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Original Article

Comparative adverse effects of low-dose oral prednisolone and oral mini pulse dexamethasone in patients of vitiligo

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Abstract

Objective To compare the adverse effects of low-dose oral prednisolone and oral mini pulse dexamethasone in patients of vitiligo.

Methods A clinical trial was carried out from January 2013 to December 2013. Total sixty patients of vitiligo were enrolled and 30 of group A patients were treated with low dose oral prednisolone (0.3 mg/kg body weight) daily and 30 of group B patients were treated with oral dexamethasone pulse therapy (10 mg per week) for 16 weeks.

Results During 12 week follow-up, increased body weight, headache, dyspepsia and fatigue were more frequent in group A as compared to group B. Similarly, in group A other side effects noted were acne (33.3%), mooning of face (26.6%), striae (26.6%), hypertrichosis 13.2%, purpura (6.7%) and among the female patients, menstrual abnormality (71.4%) whereas in group B, no patient developed these problems from baseline to follow-up period ($p<0.05$).

Conclusion Low dose oral prednisolone was found to be associated with more adverse effects than oral dexamethasone pulse therapy in treating vitiligo.

Key words
Adverse effects of oral corticosteroids, adverse effects of mini pulse dexamethasone, vitiligo.

Introduction

Vitiligo is a common, acquired, discoloration of the skin, characterized by well-circumscribed, ivory or chalky white macules which are flushed to the skin surface.[1] The cause is unknown but may involve genetic factors, autoimmunity, toxic metabolites and/or a higher vulnerability of melanocytes.[2-4] Abnormalities in both humoral and cell-mediated immunity have been documented in vitiligo patients and they present a basis for using steroids in the treatment of vitiligo.[5] There are numerous treatment options available for vitiligo, but none is universally effective. All approaches have advantage and disadvantages; and none is appropriate for every patient with vitiligo.[6]

Few studies have been published regarding treatment modalities of vitiligo and these studies have shown inconsistent results regarding the efficacy and safety of oral corticosteroids. Systemic corticosteroids suppress immunity, arrest the progression of vitiligo and lead to repigmentation. Systemic steroids may also produce unacceptable side effects.[6,7] Oral

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corticosteroid low-dose treatment may be associated with less severe and fewer side effects than usual-dose treatment. Some studies showed that low-dose oral corticosteroids were effective without serious side effects in preventing the progression and inducing repigmentation of actively spreading vitiligo. Several data showed that oral dexamethasone pulse treatment was effective in arresting progression of vitiligo but observed no side effects. Oral corticosteroid, either low-dose or pulse, therapy has provided inconsistent results regarding the adverse effects in the treatment of patients with vitiligo in some studies. To minimize the adverse effects associated with corticosteroids in daily dose, the adverse effects of low-dose oral prednisolone and mini pulse dexamethasone therapy were assessed in vitiligo patients.

Methods

The study was carried out in the outpatient Department of Dermatology and Venereology, Bangabandhu Sheikh Mujib Medical University (BSMMU) and Combined Military Hospital (CMH), Dhaka. The duration of the study was from January 2013 to December 2013 and patients of vitiligo were the study population. Inclusion criteria were patients aged 18-55 years, of both sexes, suffering from vitiligo for more than six months, having focal, segmental and generalized type of vitiligo, either stable or progressive, who had not received any treatment for vitiligo (both systemic and topical) in the previous 2 months prior to inclusion, and who gave informed consent comply with the study procedure. Exclusion criteria were pregnant and lactating mothers, patients suffering from systemic illnesses like diabetes mellitus, hypertension, ischemic heart disease, thyroid disorder or any other systemic autoimmune disorder, known case of prednisolone and dexamethasone sensitivity and vitiligo universalis and mucosal variety of vitiligo. By consecutive type of purposive sampling, 60 patients of vitiligo were enrolled and divided into group A and group B. Thirty group A patients were treated with oral prednisolone and 30 group B patients were treated with dexamethasone. The group A patients were given daily doses of oral prednisolone, 0.3 mg/kg body weight, initially for 2 months; the dosage was reduced to half of the initial dose for the third month and was halved again for the fourth month. The patients of group B were given 5 mg dexamethasone as a single oral dose after breakfast on 2 consecutive days per week (10 mg/week) for 16 weeks. Adverse effects were assessed during treatment and at each follow-up period.

Prior to the commencement of this study, the aims and objectives of the study along with its procedure, alternative methods, risks and benefits of this study were explained to the patients in easily understandable local language and then informed written consent were taken from each patient. It was assured that all information and records were kept confidential. The patients were explained that they had the right to refuse or accept to participate in the study and they would not receive any financial benefit from this study.

Data were collected by face-to-face interview and were recorded in a questionnaire. Information was collected by undertaking medical history and clinical examination. Type of vitiligo, whether progressive or stable, was determined by history and physical examination. The disease was considered stable if no new lesion had appeared and preexisting lesion did not enlarge during last six months. Baseline laboratory investigations were carried out for purpose of exclusion and monitoring of side effects. Laboratory investigations included complete blood count, serum urea, serum

creatinine and electrolytes, plasma glucose fasting and 2 hours after breakfast, liver function tests and serum cortisol levels. All the patients were weighed before starting treatment. Wood's lamp examination of lesions was done to confirm the clinical diagnosis. In the first and fourth week of therapy, plasma cortisol levels were determined in all patients.

The clinical response was evaluated at 4 weekly intervals for 12 weeks after completion of therapy and type and frequency of side effects were recorded at each visit. At the end of study, complete blood count, serum urea, serum creatinine and electrolytes, blood glucose fasting and 2 hours after breakfast and liver function tests were performed in all patients.

Data analysis was performed by Statistical Package for Social Science (SPSS), version-12. Level of significance was measured by using appropriate procedures like chi square test (χ^2) and t-test, where applicable. *p* value was set at 0.05 and confidence interval at 95%.

Results

The two groups were well matched in terms of pretreatment clinical characteristics and response to treatment (**Table 1**). Majority of patients in both groups were >25 year old i.e. 73.3% and 76.7%, respectively, χ^2 value=0.089. df=1, *p*=0.766 (*p*> 0.05). Disease was stable in the vast majority, 86.7% in group A and 90% in group B had stable disease, χ^2 value=0.089. df=1, *p*=0.766 (*p*> 0.05). About equal number of patients in both groups had single or multiple lesions, χ^2 value = 0.067, df =1, *p*=0.796 (> 0.05). Regarding the recovery rate after treatment, 27 (90%) and 25 (83.3%) patients improved, respectively in group A and B, χ^2 value= 0.577, df=1, *p*=0.448 (>0.05).

Table 2 compares mean pulse rate, systolic blood pressure, diastolic blood pressure, weight, SGPT and random plasma glucose levels in the studied patients at baseline and during study period. Unpaired student's t test revealed that no statistically significant mean difference was found between group A and group B in terms of pulse rate, systolic blood pressure and diastolic blood pressure. Analysis revealed that body weight was significantly increased from baseline to 12th week follow-up, in group A from 55.9±2.4kg to 56.5±2.4kg and in group B from 58.7±2.6kg to 61.5±2.5kg. An increasing trend of SGPT rise was observed in both groups up to 8th week of treatment and then it decreased, (*p*>0.05). No statistically significant difference of mean random plasma glucose levels was found in different stages of study (*p*>0.05).

Table 1 Distribution of patients by age, history of progression, number of lesion and rate of recovery.

Variables	*Characteristics*	*Group-A (n=30)*	*Group-B (n=30)*	*Level of significance*
Age in years	≤ 25 years	08 (26.7%)	07 (3.3%)	χ^2 value = 0.089
	> 25 years	22 (73.3%)	23 (76.7%)	*p*=0.766, NS
History of progression	Stable	04 (13.3%)	03 (10%)	χ^2 value = 0.162
	Progressive	26 (86.7%)	27 (90%)	*p*=0.688, NS
Number of lesion	Single	15 (50%)	14 (46.7%)	χ^2 value = 0.067
	Multiple	15 (50%)	16 (53.3%)	*P*=0.796, NS
Rate of recovery	Improved	27(90)	25 (83.3%)	χ^2 value = 0.577
	Not improved	3(10)	05 (16.7%)	*p*=0.448, NS

Table 2 Findings of pulse, blood pressure, weight, SGPT and random plasma glucose from baseline to 12th week.

Characteristics	*Group-A* □*n=30*□	*Group-B* □*n=30)*	*p value*
Pulse rate /min			
Baseline	80.1±1.7)	81.9±2.4	*p*>0.05
4th week	78.7±1.6	81.8±1.7	*p*>0.05
8th week	80.7±1.1	78.0±0.9	*p*>0.05
12th week	82.8±1.0	80.8±1.0	*p*>0.05
Systolic blood pressure (mm Hg)			
Baseline	121.0±2.9	118.3±3.0	*p*>0.05
4th week	121.9±2.8	117.0±2.5	*p*>0.05
8th week	129.5±3.2	123.5±2.6	*p*>0.05
12th week	133.8±3.3	124.8±2.2	*p*>0.05
Diastolic blood pressure (mm Hg)			
Baseline	75.7±1.6	75.4±1.7	*p*>0.05
4th week	74.3±2.3	76.5±1.6	*p*>0.05
8th week	78.1±1.3	77.4±1.6	*p*>0.05
12th week	81.4±1.3	79.4±0.9	p>0.05
Weight (kg)			
Baseline	58.7±2.6	55.9±2.4	*p*>0.05
12th week	61.5±2.5	56.5±2.4	*p*>0.05
SGPT (U/L)			
Baseline	24.2±2.7	31.4±4.1	*p*>0.05
4th week	29.3±3.9	37.1±8.2	*p*>0.05
8th week	41.2±10.9	43.4±12.4	*p*>0.05
12th week	28.0±2.8	34.2±4.2	*p*>0.05
Random plasma glucose (mmol/L)			
Baseline	5.4±0.2	5.3±0.2	*p*>0.05
12th week	5.3±0.2	5.6±0.3	*p*>0.05

Group A= Oral prednisolone, group B= Oral dexamethasone pulse therapy, *p* value reached from unpaired student's t test.

Table 3 shows that complaints of diarrhea and nausea appeared to be more or less similar in both groups of patients whereas headache, alopecia, dyspepsia and fatigue, were marginally more frequent in group A as compared to group B and the difference was not statistically significant (*p*>0.05) in two groups. **Table 4** reveals that in group B, no patient developed acne, mooning of face, striae, purpura, hypertrichosis and menstrual abnormalities; but in the group A, acne (33.3%), mooning of face (26.6%), striae (26.6%), purpura (6.7%), hypertrichosis (13.2%) and menstrual abnormalities (71.4%) were observed (*p*<0.05). On the contrary, mouth ulcers developed in both groups of patients; however, no statistically significant difference was found between two groups of patients (*p*>0.05).

Discussion

The results of our study were similar to study findings of Habib *et al*.,[8] Kim *et al*.[9] and Radakovic-Fijan *et al* [10] Habib *et al*.[8] conducted a study with thirty patients with vitiligo. The patients were given weekly pulses of 10mg dexamethasone on 2 consecutive days every week followed by 5 days off treatment for a maximum of 24 weeks. The mean age was 32.3 years (range, 21-51 years, standard deviation=7.68), and the disease was stable in 9 (30%) patients and progressive in 21 (70%) patients. Repigmentation was noted in 14 (46.6%) patients out of 30 patients at the end of 24 weeks. No response was observed in the remaining 16 (53.3%) patients. There was a tendency towards better treatment results with

Table 3 Comparison of diarrhea, nausea, dyspepsia, headache, alopecia and fatigue during follow-up period.

Characteristics	*Group A* □*n=30*□	*Group B* □*n=30)*	*p value*
Diarrhea			
Baseline	0 (0%)	0 (0%)	-
4th week	1 (3.3%)	1 (3.3%)	*p*>0.05
8th week	0 (0%)	1 (3.3%)	*p*>0.05
12th week	1 (3.3%)	1 (3.3%)	*p*>0.05
Nausea			
Baseline	0 (0%)	0 (0%)	-
4th week	7 (23.3%)	5 (16.7%)	*p*>0.05
8th week	7 (23.3%)	7 (23.3%)	*p*>0.05
12th week	7 (23.3%)	7 (23.3%)	*p*>0.05
Dyspepsia			
Baseline	0 (0%)	0 (0%)	-
4th week	12 (40.0%)	4 (13.3%)	*p*>0.05
8th week	15 (50.0%)	7 (23.3%)	*p*>0.05
12th week	15 (50.0%)	11 (36.6%)	*p*>0.05
Headache			
Baseline	2 (6.7%)	0 (0%)	*p*<0.05
4th week	5 (16.7%)	3 (10.0%)	*p*>0.05
8th week	6 (20.0%)	5 (16.7%)	*p*>0.05
12th week	7 (23.3%)	6 (20.0%)	*p*>0.05
Alopecia			
Baseline	0 (0%)	1 (3.3%)	*p*>0.05
4th week	0 (0%)	1 (3.3%)	*p*>0.05
8th week	0 (0%)	3 (10.0%)	*p*>0.05
12th week	1 (3.3%)	4 (13.3%)	*p*>0.05
Fatigue			
Baseline	0 (0%)	0 (0%)	-
4th week	7 (23.3%)	5 (16.7%)	*p*>0.05
8th week	11 (36.6%)	5 (16.7%)	*p*>0.05
12th week	11 (36.6%)	8 (26.6%)	*p*>0.05

Group-A= Oral prednisolone, Group-B= Oral Dexamethasone pulse therapy, *p* value reached from Fisher's exact test.

an increasing number of dexamethasone pulses. They also showed that side effects were quite common with dexamethasone pulse therapy. Twenty-one (70%) patients reported one or more side effects such as epigastric burning or pain, bloating, weight gain, insomnia, acne and menstrual disorders. Plasma cortisol levels were markedly decreased 48 hours after the second dexamethasone pulse. However, dexamethasone-induced suppression of endogenous cortisol production was only transitory and plasma cortisol values returned to baseline levels before administration of the next corticosteroid pulse. They concluded that oral dexamethasone pulse therapy is an effective treatment modality to arrest progressive vitiligo but treatment associated reversible side effects are frequent.[8] Kim *et al.*[9] evaluated 81 patients with vitiligo. The patients took daily doses of oral prednisolone (0.3 mg/kg body weight) initially for 2 months; the dosage was then reduced to half of the initial dose for the third month and was halved again for the fourth and final month. Arrested progression of vitiligo and repigmentation were noted in 87.7% and 70.4% patients, respectively. Adverse effects were assessed at the first, second, third and fourth month of treatment. The side-effects of treatment were minimal and did not affect the course of treatment.[9]

Table 4 Comparison of adverse effects like acne, mooning face, striae, purpura, hypertrichosis, menstrual abnormality and mouth ulcers during treatment.

Characteristics	*Group-A (n=30)*	*Group-B (n=30)*	*p value*
Acne	*N (%)*	*N (%)*	
Baseline	0 (0%)	0 (0%)	-
4th week	0 (0%)	0 (0%)	-
8th week	4 (13.3%)	0 (0%)	$p<0.05$
12th week	10 (33.3%)	0 (0%)	$p<0.05$
Mooning of face			
Baseline	0 (0%)	0 (0%)	-
4th week	1 (3.3%)	0 (0%)	$p>0.05$
8th week	6 (20.0%)	0 (0%)	$p<0.05$
12th week	8 (26.6%)	0 (0%)	$p<0.05$
Striae			
Baseline	0 (0%)	0 (0%)	-
4th week	1 (3.3%)	0 (0%)	$p>0.05$
8th week	6 (20.0%)	0 (0%)	$p<0.05$
12th week	8 (26.6%)	0 (0%)	$p<0.05$
Purpura			
Baseline	0 (0%)	0 (0%)	-
4th week	0 (0%)	0 (0%)	-
8th week	0 (0%)	0 (0%)	-
12th week	2 (6.7%)	0 (0%)	$p<0.05$
Hypertrichosis			
Baseline	0 (0%)	0 (0%)	-
4th week	0 (0%)	0 (0%)	-
8th week	4 (13.2%)	0 (0%)	$p<0.05$
12th week	4 (13.2%)	0 (0%)	$p<0.05$
Menstrual abnormality			
Baseline	0 (0%)	0 (0%)	-
4th week	1 (14.3%)	0 (0%)	$p>0.05$
8th week	3 (42.86%)	0 (0%)	$p<0.05$
12th week	5 (71.4%)	0 (0%)	$p<0.05$
Mouth ulcer			
Baseline	0 (0%)	0 (0%)	-
4th week	0 (0%)	0 (0%)	-
8th week	1 (3.3%)	1 (3.3%)	$p>0.05$
12th week	2 (6.7%)	3 (10.0%)	$p>0.05$

Group-A= Oral prednisolone, group-B= Oral dexamethasone pulse therapy, *p* value reached from Fisher's exact test

Radakovic-Fijan *et al.*[10] conducted a study to evaluate the efficacy, safety, and tolerability of oral dexamethasone pulse therapy in a cohort of Austrian patients with vitiligo. Twenty-nine patients with vitiligo were included in the study and of these, 25 had progressive and 4 had stable disease. They were evaluated clinical response in monthly intervals. The patients were given weekly pulses of 10 mg dexamethasone each on 2 consecutive days followed by 5 days off treatment for a maximum period of 24 weeks. After a mean treatment period of 18.2+/-5.2 weeks, the disease activity was arrested in 22 of 25 patients (88%) who had active vitiligo before the study. Marked repigmentation occurred in 2 patients (6.9%) and moderate or slight repigmentation in 3 patients (10.3%) each. No response was noted in 21 patients (72.4%). They evaluated side effects at monthly intervals. Plasma cortisol and corticotropin levels were monitored before and up to 6 days after the dexamethasone pulse in the first and fourth week of treatment in 14 patients. Side effects were recorded in 20 patients (69%) and included

weight gain, insomnia, acne, agitation, menstrual disturbance, and hypertrichosis. Plasma cortisol and corticotropin values were markedly decreased 24 hours after the second dexamethasone dose, yet returned to baseline values within the off treatment period before the next dexamethasone pulse. They concluded that mild to moderate side effects are common with this treatment modality.[10]

Conclusion

We conclude that low-dose oral prednisolone was found to be associated with more adverse effects than oral dexamethasone pulse therapy in treating vitiligo. Further multicenter, randomized, double-blind study should be conducted with large sample size.

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