Evaluation of Response of Parenteral Dexamethasone in Pemphigus Vulgaris

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Abstract

A clinical trial was carried out in the Department of Dermatology and Venereology, Bangabandhu Sheikh Mujib Medical University, Dhaka. The total number of patients was thirty and among them fifteen patients were treated with injection dexamethasone (Group-A) and other fifteen were treated with oral prednisolone (Group-B). The study showed that in Group-A, on admission and after 6 weeks, the mean number (±SD) of skin lesion of pemphigus was 36.87±8.40 and 5.27±1.624 respectively. In Group-B, on admission and after 6 weeks, the mean number (±SD) of skin lesion of pemphigus was 36.27±8.980 and 7.73±1.007 respectively. The study also observed that in group-A, on admission and after 6 weeks, the mean number (±SD) of mucous membrane lesion of pemphigus was 3.40±2.633 and 1.00±0.926 respectively. In Group-B, on admission and after 6 weeks, the mean number (±SD) of mucous membrane lesion of pemphigus was 3.33±2.225 and 1.87±1.246 respectively. Statistically significant improvement was observed in both groups in all clinical parameter after 6 weeks. Dexamethasone group showed statistically higher significant improvement than prednisolone group in all clinical parameter except Nikolsky's sign. Injection dexamethasone appears to be more effective than oral prednisolone in early management of pemphigus vulgaris.

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Introduction

The term pemphigus refers to a group of autoimmune blistering disease of skin and mucous membranes which is characterized histologically by intraepidermal blisters due to acantholysis (i.e, separation of epidermal cells from each other) and immunopathologically by in vivo bound and circulating IgG directed against the cell surface of keratinocytes. About 0.8% of all dermatologic patients suffer from pemphigus[2]. Pemphigus vulgaris (PV) is the most common type of pemphigus and comprises about 80% of patients with pemphigus[1]. The prevalence of pemphigus vulgaris is about equal in men and women. The mean age of onset is fourth to sixth decades. But it may be seen in children and the elderly[3]. There is strong genetic background to pemphigus vulgaris and there is also HLA association in pemphigus vulgaris. Most patients are of HLA phenotype DR4 or DR6 [2]. In about 50-70% of the cases the disease begins with oral lesion, which may precede the cutaneous lesions by several months. Cutaneous lesions can be localized or generalized and usually present primarily as flaccid vesicles or bullae varying in size from less than 1 cm to several centimeter.

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The scalp, pre-sternal, genitals, axillae and groin are frequent sites of involvement. The blisters rupture easily and produce painful raw denuded areas[4]. The Nikolsky's sign is present. There is an absence of cohesion in the epidermis, so the upper layers of the epidermis may easily be removed by a twisting pressure with the fingertip, leaving a moist surface. The bulla spreading phenomena can be tested by pressure on an intact bulla, gently forcing lead the fluid to wander under the skin away from site [3]. Pemphigus vulgaris is associated with high morbidity as well as significant mortality rate, before the advent of systemic corticosteroid therapy in 1950s. The mortality rate was reported 70% to 100% at that time. The use of corticosteroid dramatically reduced the death rate from this to a mean of 30%[5]. The course of pemphigus vulgaris is almost chronic. Today the risk of death in pemphigus from the side effect of oral prednisolone is greater than risk of death from the disease itself. Death from sepsis and other complications of therapy occurs in 5% to 10% of treated cases. Untreated disease is usually fatal [6]. To minimize the cumulative steroid affects in pemphigus, there has been a continuous search for alternative therapies concerning treatment of this disease. Pulse therapy, the 'big shot', refers to discontinuous intravenous infusion of very high-dose corticosteroid over a short period. Due to lack of available monitoring facility after giving so large dose of steroid, we intended to use 5mg of dexamethasone intravenously eight hourly for early control of disease. It is evident that no trial with dexamethasone has been yet done in Bangladesh. Since there is no recorded study in Bangladesh, this study was undertaken to find out the efficacy of parenteral dexamethasone compared with oral prednisolone in early management of pemphigus vulgaris.

Methods

A clinical trial was conducted in the department of Dermatology and Venereology, Bangabandhu Sheikh Mujib Medical University, Dhaka. The period of study was from January 2004 to June 2005. The total number of patients was thirty. Among them 15 patients were treated with injection dexamethasone (Group-A) and other 15 were treated with oral prednisolone (Group-B). Random sampling method was followed. A detailed history was taken from the patient. In case of female, special attention was given regarding menstrual history and use of contraceptives. Clinical assessment was done at baseline, after every one week and lastly one and half months later. Clinical assessments include number of skin lesions of pemphigus, number of mucous membrane lesion of pemphigus, positive Nikolsky's sign, presence of bulla spreading phenomena and other physical examination. Laboratory assessment was done at baseline and after two weeks and at the end of six weeks information obtained from history, physical examination and laboratory investigation (Routine blood examination-Total count (TC), Differential count (DC), Hb% and ESR, urine routine examination, blood sugar, blood urea, serum creatinine, liver function test, ECG, skin biopsy for histopathology and direct immunofluorescence test) were recorded in patient data sheet. Due to lack of available facility we could not done follow up histopathology and immunofluorescence test in this study.

Procedure of treatment

Thirty patients were included in this study using random number table. Fifteen patients were given injection Dexamethasone (Group-A) and fifteen patients were enrolled oral prednisolone (Group-B). First on admission we gave 5mg injection Dexamethasone eight hourly intravenously. It was continued until cessation of new bulla appeared. Then the dose was reduced 5mg twelve hourly. After gradual, improvement of patient's condition the dose was reduced to 5mg intravenously daily. After further improvement of patient condition we turned 5mg dexamethasone to equivalent dose of prednisolone which was 40mg (which was actually 34mg of prednisolone. But easier to take and remember we gave 40mg). After six weeks we assessed the patient's outcome. The initial dose of prednisolone was (equivalent to 15mg dexamethasone) 100 mg daily divided doses. It was continued until cessation of new bulla appeared. After gradual improvement, it

was reduced 5-10mg weekly. After six weeks, we assess the patient's condition.

Statistical Analysis

All statistical analysis was done by SPSS 12 software package as mean ± Standard deviation (SD). 95% confidence limit was taken as level of significance. Comparison between two groups were done by unpaired 't' test and some qualitative data by 'Chi-square test. Comparison within group was done by paired 't' test. P<0.05 was considered as a level of significance.

Results

Thirty patients of pemphigus vulgaris were enrolled in this study and of them 15 were enrolled in the injection dexamethasone group A (odd random table number) and 15 in the oral prednisolone group B. The age range of most of the patient of dexamethasone group was 30-39 yrs and 50-59 yrs. The age range of most of the patient of prednisolone group was 50-59 yrs and 40-49yrs. The mean±SD of ages in dexamethasone and prednisolone group were 41.60±13.271 and 46.67±10.342 years respectively. There is no significant (P>0.05) difference of ages between the two groups. All demographic, clinical parameter were almost identical in two groups (P>0.05. Nikolsky's sign and bulla spreading phenomena expressed as number of patient. Table-1 showed that in Group-A, on admission and after 6 weeks, the mean±SD number of skin lesion of pemphigus was 36.87±8.40 and 5.27±1.624 respectively. In Group-B, on admission and after 6 weeks, the mean±SD number of skin lesion of pemphigus was 36.27±8.980 and 7.73±1.007 respectively. Significant difference was observed after 6 weeks (P< 0.001). Table 2 showed that in group-A, on admission and after 6 weeks, the mean±SD number of mucous membrane lesion of pemphigus was 3.40±2.633and 1.00±0.926 respectively. Significant difference was observed after 6 weeks (P< 0.001). In Group-B, on admission and after 6 weeks, the mean±SD number of mucous membrane lesion of pemphigus was 3.33±2.225 and 1.87±1.246 respectively. Significant difference was observed after 6 weeks (P< 0.001). In table-3, statistically significant differences of bulla spread phenomena of pemphigus were observed after 6 weeks between two groups (P<0.05) but regarding Nikolski's sign, no statistically significant differences were observed between two groups. Table-4 showed that statistically significant differences of skin lesion of pemphigus were observed after 6 weeks between two groups (P<0.05).

Table-1: Detection of number of skin lesion of pemphigus in both groups on admission and after 6 weeks therapy

Group-A	Number of skin lesion of pemphigus Mean ± SD	Level of significance	
		Paired t value	P value
On admission After 6 weeks	36.87 ± 8.40 5.27 ± 1.624	16.861	< .001
Group-B	Number of skin lesion of pemphigus Mean ± SD	Level of significance	
		Paired t value	P value
On admission After 6 weeks	36.27 ± 8.980 7.73 ± 1.007	14.337	<0.001

Table-IV: Detection of number of mucous membrane lesion of pemphigus in both groups on admission and after 6 weeks therapy

Group-A	Number of mucous membrane lesion Mean ± SD	Level of significance	
		Paired t value	P value
On admission After 6 weeks	3.40 ± 2.633 1.00 ± 0.926	5.041	< 0.001
Group-B	Number of mucous membrane lesion Mean ± SD	Level of significance	
		Paired t value	P value
On admission After 6 weeks	3.33 ± 2.225 1.87 ± 1.246	5.358	<0.001

Table-3: Outcome of Nikolski's sign and Bulla spread phenomena between Dexamethasone (Group-A) and prednisolone (Group-B) after 6 weeks.

Study group	Nikolski's sign		Chi-square value
	Positive	Negative	
Group A	4	11	1.292(P value >0.05)
Group B	7	8	
Study group	**Bulla spread phenomena**		**Chi-square value**
	Positive	Negative	
Group A	0	15	9.130 (P value <0.05)
Group B	7	8	

Table-4: Out come of number of skin lesions and lesion of mucous membrane after 6 weeks between two groups.

Grouping	No. of skin lesion of pemphigus (mean ± SD)	Level of significance	
		t value	P value
Group A	5.27 ± 1.624	-3.813	< 0.05
Group B	7.73 ± 1.907		
Grouping	**No. of mucous membrane lesion of pemphigus (mean ± SD)**	**Level of significance**	
		t value	**P value**
Group A	1.00± 0.926	-2.162	< 0.05
Group B	1.87 ±1.246		

Discussion

In this study the age of the patients ranged from 20-69 years with mean age was in dexamethasone group 41.60±13.27 years and prednisolone group 46.67±10.34 years. However Toth et al found that the average age was 47.7 years [7]. It is important to note from this study that statistically significant improvement was evidenced in dexamethasone group in all clinical parameters i.e number of skin lesion of pemphigus, number of mucous membrane lesion of pemphigus and bulla spreading phenomena. But on Nikolsky's sign we did not find any significance difference between dexamethasone and prednisolone group after 6 weeks. These results were consistent with finding of study by Toth et al [7]. However in their study, the dose of dexamethasone was higher, 200 mg daily. In another study by Amrinder et al, they included cyclophosphamide with dexamethasone in the treatment of pemphigus vulgaris. [8] In this study the dose of dexamethasone was 136 mg daily and cyclophosphamide 500 mg monthly. In between pulse they used oral corticosteroid (low tapering dose) and 50 mg daily. Their follow up period was also for long duration. They found significance improvement with this therapy. Leela et al, used cyclophosphamide with dexamethasone in treatment of pemphigus vulgaris. They found complete remission in 82% of patient in their study. Their follow up period was one year [9]. Harman et al used azathioprine and in some patients used methotrexate with dexamethasone. Their dexamethasone dose was also high. They found significance improvement in their study[10]. In our study we could not do follow up histopathology and immunofluronce Test. But in others study they found significance reduction of antibody titer in direct and indirect immunofluronce test [11, 12]. Statistically we found that both injection dexamethasone and oral prednisolone were significant in early management of pemphigus vulgaris. These results furnished consistency with the finding of other study[12]. It appeared that injection dexamethasone and oral prednisolone had similar efficacy in the early management of pemphigus vulgaris.

Conclusion

This study evidenced that parenteral Dexamethasone could provide clinically significant benefit to patient in early management of pemphigus vulgaris. At the present time the clinicians although could depend on this therapy, but in future a study of long duration follow up of all cases is recommended to prove the efficacy of dexamethasone in early management of pemphigus vulgaris.

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