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Original Article

Efficacy of Oral Mini Pulse Betamethasone in the Treatment of Vitiligo-A Study in FMCH

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Abstract:

Vitiligo is an acquired multifactorial polygenic disorder with a complex pathogenesis, characterized by depigmented macules in skin. A clinical trial was conducted to evaluate the efficacy of oral mini pulse betamethasone in the treatment of vitiligo patients. The study was done in the department of Dermatology and Venereology, Faridpur Medical College Hospital (FMCH), Faridpur, Bangladesh from July 2014 to June 2015. Among thirty patients of vitiligo, most of the male patients (53.33%) and most of the female patients (40%) were between 20 to 25 years of age. Majority of patients (70%) had been suffering from vitiligo for less than 3 years and 50% patients had positive family history. Eighteen (60%) patients had acro-facial type of vitiligo and 20 (66.67%) cases were progressive in nature. In this study, response was slight in 36.67%, moderate in 33.33%, marked in 20% and excellent in 10% of cases after 12 weeks. Eight (26.66%) of total patients were seen to be with clinical side effects. Among the side effects, weight gain 4 (13.33%) was most prevalent, others include general weakness in 2 (6.66%) and acne in 2 (6.66%) patients. In conclusion, oral mini pulse betamethasone seems to be an effective treatment modality to arrest the progression of vitiligo and induction of repigmentation.

Key words: Efficacy, Betamethasone, Vitiligo.

Introduction:

Vitiligo is an acquired pigmentary anomaly of the skin manifested by depigmented white patches surrounded by a normal or a hyperpigmented border[1]. The cause is unknown but may involve genetic factors, autoimmunity, toxic metabolites and/or a higher vulnerability of melanocytes[2-4]. Vitiligo is associated with a number of autoimmune disorders, most common of which is hypothyroidism[5]. Since the 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 as the first line of 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[1,6].

One of the most probable pathogenesis of vitiligo is autoimmunity. Systemic corticosteroids suppress immunity and may arrest the progression of vitiligo and lead to repigmentation. Systemic steroids may also produce unacceptable side effects[5-7]. To minimize the side effects, we tried a new approach using oral mini pulse betamethasone in vitiligo patients.

Materials and Methods:

A clinical trial was carried out to assess the efficacy of oral mini pulse betamethasone in patients of vitiligo.

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The study was conducted in the department of Dermatology and Venereology, Faridpur Medical College Hospital, Faridpur, Bangladesh from July 2014 to June 2015. The patients were given 5mg betamethasone as a single oral dose after breakfast on 2 consecutive days per week for 16 weeks. The effects of treatment were evaluated using photographs of before and after the study. Side-effects were assessed at the first, second and third month of treatment. A total of thirty patients who fulfilled the inclusion criteria were enrolled in the study on an outpatient 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 were enrolled. Age of the patients was between 15 and 55 years. Patient with pregnancy, lactating mothers, patients receiving any treatment or those who received any treatment during last 3 months which might influence the course of disease, including photo chemotherapy, Ultraviolet B phototherapy, systemic illnesses like diabetes mellitus, hypertension, ischaemic heart disease, thyroid disorders or any other systemic autoimmune disorder were also excluded from the study. 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 counting lesion 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 appeared and pre-existing lesion was 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 starting of treatment. Photographic documentation with close-up photographs of all the depigmented macules was done in all patients after getting informed consent from the patient. In the first and fourth week of therapy plasma cortisol levels were determined in all patients before the first dose (day 0) as well as 48 hours after, before 4th dose and 48 hours after. The clinical response was evaluated at monthly intervals. Percentage of repigmentation was estimated on each visit by counting the lesion 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 general weakness, weight gain, mild headache, acne, epigastric pain and menstrual abnormality in case of female. 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 repigmentation. 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. Repigmentation 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:

Among thirty patients of vitiligo, most of the male patients (53.33%) and most of the female patients (40%) were between 20 to 25 years of age. Majority of patients (70%) had been suffering from vitiligo for less than 3 years and 50% patients had family history of vitiligo Table-I. Eighteen (60%) patients had acro-facial and 12 (40%) patients had generalized vitiligo Fig.-1. The disease was stable in 10 (33.33%) and progressive in 20 (66.67%) cases. The extent of cutaneous involvement was less than 30% area in 18 (60%) patients, 31 to 50% area in 6 (20%) patients and more than 50% area in 6 (20%) patients. In this study, response was noticed at Table-II first follow-up after 4 weeks, then after 8 weeks and lastly after 12 weeks. Response was slight in 60%, moderate in 26.60%, marked in 6.66% and excellent in 6.66% of cases after 4 weeks. Response was slight in 46.66%, moderate in 40%, marked in 6.66% and excellent in 6.66% of cases after 8 weeks. Response was slight in 36.66%, moderate in 33.33%, marked in 20% and excellent in 10% of cases after 12 weeks Table-III. In the present study 26.66% of total patients were seen to be with clinical side effect. Among the side effects, weight gain (13.33%), acne (6.67%), and general weakness (6.67%) were most prevalent Table-IV. Plasma cortisol levels were markedly decreased 48 hours after the second oral mini pulse betamethasone. However, betamethasone induced suppression of endogenous cortisol production was only transitory since plasma cortisol value returned to baseline levels before administration of the next of the oral mini pulse betamethasone therapy.

Table I: Characteristics of patients of vitiligo.

Age in years	Male		Female	
	No.	Percentage	No.	Percentage
15-20	4	26.67	5	33.33
20-25	8	53.33	6	40
25-30	2	13.33	2	13.33
30-35	1	6.67	2	13.33
Duration in year	**Number**		**Percentage**	
<3	21		70	
3-6	9		30	
Family History	**Number**		**Percentage**	
Positive	15		50	
Negative	15		50	

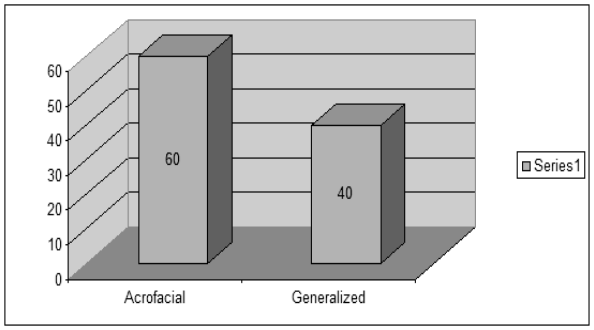

Figure 1: Distribution of the patients by varieties of vitiligo.

Table II: Distribution of patients by status and extent of vitiligo (n=30)

Status of vitiligo	Number	Percentage
Stable	10	33.33
Progressive	20	66.67
Extent of involvement	**Number**	**Percentage**
>30%	18	60
31-50%	6	20
>50%	6	20

Table III: Distribution of response rate according to duration (n=30)

Efficacy	Week-4	Week-8	Week-12
No	Percentage No.	Percentage No.	Percentage
Excellent 2	6.66 2	6.66 3	10
Marked 2	6.66 2	6.66 6	20
Moderate 8	26.66 12	40 10	33.33
Slight 18	60 14	46.66 11	36.67

Table IV: Distribution of patients by side effects of therapy.

Side effects	No. of patients(n=8)	Percentage(n=30)
General weakness	2	6.67%
Weight gain	4	13.33%
Acne	2	6.67%

Discussion:

Among thirty patients of vitiligo, most of the male patients (53.33%) and most of the female patients (40%) were between 20 to 25 years of age, having consistent with the study of Amir Habib et al[8]. They observed 80% males and 20% females in a cohort Pakistani vitiligo patient[8]. Majority of patients (70%) had been suffering from vitiligo for less than 13 years. In the study by Kim et al[9]. in the department of Dermatology, Samsung Cheil Hospital, Sungkyunkwan University School of Medicine, South Korea also observed that the duration of disease were 2 years or less[9].

In our study 18(60%) patients had acro-facial and 12(40%) patients had generalized vitiligo. The disease was stable in 10(33.33%) and progressive in 20(66.67%) cases. The extent of cutaneous involvement was less than 30% area in 18(60%) patients and 31 to 50% area in 6(20%) patients in the study by Radakovic-Fijan et al. in the department of Dermatology, University of Vienna Medical School, Austria. Of these, 25 had progressive and 4 had stable disease[6]. Amir Habib et al. observed that the disease was stable in 9 (30%) patients and progressive in 21 (70%) patients. They observed that 7 (23.3%) patients had acrofacial vitiligo and 23(76.7%) patients had generalized vitiligo, not similar to our findings. The extent of cutaneous involvement was 1% to 10% of body surface area in 15 patients, 11% to 30% in 3 patients, 31% to 50% in 6 patients and more than 50% in 6 patients, similar to our findings[8]. In our study, response was noticed at first follow-up after 4 weeks and after 12 weeks. Response was slight in 60%, moderate in 26.66%, marked in 6.66% and excellent in 6.66% of cases after 4 weeks. Response was slight in 36.57%, moderate in 33.33%, marked in 20% and excellent in 10% of cases after 12 weeks. In the study by Radakovic-Fijan et al. after a mean treatment period of 18.2$\pm$5.2 weeks, marked repigmentation occurred in 2(6.9%) patients and moderate or slight repigmentation in 3 (10.3%) patients of each. No response was noted in 20 (72.4%) patients[6]. A study by pasricha et al. conducted with forty patients having extensive and/or fast-spreading vitiligo were given 5 mg betamethasone as a single oral dose after breakfast on 2 consecutive days in a week. Within 2-4 months of treatment, 80% of the patients started having spontaneous repigmentation of the existing lesions which progressed with continued treatment. The extent of repigmentation varied in different and even in different lesions in the same patient. It was less than 10% in 14 (35%) patients and almost complete (>90%) in three patients[7]. In the study by Amir Habib et al. they observed that repigmentation was noted in 14 (46.6%) patients out of 30 patients.

Out of the total 14 patients with repigmentation, 10 (71.43%) patients had slight, 3 (21.43%) patients had moderate and one (7.14%) patient had marked repigmentation. None had excellent repigmentation. No response was observed in the remaining 16 (53.3%) patients[8]. Kim et al conducted a study in the department of Dematology, Samsung Cheil Hospital, Sungkyunkwan University School of Medicine, Suwon, South Korea. Eighty-one patients with vitiligo were evaluated for 4 months and repigmentation were noted in 40.4% of patients[9]. In the present study, 26.67% of total patients were seen to be with clinical side effects. Among the side effects- weight gain (13.33%), acne (6.67%) and general weakness (6.67%) were predominant. Side effects were recorded in 20 patients (69%) by Radakovic-Fifan et al. and included weight gain, insomnia, acne, agitation, menstrual disturbance, and hypertrichosis[6]. The side effects by pasricha et al included weight gain of 5 and 7 kg in two patients, mild headache in two patients, transitory general weakness for 2 days after the pulse in two patients, and bad tastes in the mouth in three patients and 23 patients, including six children, had no side effects[7]. In the study by Amir Habib et al. twenty-one (70%) patients reported one or more side effects such as epigastric burning or pain, bloating, weight gain. Insomnia, acne and menstrual disturbances were seen in the study done by Kim et al[9].

Plasma cortisol levels were markedly decreased 48 hours after the second oral mini pulse betamethasone. However, betamethasone induced suppression of endogenous cortisol production was only transitory since plasma cortisol values returned to baseline levels before administration of the next oral mini pulse betamethasone therapy, which is consistent with the study by Amir Habib et al[8]. The side-effects of treatment were minimal and did not affect the course of treatment by the study done by Kim et al[9].

Conclusion:

Oral mini pulse betamethasone seems to be an effective treatment modality with minimal side-effects to arrest the progression of vitiligo and induction of repigmentation. It deserves to be tried on a large scale to evaluate its advantages over the currently available methods of treatment of vitiligo.

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