0	0
Total	37	29	78.3	6	16.3	2	5.4

DISCUSSION:

The mean age of our patients in this study was 23 ± 10.1 years, which is lower by about 10 years than European studies^(9,10), but similar to African studies^(11,15). This low age may be the reflection of the age strata of different populations.

Gender was almost similar to other studies, which showed female predominance of 3:1^(2,7).

Steroid therapy is indicated for all patients with symptomatic thrombocytopenia, and probably for all patients with platelet count of < 30 X 10⁹/L, who may be at risk of haemorrhagic complications⁽⁵⁾.

When treatment is indicated, steroids followed by splenectomy if necessary can be expected to achieve a remission of about 80% of patients⁽²⁾.

In this study most of our patients responded initially to steroid therapy, however the disease relapsed when steroids were tapered, and PCR was achieved only in 10 (12.5%) patients which is less than those reported by Meyers (14%)⁽¹²⁾, Thompson (23%)⁽¹³⁾, Difino (23%)⁽⁹⁾ and Shamebo (23.3%)⁽¹⁴⁾.

TCR was achieved in 60 (75%) patients which is much higher than those reported by Myers (44%)⁽¹²⁾, Thompson (23%)⁽¹³⁾, Difino (42%)⁽⁹⁾ and Shamebo (46%)⁽¹⁴⁾.

PR was achieved in 8 (10%), and this was less than what was reported by Schiffman of (30%)⁽¹⁵⁾.

Our results confirmed what was found by Shamebo⁽¹⁴⁾, where there was no significant effects of gender, age and platelet count at presentation on type of response to steroid therapy, but differed regarding duration of bleeding. We found a highly significant effect in those presenting with a duration of bleedin of ≤ 3 weeks in favor of achievement of PCR, and this is compatible with what was found by Difino, who concluded a favorable response in patients treated within 2 weeks of symptoms⁽⁹⁾.

Our results of PCR of 78% after splenectomy were slightly higher than what were reported by other studies which were 50% - 70%^(8,16,17).

Schiffman has found that prior response to corticosteroids is predictive of good response to

splenectomy⁽¹⁵⁾, contrary to what bell concluded, that there is no consistent effective method to predict an individual ITP patients response to splenectomy⁽¹⁶⁾, and to what Handin mentioned, that even some patients who don't respond to steroid may still respond to splenectomy⁽³⁾.

The last two references^(16,3), confirmed what we have concluded in our study, that there is no significant relation between type of response to steroid therapy and the outcome of splenectomy.

CONCLUSION:

The only significant predictor to successful steroid therapy is the duration of bleeding before starting treatment, and there is no significant relation between types of response to steroid therapy and response to splenectomy.

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