Pemphigus Vulgaris Recurrence Rate and its Relationship with Initial Corticosteroid Dose

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Background: Pemphigus vulgaris (PV) is a rare autoimmune blistering disease with a high rate of morbidity and mortality without treatment. Until now, treatments consist mostly of the use of corticosteroid and immunosuppressive drugs. Optimum dosage for corticosteroid therapy is yet to be determined. The aim of the present study was to clear whether different initial corticosteroid therapeutic dosages change the recurrence rate of the disease.

Methods: Patients hospitalized with confirmed PV from 2000 to 2006 were enrolled if they received systemic corticosteroids without any adjuvant therapy for no more than three weeks when hospitalized, received their first treatment in the period of the study and were followed for at least two years in the PV clinic of Razi Hospital periodically. Initial steroid dosage as well as the number and type of the recurrence(s) were documented and analyzed.

Results: A total of 62 patients with a mean age of 46.8 (± 15.9) were enrolled. Twenty-one patients were female (33.9%) and 41 patients (66.1%) were male. According to the initial dose of systemic corticosteroid, patients were divided into two groups: group A included patients treated with less than 2mg/kg (10 patients or 16.1%) while group B included patients treated with 2mg/kg systemic steroids (52 patients or 83.9%). There was no significant difference in the recurrence rate between the two groups. Recurrence rate was 40% in group A and 51% in group B ($P>0.05$). According to the type of recurrence, there was a significant difference between the two groups; in group A, the first recurrence was major in 33% of the patients while in group B, this rate was about 28.8% ($P<0.05$).

Conclusion: According to the present study, initial therapeutic dosage did not influence the recurrence rate although the type of recurrence was influenced. Patients treated with higher initial steroid dosages experienced their first episode as a minor recurrence while patients treated with lower initial steroid dosages experienced major recurrences with a higher probability as their first episode.

Keywords: corticosteroid dosage, pemphigus vulgaris, recurrence, treatment

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INTRODUCTION

Pemphigus vulgaris (PV) is a rare autoimmune disease which results in the formation of blisters, erosions or crusts of the skin and/or mucosa membranes through circulating auto-antibodies against Desmoglein 3 (DSG3) and/or Desmoglein 1 (DSG1) antigens [1-6]. The incidence of this disorder is estimated to be about 1/100,000 of the population per year [7]. According to other references [8-10], it seems that pemphigus is more prevalent in Iran, India and eastern countries. Pemphigus vulgaris has a high morbidity and mortality rate without treatment [11]. Until now, treatment consists mostly of the use of corticosteroid and immunosuppressive drugs. Because of the rarity of the disease, there is not yet a standard treatment regimen. Prednisolone was the first drug used to treat this disease and almost in all situations, is the first line of treatment [12-14]. Other drugs used as second line therapies are azathioprine, cyclophosphamide, mycophenolate mofetil, dapsone, gold salts, methotrexate, cyclosporine, dexamethasone and cyclophosphamide pulse therapy and much more [15-21]. As one can see, there are many drugs and treatment regimens with different response rates and in fact, it has been shown that the selected therapy depends greatly on the experience of the physician in different parts of the world [22]. There are some discrepancies in the recommended dosage of prednisolone at the commencement of therapy [23]. The aim of this study was to determine whether the initial dose of prescribed prednisolone influenced the treatment outcome.

PATIENTS AND METHODS

Patients hospitalized with clinical diagnosis of pemphigus vulgaris (PV) confirmed through pathologic examination, provided that they met our inclusion criteria, were enrolled in this cohort retrospective study. Patients were selected if they had clinical diagnosis of PV confirmed through pathologic and direct immunofluorescence examination, received systemic corticosteroids without any adjuvant therapy for no more than three weeks when hospitalized, received their first treatment in the period of the study and were followed for at least two years in the PV clinic of Razi Hospital periodically. They were excluded if they had received systemic corticosteroids with or without adjuvant for more than three weeks before hospitalization and if their clinical records were not complete. The study included patients hospitalized from spring 2000 to winter 2006. All clinical records were analyzed and target data including primary remission time, number of recurrences (minor and major), extension of the lesions during recurrences, and overall patient condition (six months and two years after the first treatment), were extracted and documented in specifically designed questionnaires. Minor recurrence was defined as the appearance of less than 20 lesions on less than three anatomic sites of the body, while major recurrence was considered when more than 20 lesions appeared on three or more anatomical sites of the body or in case of the generalized disease. Recorded data was then analyzed with SPSS version Ver. 16. Fisher exact test and chi-square test were used when required.

RESULTS

A total of 62 patients were enrolled in the study. Mean age of the patients was 46.8 (± 15.9) years (ranging from 15 years to 88 years old). Twenty-one patients were female (33.9%) and 41 patients (66.1%) were male. According to the initial dose of systemic corticosteroid, patients were divided into two groups: group A included patients treated with less than 2mg/kg (10 patients or 16.1%) while group B included patients treated with 2mg/kg systemic steroid (52 patients or 83.9%). In group A, three cases (33.3%) had one recurrence and one patient (10%) had two recurrences in the period of the follow-up. In group B, 12 patients (23%) had one recurrence and 13 patients (48.1%) had two recurrences while one patient had three and one had four recurrences in the period of the follow-up. As a whole, the recurrence rate was 40% in group A and 51% in group B ($p>0.05$) (Table 1).

In group A, three cases had a major recurrence (33.3%) and one patient (10%) had both a minor and a major recurrence while in group B, seven cases had a minor recurrence (13%), 15 cases had a major recurrence (28.8%) and five cases had both (9.6%). In summary, group A had fewer number of recurrences in comparison with group B ($P>0.05$).

In group A, the first recurrence was major in 33% of the patients while in group B, this rate was about 28.8% ($P<0.05$).

Table 1. Number and type of recurrences

	Number of Recurrences (patients, recurrence number)	Recurrence Type	First Recurrence	Summary
Group A	(3,1) (1,2)	1 (10%): Both Minor & Major 3 (33.3%): Major	3 (33%) Major**	4 (40%)*
Group B	(12,1) (13,2) (1,3) (1,4)	7 (13%): Minor 15 (28.8%): Major 5 (9.6%): Both Minor & Major	15 (28.8%) Major**	27 (51%)*

*Not significant (p>0.05)
**Significant (p<0.05)

DISCUSSION

Pemphigus vulgaris is a potentially life threatening disease without treatment. Treatment with immunosuppressive agents such as prednisolone has the advantage of clearing vesicles but is accompanied by many adverse effects such as opportunistic infections, osteoporosis, prednisolone induced diabetes mellitus and much more. So, it is wise to call for regimens with a lower initial dose of corticosteroids with the least effect on treatment outcome. Early studies advocated high doses of systemic corticosteroids, e.g. initial doses of 120–180 mg prednisolone daily [24] but it was noted that steroid side-effects were common and dose related [25,26]. One study proved that more than 70% of the deaths during the treatment period of this disorder were steroid related [25]. This high mortality rate has encouraged physicians to find protocols using lower steroid dosages and therefore controlled studies have been performed to support low dose steroid treatment. Dosing schedules consider 45-60 mg/day steroids as low-dose, compared to 120-180 mg/day as high-dose. It has been shown that there was no significant difference in the duration to achieve remission and in relapse rates after 5 years, and there were no deaths [27]. Our study showed that the recurrence rate in both groups was to some extent identical and there were no significant differences, but there was an interesting discrepancy: the first recurrence in patients treated with lower steroid doses was major in about 33% while in patients treated with 2mg/kg steroid, this rate was 28.8% and this difference was significant ($p<0.05$). Therefore, one can conclude that lower steroid dose schedules may be comparable to higher doses from the view point of general recurrence rate- this finding is in agreement with other studies [27]- but patients treated with lower steroid doses are more prone to experience a major recurrence as their first recurrence. It has been shown that disease activity decreases with time and most cases of recurrence occur in first two years [28] . According to the results of the present study, patients may benefit from treatment with higher dosage schedules because of the lower rate of major recurrences in the first attack after commencement of the treatment. On the other hand, as mentioned earlier, it seems that higher dose schedules have no significant difference with lower dosage regimens in terms of general outcome. Furthermore, higher dosages of steroid may have more adverse effects on patients' health. The authors believe that more in-depth studies with larger samples sizes are required to clarify this situation.

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