Original Article

Role of Topical Calcipotriol to Potentiate the Effect of Photochemotherapy (PUVA) in Treatment of Vitiligo

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Abstract

Introduction: Vitiligo is a specific, common, often heritable acquired disorder characterized by well-circumscribed milky white cutaneous macules and patches devoid of identifiable melanocyte. Treatment of vitiligo, though quite frustrating, includes repigmentation therapies like Topical glucocorticoids, Topical calcipotrieinene, Topical PUVA (Psoralen + Ultraviolet Light A). The combination of calcipotriol and PUVA proves quite effective for management of this condition.

Objectives: To compare the effectiveness of PUVA and the combination of topical calcipotriol and PUVA in treatment of vitiligo.

Materials and Methods: This quasi experimental study was undertaken at Combined Military Hospital, Dhaka Cantonment, Dhaka from March to October 2015. A total of 32 patients suffering from vitiligo diagnosed clinically and confirmed by Wood's lamp examination were selected as study population. Systemic PUVA, thrice weekly was given but Topical calcipotriol applied twice daily at one side of the body and other side used nothing Topically. Response was assessed clinically every 4 weeks along with photographic record and compared between two sides of the body.

Results: During the course of the treatment, the calcipotriol plus PUVA treated side showed considerably better improvement than only PUVA treated side. The response was Excellent; 37.8% (12/32), Good; 31.3% (10/32), Fair; 18.8% (6/32), *Poor*; 12.5% (4/32) in calcipotriol plus PUVA treated side whereas Excellent; 12.5% (4/32), Good; 25% (8/32), Fair; 43.8% (14/32) and Poor; 18.8% (6/32) in only PUVA treated side.

Conclusion: This study shown that concurrent topical calcipotriol potentiates the efficacy of PUVA in the treatment of vitiligo along with the fact that this combination achieves earlier pigmentation with a lower total UVA dosage in comparison to only PUVA therapy.

***Key-words*:** Vitiligo, PUVA, Topical calcipotriol

Introduction

The word vitiligo is derived from Greek word 'vitilus', means spotted calf[1]. Vitiligo is a specific, common, often heritable acquired disorder characterized by well-circumscribed milky white cutaneous macules and patches devoid of identifiable melanocyte[2]. The loss of melanocytes alters both structure and function of the affected skin and mucous membrane and results in the absence of pigment[3]. Vitiligo usually begins in childhood or young adult-hood with about half of cases beginning before age 20 and overall prevalence is between 1 and 2 percent[4]. All races are affected. Both sexes are affected equally, but female prevalence in some studies has been shown. It appears to be observed more commonly in sun exposed areas and in darker skin type (SPT IV). The etiology of vitiligo is complex. There appears to be a certain genetic predisposition and 30-40% of patient having positive family history. Inheritance may be polygenic or autosomal dominant of variable penetrance[5]. Many studies show relationship between HLA system and vitiligo. An association between the catalase gene, VIT-1 gene and vitiligo has been suggested. Vitiligo also has some potential precipitating factors, as crisis or illness, physical injury, sun exposure. Again, recent studies have suggested that there's a defect in calcium homeostasis in vitiligous skin[6,7]. Four possible mechanisms have been proposed to induce vitiligo. These are autoimmune hypothesis, neural hypothesis, self-destruct hypothesis and melanocytorrhagy.

Vitiligo is a frustrating condition to treat. Spontaneous repigmentation occurs in 15-25% of cases. All patients should be encouraged to use sunscreens to protect vitiliginous areas. Cosmetics that are makeup dyes and self-tanning preparations can temporarily conceal the lesions. For repigmentation, various options are available. These are topical glucocorticoids for limited vitiligo, topical PUVA for focal and segmental types, PUVA-grafting for refractory segmental vitiligo or stable vitiligo narrow band UVB (ultraviolet B) therapy and systemic PUVA for segmental or generalized vitiligo[8,9]. PUVA is treatment involving the use of psoralen, an exogenous photosensitizer followed by ultraviolet A (UVA) irradiation[10]. Concurrent topical calcipotriol potentiate the efficacy of PUVA in the treatment of vitiligo[11]. Calcipotriol, a vitamin D analogue, influences melanocyte maturation and differentiation[12]. Numerous surgical techniques are also available. These are epidermal grafting, autologous minigrafts and transplantation of cultured and non-cultured melanocytes. Other modalities for repigmentations are multivitamin therapy, melagenina, phenylalanine and UVA, combination of calcium, pseudocatalase and UVB.

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Depigmentation can be done with monobenzyl ether of hydroquinone (MBEH) 20% cream. This study was performed in order to assess the role of calcipotriol as an effective adjunct to the traditional PUVA therapy in the treatment of vitiligo patients in Bangladesh.

Materials and Methods

A quasi experimental study was conducted from May to October 2015 at Department of Dermatology and Venereology, CMH, Dhaka. A total of 32 patients suffering from vitiligo affecting 5-40% of their skin who gave consent were selected as study population. They were between 15-45 years. However, the patients who had history of hypersensitivity to phototherapy or with severe impairment of renal or hepatic function, diabetes mellitus, thyroid disease were also not included. Pregnant and lactating mothers too were excluded. An informed consent was sought from the patient to take part in the study. Patient's data were recorded on predesigned record form. The diagnosis was made on clinical basis and wood's light examination. As for the treatment protocol, oral dose of 0.6 mg/kg 8-methoxypsoralen was given 2 hours before exposure to UVA. The exposure was given thrice in a week. The patient was advised to apply calcipotriol 50 micrograms/g topically on one side of the body twice daily and other side of the body nothing to use topically. All patients received at least forty-five sessions and maximum 60 sessions of PUVA therapy over whole body. In addition to clinical examination by wood's lamp the following investigations were done in all cases like; CBC and urine R/E, liver function test, blood sugar level, serum urea and creatinine, thyroid function test, thyroid autoantibody if necessary and serum calcium level. In each patient, the size of depigmented areas is assessed according to the rule of nines before treatment. During treatment patients are assessed clinically by two investigators in every 4 weeks interval. In addition, photographic records are taken before and after treatment. Treatment efficacies are classified into 4 groups: Poor; 0-25% repigmentation, Fair; 26-50% repigmentation, Good; 51-75% repigmentation and Excellent; more than 75% repigmentation. The scoring was done on the basis of induced repigmentation in vitiligo; the responses in each visit were endorsed into study protocol. By the end of the therapy, the percentage, score for each patient was evaluated by statistical analysis which was performed with significant level set as $p < .05$ by Chi-square test. Mean median, standard deviation and 95% confidence interval was estimated when appropriate.

Results

The mean age of the patients was 28.9 years (range 16-45 years). The median duration of disease is 5.2 years and range 1-16 years. Evidence of initial pigmentation was obtained earlier in lesions treated with the combination of PUVA and calcipotriol than with PUVA therapy alone. After 02 months of therapy 20 out of 32 (62.5%) patients showed fair response (26-50% repigmentation) in calcipotriol+ PUVA treated side whereas 06 of 32 (18.8%) patients showed fair response in only PUVA treated side. After 04 months of therapy in PUVA+ calcipotriol treated side 14 patients showed good response (51-76% repigmentation) and 10 patients showed fair response (26-50% repigmentation) whereas 08 patients showed good response and 08 patients showed fair response in only PUVA treated side. After 06 months of therapy in PUVA+ calcipotriol treated side 12 of 32 patients (37.8%) showed excellent response (76-100% repigmentation), 10 patients (31.3%) showed good response (51-75% repigmentation) and 06 patients (18.8%) showed fair response (26-50% repigmentation). Whereas in only PUVA treated side 04 patients (12.5%) showed excellent response, 08 patients (25%) showed good response and 14 patients (43.8%) showed fair response and 04 patients of PUVA+ calcipotriol treated side and 06 patients of only PUVA treated side showed poor response (0-25% pigmentation) (Table-I). Four patients had mild to moderate erythema and itching on the calcipotriol applied sites and two patients had nausea and headache as side effects. No new lesions occurred during the treatment.

Table-I: Therapeutic response of study group after 2, 4 and 6 months of therapy (n=32)

Treatment Response (Percentage of re-pigmentation)		**PUVA+Calcipotriol**	**Only PUVA**
After 2 months	Excellent (76-100)	00	00
	Good (51-75)	00	00
	Fair (26-50)	20	06
	Poor (0-25)	12	26
After 4 months	Excellent (76-100)	00	00
	Good (51-75)	14	08
	Fair (26-50)	10	08
	Poor (0-25)	08	16
After 6 months	Excellent (76-100)	12	04
	Good (51-75)	10	08
	Fair (26-50)	06	14
	Poor (0-25)	04	06

Discussion

Various agents including khellin, oral and topical phenylalanine, pseudocatalase and calcium has been combined with UVA or UVB to increase their effectiveness in vitiligo treatment but none has been found to be superior and safer than PUVA therapy alone[13]. However, recent studies suggest that the efficacy of PUVA can be enhanced when it is used in combination with topical calcipotriol[14]. Parsad D et al conducted a randomized double-blind right/left comparative study of 18 months' duration. They reported a marked complete repigmentation with topical calcipotriol and PUVA in 12(70%) of 19 vitiligo patients whereas placebo treated side showed success of 35% at 06 months[15,16]. Ermis O et al conducted a placebo-controlled double-blind study on 27 patients with generalized vitiligo. Calcipotriol 0.05 μg cream or placebo was applied to the lesions before PUVA treatment. They reported that treatment with calcipotriol and PUVA resulted in significantly higher response for both initial (81%) and complete pigmentation (63%) in comparison to placebo and PUVA (7 and 15%, respectively)[17]. Simillar result also found by Hartmann A and Lurz C[18].

This study has also indicated that combination treatment with calcipotriol and PUVA is much more effective in initial and also in final stage for reaching complete repigmentation than PUVA alone. After 06 months of treatment with PUVA and topical calcipotriol excellent and good response have been achieved in 68.75% (22/32) cases whereas only 37.5% (12/32) showed excellent and good response with systemic PUVA alone which correlates with the results achieved by Parsad D et al[15] and Emris O et al[17]. Baisal V et al[13] conducted an open study on 22 patients with generalized vitiligo. PUVA treatment was applied on a twice weekly schedule. Calcipotriol cream was applied to one of the two symmetric lesions of each patient twice daily. They reported that the addition of topical calcipotriol to PUVA treatment did not lead to a significant increase in response rate to patients with vitiligo compared with PUVA treatment alone. Their study does not correlate with this study. Mild to moderate pruritus, irritation and erythema was noticed on calcipotriol applied site in 4 patients, Nausea and headache were observed in 2 patients. In this study 75% (24) patients were between 15 to 35 years and the mean age group is 28.9 years. This occurs with the observation that vitiligo most common in these age groups. In this study male and female ratio was equal that is 1:1 which reflects that in vitiligo both sexes are equally affected.

Conclusion

The combination of calcipotriol and PUVA in vitiligo seems to be safe and effective. These studies have shown that concurrent topical calcipotriol potentiates the efficacy of PUVA in the treatment of vitiligo, and this combination achieves earlier pigmentation with a lower total UVA dosage. No significant side effects seen with these treatment modalities. Study with large number of patients for longer period needs for confirmation of this results.

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