Safety of parenteral dexamethasone vs. oral prednisolone in the treatment of pemphigus vulgaris

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Abstract

Objective To observe the safety of parenteral dexamethasone compared with oral prednisolone in the treatment of pemphigus vulgaris.

Patients and methods A clinical trial was carried out in the department of Dermatology and Venereology, Bangabandu Sheikh Mujib Medical University, Dhaka, Bangladesh. Total number of patients was thirty. Among them fifteen patients were treated with injection dexamethasone (group A) and other fifteen were treated with oral prednisolone (group B).

Results Statistically significant improvement was observed in both groups in all clinical parameters after 6 weeks. But dexamethasone group showed statistically more significant improvement than prednisolone group in all clinical parameters except Nikolsky's sign. Most common adverse effects in both groups were weight gain, increased appetite, puffy face and hyperglycemia. In dexamethasone group other side effect was sleep disturbance. In prednisolone group other side effects were gastritis, sleep disturbance, nausea and vomiting, herpes zoster infection, reactivation of tuberculosis and mood change.

Conclusion Parenteral dexamethasone appears to be safer than oral prednisolone in the management of pemphigus vulgaris with an acceptable efficacy profile.

Key words
Safety, parenteral dexamethasone, treatment, pemphigus vulgaris.

Introduction

Pemphigus vulgaris (PV) is the most common type of pemphigus and comprises about 80% of patients with pemphigus.[1] About 0.8% of all dermatologic patients suffer from pemphigus.[2]

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The prevalence of pemphigus vulgaris is almost equal in men and women. The mean age of onset is fourth to sixth decades.[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 lesions, which may precede the cutaneous lesions by several months. Cutaneous lesions arelocalized or generalized and usually present primarily as flaccid vesicles or bullae varying in size from less than 1 cm to several cm. The scalp, presternal, 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 phenomenon 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%. The use of corticosteroids dramatically reduced the death rate to be to a mean of 30%.[5]

Dexamethasone is a long-acting synthetic steroid. The glucocorticoid effect in per mg is about 6.7 times stronger than prednisolone. Prednisolone is an intermediate acting synthetic corticosteroid.[2] 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 side effects 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. But due to lack of available monitoring facility after giving so large dose of steroid, we used 5mg of dexamethasone intravenously eight hourly for early control of disease.

There is scanty data regarding the use of parenteral dexamethasone in pemphigus in Bangladesh. This study was undertaken to see the safety level of parenteral dexamethasone compared with prednisolone in early management of pemphigus vulgaris.

Patients and methods

This clinical trial was carried out in the department of dermatology and venereology, Bangabandu Sheikh Mujib Medical University, Dhaka, from January 2010 to June 2011. Thirty patients of pemphigus were enrolled; 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 females, special attention was given regarding menstrual history and use of contraceptives. Clinical assessment was done at baseline, then weekly up to 6 weeks. Clinical assessment included number of skin lesions of pemphigus, number of mucous membrane lesions, 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.

Monitoring of adverse effect was done after two weeks, at the end of 4 weeks and after 8 weeks by query of symptoms of different system, physical examination and laboratory test. Information obtained from history, physical examination and laboratory investigation complete blood count and ESR, urinalysis, blood sugar, blood urea, serum creatinine, liver function tests, ECG, skin biopsy for histopathology and direct immunofluorescence test were recorded in patient data sheet.

Procedure of treatment

Group A (n=15) patients were treated with 5mg intravenous dexamethasone eight hourly. It was continued until cessation of new bullae. 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, we changed 5mg dexamethasone to equivalent dose of prednisolone i.e. 40mg (actually equivalent to 34mg of prednisolone, but as it was easier to take and remember, we gave 40mg). After six weeks we assessed the patient's outcome.

In group B, the initial dose of prednisolone was 100 mg daily in divided doses. It was continued until cessation of new bullae. After gradual improvement, it was reduced by 5-10mg weekly. After six weeks, we assessed the patient's condition.

Statistical analysis

All statistical analysis was done by SPSS 12 software package. 95% confidence limit was taken as level of significance. Comparison between two groups was 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

Table 1 showed that all demographic, clinical parameter were almost identical in two groups ($P>0.05$).

Table 2 showed statistically significant differences of skin lesion of pemphigus were observed after 6 weeks between two groups ($P<0.05$). Nikolsky's sign and bulla spreading phenomenon were present in all patients. In **Table 3**, statistically significant difference of bulla spread phenomenon was observed after 6 weeks between two groups ($P<0.05$) but regarding Nikolsky's sign, no statistically significant differences were observed between two groups.

Table 1 Baseline characteristics of two groups, dexamethasone (group A) and prednisolone (group B).

Characteristics	Group-A Dexamethasone (n=15)	Group-B Prednisolone (n=15)	P value
Age (years)	41.60±13.271	46.67±10.342	>0.05
Sex (male/female)	8/7	9/6	---
Duration of disease (months)	4.53±1.846	4.30±1.859	>0.05
Number of skin lesions	36.87±8.400	36.27±8.980	>0.05
Number of mucous membrane lesions	3.40±2.613	3.33±2.225	>0.05
Nikolsky's sign	15 (100%)	15 (100%)	--
Bulla spreading phenomenon	15 (100%)	15 (100%)	

Table 2 Comparison of number of skin and mucous membrane lesions in dexamethasone (A) and prednisolone (B) groups after 6 weeks.

	Group A (n=15)	Group B (n=15)	P value
No. of skin lesion of pemphigus (mean±SD)	5.27±1.624	7.73±1.907	<0.05
No. of mucous membrane lesion of pemphigus (mean±SD)	1.00±0.926	1.87±1.246	<0.05

Table 3 Outcome of Nikolsky's sign and bulla spread phenomena between dexamethasone (group A) and prednisolone (group B, prednisolone) after 6 weeks.

	Group A		Group B		P value
	Positive	*Negative*	*Positive*	*Negative*	
Nikolsky's sign	4	11	7	8	>0.05
Bulla spreading phenomenon	0	15	7	8	<0.05

Table 4 Frequency of adverse effects in dexamethasone (group A) and prednisolone (group B).

Adverse effects	Group A (N=15)	Group B (N=15)
Increased body weight	6 (40%)	9 (60%)
Increased appetite	6 (40%)	9 (60%)
Puffy face	6 (40%)	9 (60%)
Hyperglycemia	5 (33.3%)	5 (33.3%)
Hypertension	4 (26.7%)	6 (40%)
Sleep disturbance	2 (13.3%)	1 (6.7%)
Nausea, vomiting	0 (0%)	2 (13.3%)
Gastritis	0 (0%)	5 (33.3%)
Herpes zoster	0 (0%)	1 (6.7%)
Reactivation of tuberculosis	0 (0%)	1 (6.7%)
Mood changes	0(0%)	1 (6.7%)

Table 4 shows that the most common adverse effects were increased body weight (40%), increased appetite (40%), and puffy face (40%) in dexamethasone group. In prednisolone group, these side effects were seen in 60% of the subjects. Other side effects in dexamethasone group were hyperglycemia (33.3%), hypertension (26.7%), and sleep disturbance (13.3%). In prednisolone group other side effects were hyperglycemia (33.3%), hypertension (40%), gastritis (33.3%), nausea, vomiting (13.3%), reactivation of tuberculosis, herpes zoster infection, sleep disturbance, and mood change were 6.7%.

Discussion

The age of the patients enrolled in the study group ranged from 20-69 years with mean age of 41.60±13.27 years in dexamethasone group and 46.67±10.34 years in prednisolone group. In study by Toth *et al.*[7] they found the average age was 47.7 years. Statistically significant improvement was observed in dexamethasone group in all clinical parameters i.e. number of skin lesions of pemphigus, number of mucous membrane lesion of pemphigus and bulla spreading phenomena. But for Nikolsky's sign we did not find any significance difference between dexamethasone and prednisolone group after 6 weeks. These results were consistent with findings of another study.[7] In that study, the dose of dexamethasone was higher i.e. 200mg daily. In study by Amrinder *et al.*[8] they used cyclophosphamide with dexamethasone in the treatment of pemphigus vulgaris. In this study the dose of dexamethasone was 136mg monthly and cyclophosphamide 500mg monthly. In between pulse they used oral corticosteroid (low tapering dose) and 50mg daily. Their follow-up period was also for long duration. They found significance improvement with this therapy. Engineer *et al.*[9] used cyclophosphamide with dexamethasone in treatment of pemphigus vulgaris. They found complete remission in 82% of patients in their study. Their follow up period was one year. Harman *et al.*[10] in their study used azathioprine and in some patients used methotrexate with dexamethasone. Their dexamethasone dose was also high. They found significant improvement in theirpatients.

We did not do any histopathology or immunofluorescence studies, but others found significance reduction of antibody titer in direct and indirect immunofluorescence tests.[11,12] We found both inj dexamethasone and oral prednisolone were effective in early management of pemphigus vulgaris. These results were also consistent with the findings of

another study.[12] It appeared that inj dexamethasone and oral prednisolone had similar efficacy in the early management of pemphigus vulgaris.

The most common adverse effects from parenteral therapy were weight gain (40%), increased appetite (40%) and puffy face (40%). Other side effects were hyperglycemia (33.3%), hypertension (26.7%) and sleep disturbance (13.3%). In study by Toth *et al.*[7] diabetes was a common side effect. They also found minor side effects like temporary facial flushing, sleep disturbance and mood change. In prednisolone group, common side effects were increased body weight (60%), increased appetite (60%), and puffy face (60%). Other side effects were hyperglycemia (33.3%), nausea, vomiting (13.3%), gastritis (33.3%), herpes zoster, reactivation of tuberculosis, and mood change (6.7%). One study reported gastritis, hyperglycemia, hypertension, increased body weight, mood change and altered calcium/phosphate metabolism in prednisolone treated patient.[8]

It appeared that parenteral dexamethasone and oral prednisolone had similar efficacy in the early management of pemphigus vulgaris. Adverse effects were almost similar. Both drug appeared to be safe and well-tolerated.

Conclusion

We conclude that parenteral dexamethasone appears to be safer than oral prednisolone in early management of pemphigus vulgaris with an acceptable efficacy profile. A study with larger sample size with long duration follow-up of all cases is recommended.

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