

Original Article

Comparative efficacy of hydroxychloroquine and griseofulvin in the treatment of lichen planus

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Abstract *Background* Lichen planus (LP) is an unpredictable disease that typically persists for 1 to 2 years, but which may follow a chronic, relapsing course over many years. Management of LP can be challenging and discouraging for both the patient and physician.

Objectives To compare the efficacy of hydroxychloroquine and griseofulvin in the treatment of LP.

Patients and methods 80 cases of age group 20-60 years were selected for the study during the period of July 2007 to June 2009 in the Department of Dermatology and Venereology of three different hospitals in Bangladesh. All cases were diagnosed clinically and confirmed by histopathological examination of skin. The patients were randomly divided into 2 equal groups. Group A was given hydroxychloroquine 400 mg daily and group B was given griseofulvin 500mg daily for a period of 6 months.

Results 53 (66%) male and 27 (34%) female were included in the study. The mean age in group A was 39.03±12.28 years and in group B was 42.87±11.16 years ($p=0.146$). The mean duration of the disease in group A was 4.37±3.87 months and in group B was 4.35±3.32 months ($p=0.975$). In group A clinical responders were 28 (70%): complete response in 7 (17.5%) and moderate improvement in 21 (52.5%) and in group B clinical responders were 17 (42.5%): complete response in 2 (5%) and moderate improvement in 15 (37.5%) [$p=0.027$].

Conclusion In this study both hydroxychloroquine and griseofulvin showed clinical improvement but hydroxychloroquine showed a relatively better response than griseofulvin in the treatment of LP.

Key words

Lichen planus, hydroxychloroquine, griseofulvin.

Introduction

Lichen planus (LP) is a common inflammatory

disorder that affects the skin, mucous membrane, nail and hair.^{1,2} This papulosquamous disease is characterized by small, flat-topped, shiny, polygonal, violaceous, pruritic papules that begin as pinpoint papules and expand to 0.5 to 1 cm plaques.^{3,4} The papules may show on its surface gray or white puncta or streaks known as Wickham's striae. Koebner's phenomenon occurs in LP.^{5,6} The disease is seen throughout

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the world in all races. It may be familial.^{6,7} The exact etiology of the disease is unknown but several etiologies have been proposed. Both endogenous, including genetic, and exogenous components such as drugs and infection interact to elicit the disease. Some conclude that the autonomic nervous system from the beginning takes an active part in the pathological process. LP is a benign disease with remission and exacerbation.⁸⁻¹¹

Various modalities of treatment such as steroids (topical, intralesional, systemic), cyclosporine, subcutaneous low molecular heparin, retinoids, metronidazole, hydroxychloroquine, griseofulvin, methotrexate, PUVA, interferon, gold, antihistamines, dapsone etc. are available but many of the advocated treatments lack conclusive evidence for efficacy.¹²⁻¹⁵

There are many studies from different countries of the world on the efficacy/benefit of hydroxychloroquine and griseofulvin in the treatment of oral LP. Many studies are also available for treatment of cutaneous lichen planus with griseofulvin but only a few data are available on the efficacy of hydroxychloroquine in the treatment of cutaneous lichen planus. Till date no such study has been conducted in Bangladesh, hence this study designed to compare the efficacy of hydroxychloroquine and griseofulvin in the treatment of lichen planus.

Patients and methods

The study was conducted on 80 patients of age group 20-60 years having classical lichen planus, with or without oral involvement in the Department of Dermatology and Venereology at Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka and Combined Medical Hospital, Dhaka Cantt. Dhaka, and Shahid

Shorwardy Hospital Dhaka, Bangladesh from July 2007 to June 2009. All the cases were diagnosed clinically and confirmed by histopathological examination of skin. The patients were randomly allocated into 2 equal group A and group B. All the patients had given informed written consent. The patients were excluded from the study if they were pregnant, nursing mothers, age below 20 and above 60 years, sensitivity to hydroxychloroquine or griseofulvin, taking medications that could interfere with trial drugs and having serious systemic illness.

Group A was given hydroxychloroquine 400 mg daily and group B was given griseofulvin 500 mg daily for 6 months.

Outcome measures were assessed at baseline and at 2 weekly intervals during treatment and then the cases was followed up monthly for another 1 year. The patients of group A were instructed to check up eye problem periodically. Clinical response was noted on the basis of following. Complete response (CR): 100% clearing of lesion; moderate improvement (MI): 50-90% clearing of lesion; and no response (NR): less than 50% clearing of lesion.

Results

This study was conducted on 80 patients of classical lichen planus with or without oral involvement. In group A, there were 40 patients (26 male, 14 female, mean age 39.03±12.28 years) and in group B, 40 patients (27 male, 13 female, mean age 42.87±11.16 years ($p=0.146$, **Table 1**). The duration of the disease in the study ranged from 15 days to 12 months. The mean duration in group A was 4.37±3.87 months and in group B was 4.35±3.32 months ($p=0.975$). Oral involvement was found in 10

Table 1 Demographic data in two groups.

	Group A (n=40)	Group B (n=40)	P value
<i>Age (years)</i>			
<30	14 (35.0)	7 (17.5)	
30-40	8 (20.0)	9 (22.5)	
40-50	8 (20.0)	11 (27.5)	
>50	10 (25.0)	13 (32.5)	
Mean ± SD (years)	39.03 ± 12.28	42.87 ± 11.16	0.146
<i>Sex</i>			
Male	26 (65.0)	27 (67.5)	0.813
Female	14 (35.0)	13 (32.5)	
<i>Site of involvement</i>			
Skin	40 (100.0)	40 (100.0)	0.999
Oral	10 (25.0)	6 (15)	0.221
<i>Duration of disease (months)</i>			
≤5	28 (70.0)	30 (75.0)	
>5	12 (30.0)	10 (25.0)	
Mean ±SD	4.37 ±3.87	4.35 ±3.32	0.975

Table 2 Comparison of improvement in two groups.

	Group A	Group B	P value
<i>Cutaneous lesions</i> (n=40)			
Complete response	7 (17.5)	2 (5.0)	0.027
Moderate improvement	21 (52.5)	15 (37.5)	
No response	12 (30.0)	23 (57.5)	
<i>Oral lesions</i> (n=10)			
Complete response	7 (70.0)	2 (33.3)	0.120
Moderate improvement	3 (30.0)	2 (33.3)	
No response	-	2 (33.3)	

(25%) cases in group A and 6 (15%) cases in group B ($p=0.221$).

Regarding the efficacy, each group of patients was observed separately. In group A, clinical response was found in 28 (70%) cases: complete response in 7 (17.5%) and moderate improvement in 21 (52.5%) and in group B, clinical response was found in 17 (42.5%) cases: complete response in 2 (05%) and moderate improvement in 15 (37.5%) ($p=0.027$, **Table 2**). In case of oral lesion in group A, clinical response was found in all cases: complete response in 7 (70%) and moderate improvement in 3 (30%) and in group B, clinical response found in 4 (66.66%) cases: complete response in 2 (33.33%) and moderate improvement in 2 (33.33%) [$p=0.120$, **Table 2**].

Discussion

LP is an inflammatory disease affecting skin, mucous membrane, hair and nail. The treatment of this condition is often disappointing and controversial.^{3,17} Various drugs or physical treatment have been proposed in the past several decades but the majority of the reports consist of small series of patients or anecdotes. Controlled studies on large number of patients are rare. It has many different clinical forms that have different natural courses and may require different treatment.¹⁷ As a result, large and randomized studies are difficult to perform. Furthermore no standardized methods exist for the evaluation of the severity of the disease, there are no consensual criteria of improvement or cure and the course of the disease is variable from one patient to another and varies according to the clinical form. Our study was designed to

compare the efficacy of hydroxychloroquine and griseofulvin in the treatment of lichen planus.

The exact mechanism of action of hydroxychloroquine and griseofulvin in LP is unknown. Among the postulates for the mechanism of hydroxychloroquine are immunosuppression, anti-inflammatory and DNA binding, and the mechanism of action of griseofulvin includes immunomodulation, anti-inflammatory and also DNA binding.^{12,15,16,17}

Males 53 (66%) were predominant in our study than females 27 (34%) which is almost consistent with the study done by Nasreen *et al.*¹⁷ where they found 62% males and 38% females and differing from the study done by Abdallat and Maaita,¹⁸ where female predominance was reported. In the present series, oral involvement was found in 25% cases of group A and 15% cases in group B which is not comparable with that by Kalmar¹⁹ where he observed more than one third cases of oral involvement.

In the present study, age varied from 20 to 60 years with mean 39.03 ± 12.28 years in group A and 42.87 ± 11.16 years in group B, which is similar to that by Nasreen *et al.*¹⁷ In another study, Anbar *et al.*²⁰ found mean age of 41.36 years which slightly differs from our series. The mean duration of the disease in group A was 4.37 ± 3.87 months and in group B 4.35 ± 3.32 months which is not consistent with Anbar *et al.*²⁰

In our study in group A with hydroxychloroquine, clinical response was found in 70% cases: complete response in 17.5% and moderate improvement in 52.5% in cutaneous lesions. No such study was available in the treatment of cutaneous LP with hydroxychloroquine, so our study is not

comparable. In group B with griseofulvin in cutaneous LP, clinical response was seen in 42.5% cases: complete response in 5% and moderate improvement in 37.5%. Cribier and Chosidow²¹ first reported 12% improvement with 1gm/day griseofulvin administered for 1 to 10 months and in their second study 86% of the patients had complete disappearance of the lesions after 3 months. Sehgal *et al.*²² showed encouraging results using griseofulvin in cutaneous lichen planus.

In group A, we found clinical response in all cases with oral involvement. Eisen²³ observed that 9 of 10 patients (90%) of oral LP had an excellent response to hydroxychloroquine. So our study is almost consistent with that study.

In group B, clinical response was found in 66.66% cases with oral involvement. In a study by Bernerd Cribier *et al.*²² 3 cases out of 7 showed dramatic response with griseofulvin in oral LP. Aufpermorte *et al.*²⁵ supported the use of griseofulvin in oral LP and found improvement in 3 cases having severe erosive oral LP with 1gm griseofulvin for 8 weeks. Naylor²⁶ failed to show any benefit in 4 patients with erosive oral LP treated with griseofulvin. Bagen *et al.*²⁷ treated seven patients with 1 gm of griseofulvin daily for 2½ months, but no improvement was found, rather worsening in four patients. Massa and Roser²⁸ showed complete remission in 6 out of 11 patients having oral LP with griseofulvin. So our study is not comparable with earlier ones. During the study period we found no serious side effects.

Conclusion

Hydroxychloroquine and griseofulvin may prove to be an alternative treatment worth considering in patients with cutaneous and oral lichen planus. Hydroxychloroquine showed better

response than griseofulvin in both cutaneous and oral LP. So large scale, multicenter, randomized, clinical comparative trials may be done to prove their effectiveness.

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