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EFFICACY AND SAFETY OF ORAL DEXAMETHASONE PULSE TREATMENT FOR VITILIGO

Aamir Habib, *Zafar Iqbal Sheikh, **Qamar ud Din Khan, ***Simeen Ber Rahman

CMH Sialkot, *AM College Rawalpindi, **141 Medical Battalion, ***MH Rawalpindi

ABSTRACT

Background: Results of previous studies on efficacy and safety of oral corticosteroid pulse treatment for vitiligo are inconsistent.

Objective: The objective of this study was to assess the efficacy and safety of oral dexamethasone pulse treatment in a cohort of Pakistani patients. This is a descriptive study.

Patients and Methods: Thirty patients with vitiligo were included in the study. Of these, 21 had progressive disease and 9 had stable disease. The patients were given weekly pulses of dexamethasone on 2 consecutive days every week followed by 5 days off treatment for a maximum of 24 weeks. Clinical response and side effects were evaluated at monthly intervals. Plasma cortisol levels were also monitored.

Results: After a mean treatment period of 16 + 4 weeks, progression was arrested in 18 (85.7%) of 21 patients with active vitiligo before the study. Overall, repigmentation was noted in 14 (46.6%) patients at the end of 24 weeks. The extent of repigmentation varied from less than 25% (slight) to 51% to 75% (marked). Twenty (66.6%) patients reported one or more side effects. Plasma cortisol values were markedly decreased 24 hours after the second dose of each pulse but returned to baseline before the next dexamethasone pulse.

Conclusion: Oral corticosteroid pulse therapy is an effective treatment modality to arrest progressive vitiligo but is only moderately effective in inducing satisfactory repigmentation. Treatment associated side effects are frequent but reversible; however, sustained suppression of endogenous cortisol production does not occur with pulse regimen.

INTRODUCTION

Vitiligo is an acquired skin disorder characterized by well-defined white patches that are often symmetrically distributed [1]. The cause is unknown but may involve genetic factors, autoimmunity, toxic metabolites and/or a higher vulnerability of melanocytes [1-5]. Vitiligo is associated with a number of autoimmune disorders, most common of which is hypothyroidism [5]. Since curative treatment is not available, current modalities are directed towards stopping progression and to achieving repigmentation in order to repair the morphology and functional deficiencies of depigmented skin areas [1,3-5]. For widespread disease, photochemotherapy is generally considered the first line treatment [4,5]. The other modes of treatment include topical and systemic steroids, broad and narrow spectrum Ultraviolet B (UVB) and grafting techniques; minigrafts and autologous cultured melanocytes [1-5].

Systemic steroids can arrest the progression of vitiligo and lead to

Correspondence: Maj Aamir Habib, Graded Dermatologist, Combined Military Hospital, Sialkot

repigmentation in significant proportion of patients but may also produce unacceptable side effects [5-8]. To minimize the side effects associated with corticosteroids in daily dose, Pasricha, et al, introduced the concept of pulse therapy for treatment of vitiligo, using mini pulse therapy with betamethasone [7]. Subsequently few other studies have been published [6,9,10]. These studies have shown inconsistent results as regards the efficacy of oral corticosteroids in inducing repigmentation and arresting progression of vitiligo [6-10]. Oral corticosteroid pulse treatment is associated with less severe and fewer side effects than continuous treatment [11]. The ethnic background and peculiar environmental conditions of different countries may have an impact on the therapeutic response. It has been observed that dark skinned patients show better repigmentation than fair skinned patients during Psoralen Ultraviolet A (PUVA) therapy as well as after topical therapy [5]. The present study was performed to assess the efficacy and safety of oral dexamethasone pulse treatment in Pakistani patients.

PATIENTS AND METHODS

An observational study was carried out to assess the efficacy and safety of oral dexamethasone pulse treatment in Pakistani patients. A total of 30 patients who fulfilled the inclusion criteria were enrolled in the study on an out patient basis after taking an informed consent. First 30 patients of either sex having vitiligo of more than six months duration whether stable or progressive reporting to Dermatology department of Military Hospital Rawalpindi were enrolled. Age of the patients was between 20 and 55 years. Patient with pregnancy, lactating mothers, patients receiving any treatment or those who had received any treatment during last 3 months which might influence the course of disease, including Photochemotherapy, Ultraviolet B Phototherapy, systemic steroids and topical steroids were excluded from the study. Patients suffering from systemic illnesses like diabetes mellitus, hypertension, ischaemic heart disease, thyroid disorders or any other systemic autoimmune disorder were also excluded from the study. Skin phenotype of patients fulfilling the inclusion criteria was determined. Detailed history was taken and physical examination was performed. Type of vitiligo whether generalized, acrofacial or focal was determined by history and physical examination. Extent of vitiligo was assessed by lesion counting and determination of percentage of body surface area affected by rule of nine. Course of disease was determined by history. The disease was considered stable if no new lesion had appeared and preexisting lesion had not enlarged during last six months. Baseline laboratory investigations that were carried out for purpose of exclusion and monitoring of side effects included, complete blood counts, 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 first pulse of dexamethasone. Photographic documentation with close up photographs of all the depigmented macules was done in all patients after getting informed consent from the patient.

The enrolled patients were given weekly pulses of oral dexamethasone for a maximum of 24 weeks. A weekly pulse consisted of 10 mg dexamethasone taken as a single oral dose after breakfast on two consecutive days every week followed by five days without treatment. In the first and fourth week of therapy plasma cortisol levels were determined in all patients before the first dexamethasone dose (day 0) as well as 48 hours after 2nd dose, before 4th pulse and 48 hrs after 2nd dose of 4th pulse.

The clinical response was evaluated at monthly intervals. Percentage of repigmentation was estimated on each visit by lesion counting and a visual comparison of the patients against their baseline

photographs. Clinical evaluation was done at baseline and at the end of the treatment. In addition to the treatment response, type and frequency of side effects were recorded at each visit by taking history of weight gain, insomnia, acne, epigastric discomfort and hypertrichosis and menstrual disturbances (in female patients) (table-2). Patients were weighed at each visit to detect any weight gain. At the end of study, complete blood counts, serum urea, serum creatinine and electrolytes, blood glucose fasting and 2 hours after breakfast and liver function tests were performed in all patients.

Efficacy parameters included arrest of progression and percentage of repigmentatioin. Progression was said to be arrested if no lesion appeared or pre-existing lesions did not enlarge during last one month. Lesion counting and a visual comparison of the patients against their baseline photographs estimated the percentage of repigmentation. Repigmentaton was considered excellent (>75%), marked (51% to 75%), moderate (26% to 50%) and slight (25% or less). Safety of treatment was assessed by incidence of side effects as judged by history, clinical examination and laboratory investigations.

RESULTS

A total of 30 patients were included in the study. There were 24 (80%) males and six (20%) females. Male to female ratio was 4:1. All the patients had Fitzpatrick skin type IV. The mean age was 32.3 years (range, 21-51 years, standard deviation [S.D.] =7.68), and the mean disease duration was 3.6 years (range, 0.5 –16 years, standard deviation [S.D.]=3.6). The disease was stable in 9 (30%) patients and progressive in 21 (70%) patients. Seven (23.3%) patients had acrofacial vitiligo and 23 (76.7%) patients had generalized vitiligo. The extent of cutaneous involvement was 1% to 10% of body surface area in 19 patients, 11% to 30% in 6 patients, 31% to 50% in 4 patents and more than 50% in one patient.

After a mean treatment period of 16 + 4 weeks, progression was arrested in 18 (85.7%) of 21 patients with progressive vitiligo, while in the remaining 3 (14.3%) patients; the progression of disease was not arrested. Repigmentation was noted in 14 (46.6%) patients out of 30 patients at the end of 24 weeks (table-1). Out of these 14 patients, 13 (92.9%) had progressive disease and one (7.1%) had stable disease (fig). It was found that the response of patients with progressive disease was significantly better ($p<0.05$) as compared to stable disease in terms of repigmentation. Out of 14 patients showing repigmentation 11 (78.6%) had generalized disease and 3 (21.4%) had acrofacial disease. It was observed that the response was not significantly different ($P>0.05$) in these two groups of patients. Out of the total 14 patients with repigmentation, 10 (71.43%) patients had slight, 3 (21.43%) patients had moderate repigmentation and one (7.14%) patient had marked repigmentation. None had excellent repigmentation. The only patient showing marked repigmentation had stable disease at the beginning of the study. No response was observed in the remaining 16 (53.3%) patients. There was a tendency towards better treatment results with an increasing number of dexamethasone pulses.

Side effects were quite common. 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 since plasma cortisol values returned to baseline levels before administration of the next corticosteroid pulse.

DISCUSSION

To minimize the side effects of systemic steroids, Pasricha, et al, introduced the concept of treatment of vitiligo by pulses of

systemic corticosteroids by using mini-pulse therapy with betamethasone [7]. Subsequently few other studies were published [6,9]. These studies have shown inconsistent results as regards the efficacy of oral corticosteroid pulse treatment in arresting active disease and inducing the repigmentation in patients with vitiligo [6-9]. However all the studies concluded that the side effects of treatment were minimal and did not affect the course of treatment [6-9].

In our study, the efficacy and safety of 10 mg dexamethasone for 2 days a week was evaluated in 30 patients with vitiligo. First 30 patients of vitiligo reporting to Dermatology department of Military Hospital who fulfilled inclusion criteria were enrolled. There were 24 (80%) males and 6 (20%) females. Male patients were more than female patients. A number of females could not be included in the study because they were reluctant to get every skin lesion photographed. All patients had Fitzpatrick's skin phenotype IV. Patients having any other systemic illness whether associated with vitiligo or not were excluded by history, clinical examination and laboratory investigations. Efficacy of systemic corticosteroids pulse treatment in arresting the progression of disease has been reported between 81 to 89 percent in previous studies [6-7,9]. Progression of disease was halted in 85.7% of our patients. Pasricha JS, et al, reported repigmentation in14 (35%) of 40 patients and almost complete repigmentation (>90%) in 3 (7.5%) patients [7]. Siester S, et al, [9] observed repigmentation in 71% of patients with progressive disease. Radakovic-Fijan S, et al, [6] reported repigmentation in 27.6% of patients and concluded that oral corticosteroid pulse treatment has got limited efficacy in inducing cosmetically acceptable repigmentation when used as a monotherapy. Recently, Handa S, et al, [10] studied combination of sun exposure and oral dexamethasone pulse treatment for vitiligo and reported repigmentation in 81% of their patients. In our study repigmentation was noted in 46.6% of patients, with only one patient showing >50% repigmentation. The difference observed in various studies in efficacy of systemic corticosteroid pulse therapy as regards repigmentation may be due to different skin types of patients. In our patients as also reported in previous studies [6-10], there was a tendency towards better repigmentation results with an increasing number of oral corticosteroid pulses. Radakovic-Fijan S, et al, [6] reported that oral dexamethasone pulse therapy was ineffective in inducing repigmentation in patients with stable disease. Our results were different from those of Radakovic-Fijan S, et al, in that in our study out of total 14 (46.6%) patients showing repigmentation, one patient had stable

Table-1: Assessment of repigmentation

Percentage of repigmentation	Number of patients showing repigmentation at different weeks			
	8 wks	12 wks	16 wks	24 wks
0	30	26	21	16
<25%	-	3	7	10
26%-50%	-	1	2	3
51%-75%	-	-	1	1
>75%	-	-	-	-

Table-2: Type and incidence of side effects

Side effects*	No of Patients (%)
Dyspeptic symptoms	15 (50%)
Weight gain	12 (40%)
Insomnia	6 (20%)
Acne	4 (13.3%)
Menstrual disturbances	6 (100%)ε

** Multiple entries per patient possible*
ε Percentage of female patients

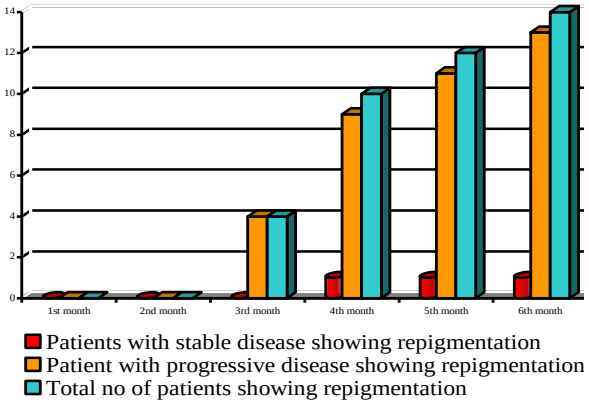

Fig: No of patients showing repigmentation.

disease when assessed at the beginning of study. In our patients 13 (61.9%) out of 21 patients with progressive disease and one (11.1%) out of 9 patients with stable disease showed repigmentation. Patients with progressive disease exhibited significantly better response ($P<0.05$) as compared to those with stable disease. In our patients 11 (47.8%) out of 23 patients with generalized disease and 3 (42.3%) out of 7 patients with acrofacial disease showed repigmentation. Treatment associated side effects were frequent but were not severe enough to warrant discontinuation of treatment in any patient. Side effects were fully reversible on discontinuation of therapy. No sustained suppression of the endogenous cortisol production was found with pulse administration of oral dexamethasone.

Our findings indicate that oral corticosteroid pulse therapy is an effective treatment modality to arrest progressive vitiligo. However it is only moderately effective in inducing substantial repigmentation when given for a period of unto 24 weeks.. The patient compliance to take oral corticosteroid pulses over extended periods is likely to be hampered by the slow pace of response and the high rate of side effects.. Advantages of oral corticosteroid pulse therapy over conventional daily dose include better patient compliance, less severe and fewer side effects and no sustained suppression of the endogenous cortisol production. The beneficial effects of oral corticosteroid pulse therapy in combination with other modalities remains to be evaluated in future studies.

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