Topical HCQS vs. Enteral HCQS in Oral Lichen Planus Comparitive Study

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Abstract

Oral lichen planus is a chronic muco cutaneous inflammatory disorder of varied etiology. It manifests in many clinical forms like reticular, erosive, bullous, atrophic and ulcerative. It usually occurs in middle aged women and malignant potential of these lesions are reported in the literature. These lesions are usually associated with severe burning sensation. There are many options available for the management of oral lichen planus. Studies have shown that hydroxychloroquine is a promising drug in the treatment of lichen planus. Objective: 1.To evaluate the efficacy of Hydroxychloroquine in the management of Oral lichen Planus. 2. To compare the efficacy of topical Hydroxychloroquine to that of systemic Hydroxychloroquine. Methods: 1.Randomly 30 consecutive symptomatic oral lichen Planus cases that were reported to the department of Oral Medicine and Radiology; PMVIDS & RC, were included in the study. All clinical variants of Oral Lichen Planus were considered for the study. 2. Subjects were screened for Oral & dermatologic lesions, routine blood tests, and an ophthalmic screening as a prerequisite. A detailed clinical examination was performed and the suspected cases of Lichen Planus based on clinical examination were subjected to incisional biopsy to confirm the diagnosis. Patients were divided into two groups, group A was treated with Topical Hydroxychloroquine gel till symptoms subsided and Group B with systemic Hydroxychloroquine tablets therapy till symptoms subsided. The obtained results were subjected to statistical analysis. Results: At the end of study Group A (Topical HCQs) showed decrease of clinical scores in 2 patients. In Group B (Systemic Group) showed decrease in the clinical scores in 8 patients. When the mean was compared (Group A) Topical Group showed a change of only 0.133, whereas Group B (Systemic Group) showed a mean change of 0.933. This showed that systemic group showed better remission of scores as compared to topical group that was statistically significant with a p value of <0.05. Conclusion: From this study it can thus be concluded that systemic Hydroxychloroquine can be used effectively to treat patients with Oral Lichen Planus when compared with Topical Hydroxychloroquine, though it is not recommended as a first line therapy, it can be used effectively as adjunctive drug.

Key Words: Mucocutaneous disorder, Potentially malignant disorders, T cell mediated disorder, Oral Lichen Planus, Topical and systemic hydroxychloroquine

Introduction

Lichen planus (LP) is a chronic inflammatory disorder that affects the skin, mucosae(oral, genital, oesophagic) and adnaexae(pilo sebaceous units,nail units) [1]. The first clinical description was given by Erasmus Wilson in 1869 and histological description was given by Dubdreuilh in 1906 [2]. Oral lesions occur in 50% to 70% of patients with LP and may be an exclusive manifestation in 20% to 30% of them [1]. Most of the cases are found incidentally during routine oral examination and are quite asymptomatic, patients presenting with symptoms include erythematous and erosive lesions that are difficult to manage and pose a challenge to oral physician. Prevalence of OLP range from 0.5%-2.2% [3] and may vary among races and geo figureic areas [4] with an estimated prevalence of 2.6% in Indian population [5]. It is predominantly seen in females [6]. The age of onset is usually between 3rd and 6th decade of life [7]. Though the etiology remains unknown except for T cell mediated chronic inflammation, a myriad of antigen specific and non-specific hypothesis have been postulated [4].

Antimalarial agents like chloroquine, hydroxychloroquine, and quinacrine, has proven efficacy in the treatment of lupus erythematosus [8-12]. These antimalarials have a wide and overlapping range of action. Apart from antimalarial actions, chloroquine has been shown to have anti- inflammatory mechanism of action as a lysosomal stabilizer that retards the release of hydrolytic enzymes, in addition chloroquine and quinacrine can both function as competitive prostaglandin antagonists. Other possible anti-inflammatory mechanism that have been proposed to account for the effects of antimalarials are chemotaxis inhibition, the antihistamine and antiserotonin effect [12]. In 1940's a hydroxylated form of the antimalarial drug chloroquine was first synthesized known as Hydroxychloroquine. It was found to be less toxic and effective when compared to chloroquine. It is now routinely used in the treatment of Systemic Lupus Eythematosus, Rheumatoid Arthritis, Q fevers [13,14] and has been used for Oral lichen Planus with excellent results. Studies have proven the efficacy of hydroxychloroquine when administered systemically caused complete remission, but very less literature is available about its efficacy on topical application. In view of the above facts, the present study was designed to evaluate the efficacy of hydroxychloroquine in topical and systemic routes of administration to treat the patients with Oral lichen Planus.

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Patients and Methods

A Total of thirty Patients were included in the study after clinical and histopathological confirmation of OLP. They were randomly categorized into two groups as Group A and Group B. Group A includes 15 patients (received 20% topical Hydroxychloroquine gel TID till symptoms subside) and Group B includes 15 patients (received Tablets Hydroxychloroquine 200-400 mg OD or BID till the symptoms subside). A specially designed proforma was used for recording demo figureic details, clinical findings and scores of clinical scale and burning sensation.

Sample inclusion criteria

- Patients those are willing to undergo treatment.
- Clinical and histopathological diagnosis of OLP irrespective of age and gender.

Sample exclusion criteria

- Patients those are not willing to undergo treatment.
- Patient with severe systemic illness. Patients with lesions in resemblance with lichen planus such as, contact allergy, lichenoid reaction which have a local or systemic etiology.
- Any prior treatment for oral lichen planus within a period of 1 month.
- Patients suffering from retinopathy and any other haematological diseases.
- Patients with cutaneous Lichen Planus.
- History of hypersensitivity to Hydroxychloroquine and chloroquine.

20% topical Hydroxychloroquine gel was prepared by College of Pharmacy.

Study design

Study sample comprised of 30 patients. They were randomly divided into two groups comprising of 15 patients each.

Group A: 15 patients – received 20% Topical Hydroxychloroquine gel.

Group B: 15 patients – received Enteral Hydroxychloroquine tablets (200-400 mg) Grading of the lesion was done clinically according to the scale given by Thongsprom.

All group A patients received 20% topical Hydroxychloroquine gel and all Group B patients received Systemic Hydroxychloroquine tablets (200-400 mg). The patients were instructed to apply the gel three times daily and were prohibited from using any emollient during application of study medication. If allergic manifestations were evident during the first application of the above medicament, patients were asked to discontinue the medication and report to the hospital immediately.

Patients were recalled for periodic review, at the interval of 2nd, 4th, 6th and 12th week respectively. Clinically the location of the lesions was recorded, with application of the clinical criteria scale developed by Thongprasom [15].

Statistical analysis

Data was collected and analysed using SPSS software version 16. The tables, Figures and charts were prepared. The Intra group and Inter group comparison was analysed using independent sample T tests and t-test for Equality of Means. And p value <0.05 was considered significant.

The present study was conducted to compare the efficacy of Topical HCQs and Systemic HCQs in the treatment of Oral Lichen Planus. The study population comprised of 30 clinically and histopathologically diagnosed cases of OLP. These patients were randomly distributed into two groups irrespective of age and gender. Group A- Comprised of 15 symptomatic OLP patients who received topical HCQ gel.Group B- Comprised of 15 symptomatic OLP patients who received systemic HCQ tablets (200-400 mg).

Age distribution

Overall age distribution showed a mean age of 46 with a range from 25-65 years (*Table 1*). The patients were randomly distributed into two groups where the mean age in Group A was 12 years with a range from 28-61 years (*Table 2*). The mean age in Group B was 48 years with a range from 25-65 years (*Table 3*).

Table 1. *Overall age distribution.*

	N	Minimum	Maximum	Mean	Std. Deviation
AGE	30	25.00	65.00	46.0000	11.38965

Table 2. *Age distribution among group A (topical group).*

	N	Minimum	Maximum	Mean	Std. Deviation
AGE	15	28	61	43.8667	10.53475

Table 3. *Age distribution among group B (systemic group).*

	N	Minimum	Maximum	Mean	Std. Deviation
AGE	15	25.00	65.00	48.1333	12.16474

Table 4. *Overall gender distribution.*

SEX	Frequency	Percent
MALE	8	26.7
FEMALE	16	73.3
Total	30	100.0

Gender distribution

Overall gender distribution (*Table 4 and Figure 1*) showed 16 females (73.3%) and 8 males (26.7%). In Group A, 60% were females and 40% were males (*Figure 2*). In Group B, 86.7% were females and the remaining 13.3% were males (*Figure 3*).

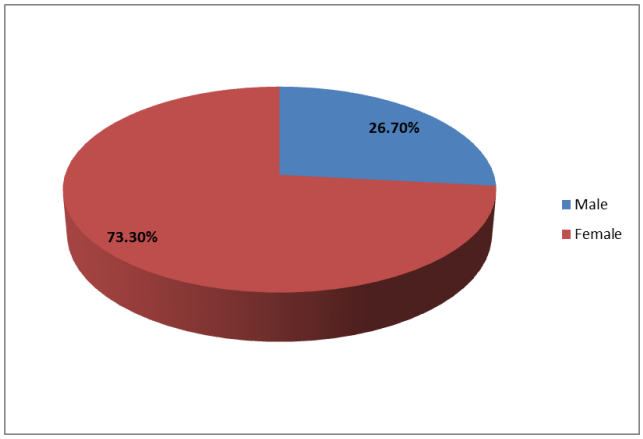

Figure 1. *Overall gender distribution.*

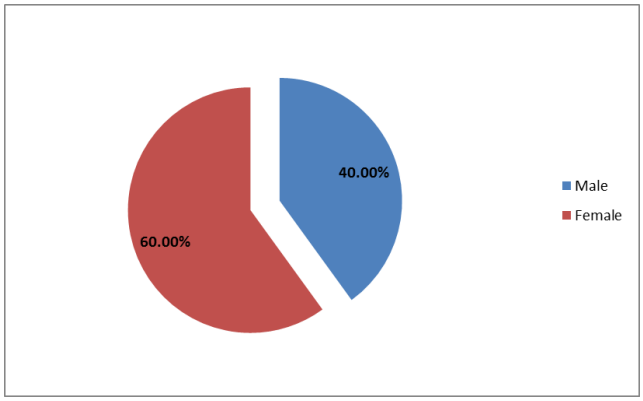

Figure 2. *Gender distribution among group A (topical group).*

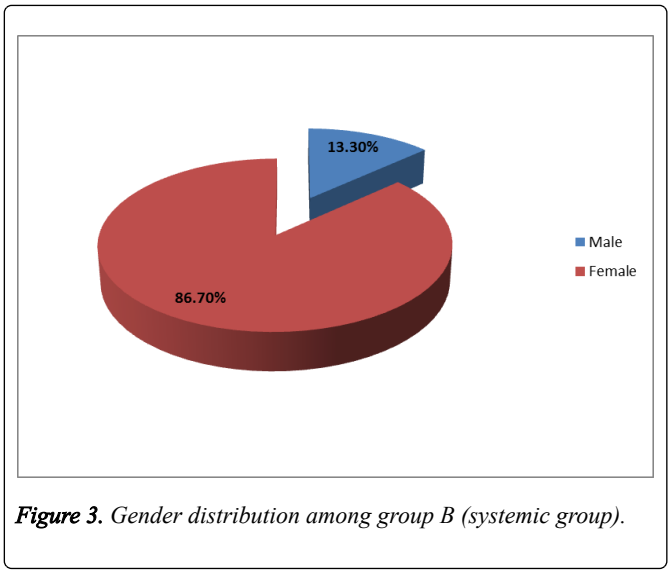

Figure 3. *Gender distribution among group B (systemic group).*

Comparison of initial lesion distribution among groups

As observed from the table, majority of the patients in the topical group had scores 3 or less, while those in the systemic group had scores 4 and 5 with only a single patient scoring 2. There was a difference observed between the trend of scores obtained in the topical and systemic groups. Topical group showed association with lower scores while the systemic group showed association with higher scores (*Table 5*).

Table 5. *Comparison of initial lesion distribution among groups.*

			INITIAL LESION					Total	Chi-Square
			Mild white striae	White striae with atrophic area less than 1cm2	White striae with atrophic area more than 1cm2	White striae with erosive area less than 1cm2	White striae with erosive area more than 1cm2 or ulcerative lesion		
Group	Group A	Count	2	8	5	0	0	15	X2 = 26.124, p < 0.001
	Topical	% within GROUP	13.30%	53.30%	33.30%	0.00%	0.00%	100.00%	
	Group B	Count	0	1	0	8	6	15	
	Systemic	% within GROUP	0.00%	6.70%	0.00%	53.30%	40.00%	100.00%	
Total		Count	2	9	5	8	6	30	
		% within GROUP	6.70%	30.00%	16.70%	26.70%	20.00%	100.00%	

Comparison of lesion distribution among groups at the end of 2 weeks

At the end of 2 weeks, scores observed were similar to the initial values, i.e., majority of the patients in the topical group had scores 3 or less, while those in the systemic group had scores 4 and 5 with only a single patient scoring 2. There was a difference observed between the trend of scores obtained in the topical and systemic groups. Topical group showed

association with lower scores while the systemic group showed association with higher scores (*Table 6*).

Table 6. *Comparison of lesion distribution among groups at the end of 2 weeks.*

			SIZE OF LESION 2ND WEEK					Total	Chi Square
			Mild white striae	White striae with atrophic area less than 1cm^2	White striae with atrophic area more than 1cm^2	White striae with erosive area less than 1cm^2	White striae with erosive area more than 1cm^2 or ulcerative lesion		
Group	Group A	Count	2	8	5	0	0	15	X2 = 26.124
	Topical	% within Group	13.30%	53.30%	33.30%	0.00%	0.00%	100.00%	p < 0.001
	Group B	Count	0	1	0	8	6	15	
	Systemic	% within Group	0.00%	6.70%	0.00%	53.30%	40.00%	100.00%	
Total		Count	2	9	5	8	6	30	
		% within Group	6.70%	30.00%	16.70%	26.70%	20.00%	100.00%	
At the end of 2 weeks, scores observed were similar to the initial values, i.e., majority of the patients in the topical group had scores 3 or less, while those in the systemic group had scores 4 and 5 with only a single patient scoring 2.									

Comparison of lesion distribution among groups at the end of 4 weeks

At the end of 4 weeks, scores observed showed a change in the trend of distribution as compared to the initial values, i.e., majority of the patients in the topical group had scores 4 or less, while those in the systemic group had scores 3, 4 and 5 with only a single patient scoring 2. There was a difference observed between the trend of scores obtained in the topical and systemic groups. Topical group showed association with lower scores while the systemic group showed association with higher scores (*Table 7 and Figure 4*).

Table 7. *Comparison of lesion distribution among groups at the end of 4 weeks.*

			SIZE OF LESION 4TH WEEK					Total	Chi-Square
			Mild white striae	White striae with atrophic area less than 1cm^2	White striae with atrophic area more than 1cm^2	White striae with erosive area less than 1cm^2	White striae with erosive area more than 1cm^2 or ulcerative lesion		
Group	Group A	Count	2	8	3	2	0	15	X2 = 13.111 p = 0.011
	Topical	% within GROUP	13.30%	53.30%	20.00%	13.30%	0.00%	100.00%	
	Group B	Count	0	1	6	4	4	15	
	Systemic	% within GROUP	0.00%	6.70%	40.00%	26.70%	26.70%	100.00%	
Total		Count	2	9	9	6	4	30	
		% within GROUP	6.70%	30.00%	30.00%	20.00%	13.30%	100.00%	
At the end of 4 weeks, scores observed showed a change in the trend of distribution as compared to the initial values, i.e., majority of the patients in the topical group had scores 4 or less, while those in the systemic group had scores 3, 4 and 5 with only a single patient scoring 2.									

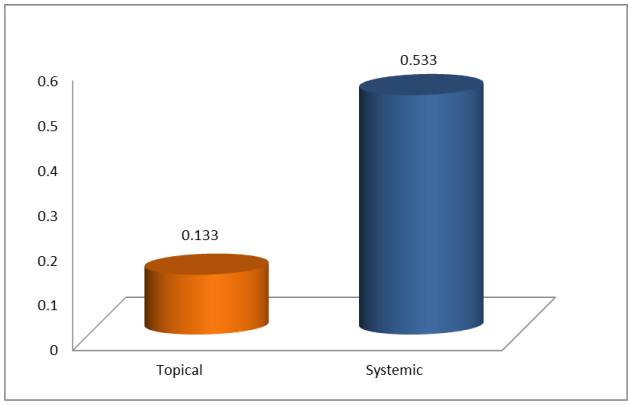

Figure 4. *Change in mean scores after 4 weeks.*

Comparison of lesion distribution among groups at the end of 6 weeks

At the end of 6 weeks, scores observed showed a change in the trend of distribution as compared to the initial values, i.e., there was an observed remission in the scores obtained in the topical group where majority of the patients had score 2 with some individuals recording 3, while in the systemic group too, remission was observed in the scores with 2 individuals recording 2, while the number of individuals scoring 4 and 5 had also declined. And this association was found to be statistically significant with a p value of <0.05 obtained in the chi square tests (*Table 8 and Figure 5*).

Table 8. *Comparison of lesion distribution among groups at the end of 6 weeks.*

			Size of lesion 6th week					Total	Chi Square
			Mild white striae	White striae with atrophic area less than 1cm^2	White striae with atrophic area more than 1cm^2	White striae with erosive area less than 1cm^2	White striae with erosive area more than 1cm^2 or ulcerative lesion		
Group	Group A	Count	2	10	3	0	0	15	X2 = 12.769 p = 0.012
	Topical	% within GROUP	13.30%	66.70%	20.00%	0.00%	0.00%	100.00%	
	Group B	Count	0	3	6	4	2	15	
	Systemic	% within GROUP	0.00%	20.00%	40.00%	26.70%	13.30%	100.00%	
Total		Count	2	13	9	4	2	30	
		% within GROUP	6.70%	43.30%	30.00%	13.30%	6.70%	100.00%	
Statistical significance with a p value of <0.05 was observed									

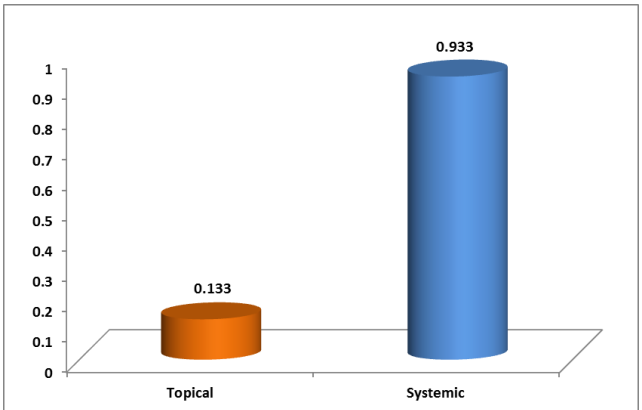

Figure 5. *Change in mean scores after 6 weeks.*

Comparison of lesion distribution among groups at the end of 12 weeks

At the end of 12 weeks too, observations reflected those at 6 weeks. Scores observed showed a change in the trend of distribution as compared to the initial values, i.e., there was an observed remission in the scores obtained in the topical group where majority of the patients had score 2 with some individuals recording 3, while in the systemic group too, remission was observed in the scores with 2 individuals recording 2, while the number of individuals scoring 4 and 5 had also declined. And this association was found to be statistically significant with a p value of <0.05 obtained in the chi square tests (*Table 9 and Figure 6*).

Table 9. *Comparison of lesion distribution among groups at the end of 12 weeks.*

			Size of lesion 12th week					Total	Chi-Square
			Mild white striae	White striae with atrophic area less than 1cm^2	White striae with atrophic area more than 1cm^2	White striae with erosive area less than 1cm^2	White striae with erosive area more than 1cm^2 or ulcerative lesion		
Group	Group A Topical	Count	2	10	3	0	0	15	X2 = 12.769 p = 0.012
		% within GROUP	13.30%	66.70%	20.00%	0.00%	0.00%	100.00%	
	Group B Systemic	Count	0	3	6	4	2	15	
		% within GROUP	0.00%	20.00%	40.00%	26.70%	13.30%	100.00%	
Total		Count	2	13	9	4	2	30	
		% within GROUP	6.70%	43.30%	30.00%	13.30%	6.70%	100.00%	
At the end of 12 weeks too, observations reflected those at 6 weeks.									

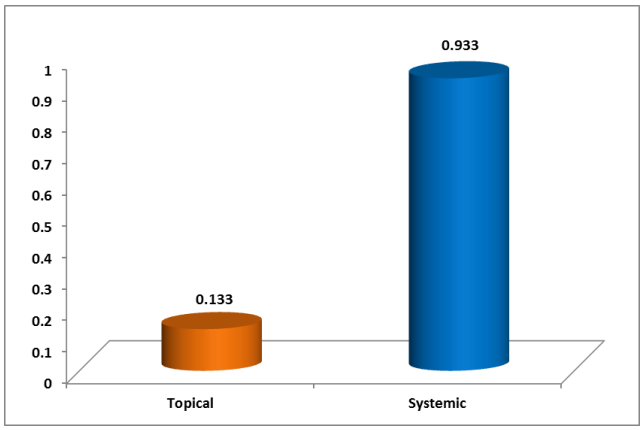

Figure 6. *Change in mean scores after 12 weeks.*

Comparison of change in mean score of lesion size between groups after 2 weeks

Since there was no difference observed in either group after 2 weeks, Independent sample T test could not be computed to assess the difference in the Mean of Difference observed (*Table 10*).

Table 10. *Comparison of change in mean score of lesion size between groups after 2 weeks.*

	GROUP	N	Mean of Difference observed	Std. Deviation	T
CHANGE IN 2 WEEKS	Group A Topical	15	0	.00000a	T = not calculated
	Group B Systemic	15	0	.00000a	P = Not applicable
a. t cannot be computed because the standard deviations of both groups are 0.					
Since there was no difference observed in either group after 2 weeks, Independent sample T test could not be computed to assess the difference in the Mean of Difference observed.					

Comparison of change in mean score of lesion size between groups after 4 weeks:

An Independent Sample T test was computed to assess the difference observed in the Mean of Difference obtained in both the groups. Systemic Group showed a mean change of 0.533 score after 4 weeks while Topical Group showed a change of only 0.133. This showed that systemic group showed better remission of scores as compared to topical group and this difference was observed statistically too, with a p value of <0.05 (*Table 11*).

Comparison of change in mean score of lesion size between groups after 6 weeks

An Independent Sample T test was computed to assess the difference observed in the Mean of Difference obtained in both the groups. Systemic Group showed a mean change of 0.933 score after 6 weeks while Topical Group showed a change of only 0.133. This showed that systemic group showed better remission of scores as compared to topical group and this difference was observed statistically too (p <0.05 (*Table 12*).

Table 11. Comparison of change in mean score of lesion size between groups after 4 weeks.

	GROUP	N	Mean of Difference observed	Std. Deviation	T
CHANGE IN 4 WEEKS	Group A	15	0.1333	0.35187	T = 3.140
	Topical				
	Group B	15	0.5333	0.74322	P = 0.005
	Systemic				
Statistical significance with a p value of <0.05 was observed.					

Comparison of change in mean score of lesion size between groups after 12 weeks:

An Independent Sample T test was computed to assess the difference observed in the Mean Of Difference obtained in both the groups. Results carried similar observations to those obtained after 6 weeks. Systemic Group showed a mean change of 0.933 score after 12 weeks while Topical Group showed a change of only 0.133. This showed that systemic group showed better remission of scores as compared to topical group and this difference was observed statistically too, with a p value of <0.05 (*Table 13*).

Table 12. Comparison of change in mean score of lesion size between groups after 6 weeks.

	GROUP	N	Mean	Std. Deviation	T
CHANGE IN 6 WEEKS	Group A	15	0.1333	0.35187	T = 3.550
	Topical				
	Group B	15	0.9333	0.79881	P = 0.002
	Systemic				
Statistical significance with a p value of <0.05 was observed.					

Table 13. Comparison of change in mean score of lesion size between groups after 12 weeks.

	GROUP	N	Mean	Std. Deviation	T
CHANGE IN 12 WEEKS	Topical	15	0.1333	0.35187	T = 3.550
	Systemic	15	0.9333	0.79881	P = 0.002

Results carried similar observations to those obtained after 6 weeks.

Discussion

This study demonstrates that systemic HCQ therapy would significantly improve Oral Lichen Planus when compared to topical HCQ therapy. The study group comprised of 30 OLP patients who were randomly distributed into two groups of 15 each in a group where Group A received 20% Topical HCQ and Group B received Systemic HCQ (200-400 mg), which was in accordance to the study done by Bendas ER [12] where 11 randomly selected OLP patients were advised to apply topical niosomal HCQ gel and 5 patients were given placebo. Furthermore, it was not in accordance to the study conducted by Eisen D [12] where only 10 erosive forms of OLP patients were given systemic HCQs for a period of 6 months.

In the present study the age range was from 25-65 years with a mean age of 46 which was in close accordance to the study done by Ingafou M et al. [6]. As Oral lichen planus is generally a disease of middle age and elderly, several authors have reported different age ranges as follows: 16-80 years with a mean age of 52 years by Silverman et al. [14], 18-73 years with a mean age of 40 years by Ingafou M et al. [6]. Eisen D [8] in his study of OLP treated with Systemic Hydroxychloroquine tablets reported age range of 40 to 66 years with a mean age of 59 years which is slightly above the mean age of the present study. Bendas ER [12] in their study regarding treatment of OLP with topical Hydroxychloroquine niosomal gel reported an average age of 45 years in topical group and 48 years in placebo group which is in close accordance to the present study.

Oral lichen planus can affect either sex, though females are affected more frequently than males. Silverman et al. [14], Boyd AS, et al. [16] reported a female predilection in their study [17]. However Mccarthy PL, et al. [18], Ingafou M et al. [6], Regezi JA, et al. [19] reported an equal sex predilection. On the other hand, Sehgal VN [20] reported a higher male to female ratio. In the present study it was seen that females were more affected than males which is in accordance with Silverman et al. [14], Boyd AS et al. [16]. The gender predilection in the present study was in accordance with the study done by Bendas ER et al. [12] where Topical HCQ gel was used in the treatment of Oral Lichen Planus, where he reported 4 males and 12 females. Eisen D [8] reported 9 women and 1 man in his study of systemic HCQ tablets for Oral Lichen Planus. In the present study even the inter group showed female predilection with Group A (topical) having 60% females and Group B (systemic) having 86.7% females.

In the present study out of 30 patients, 18 patients had reticular form, 10 patients had erosive form, 1 patient had atrophic form and 1 patient had bullous form. These patients were randomly distributed into two groups as in Group A (Topical) 13 patients had reticular form, 2 patients had erosive form and Group B (Systemic) 8 patients had erosive form, 5 patients had reticular form, 1 patient each had bullous and atrophic form. This was not in accordance with Eisen D et al. [12] where only erosive forms of OLP were included in his study.

On intra group comparison of Group A, at the end of 2 weeks there was no much change noticed in the size of clinical lesion when compared to the initial size of the clinical lesion. At the end of 4 weeks, Group A showed initial rise in size of clinical lesion in 1 patient. And other patients showed no change in size of the clinical lesion when compared to the initial size of clinical lesion.

At the end of 6th week and 12th week Group A showed an observed moderate remission in the size of clinical lesion in 2 patients when compared to the size of the initial lesion.But the results of the study that of Group A were not in accordance with Bendas ER [12] who concluded in his study that topical HCQ niosomal gel reduced the clinical scores in 11 patients by 64.28% when compared to placebo that decreased clinical scores by 3.94% after a treatment period of 2 months. Data regarding the evaluation of the two major parameters (size of lesions and pain) were taken into consideration in their study and there was significant difference between the results of the group treated with HQ niosomal gel (after treatment) and the Placebo group (after treatment). The results of the present study can be attributed to the poor drug penetrability, less contact time with the lesion and potential errors during the drug preparation.

On Intra Group comparison of Group B (Systemic HCQs), at the end of 2 weeks there was no much change in the size of clinical lesion when compared to the initial size of the lesion. There was no change in the size of lesion or oral discomfort, that can be attributed to the pharmacokinetics of the drug and the achievement of therapeutic dose as it takes to 4-6 weeks to attain therapeutic dose.

At the end of 4th week, out of 15 patients 6 patients showed decrease in the size of the clinical lesion, when compared to the initial size of clinical lesion in the same group. The group had scores 3, 4 and 5 with only a single patient scoring 2. In addition to it there was a decrease in oral discomfort at the end of 4th week that was similar to the findings noted by Eisen D [8] where there was decrease of oral discomfort after 1 to 2 months of therapy.

At the end of 6th week and 12th week Group B (Systemic Group) showed decrease in the size of clinical lesion in 8 patients when compared to the initial size of clinical lesion that was observed. Scores observed showed a change in the trend of distribution as compared to the initial values, a remission in the size of clinical lesion was observed with 2 individuals recording 2, while the number of individuals scoring 4 and 5 had also declined. In addition to it there was a decrease in erythema in present study similar to the findings noted by Eisen D [8] where out of the six patients with erosions at the start of the study, three had complete healing that required 3 to 6 months of therapy. In the remaining three patients the erosions were persistent after 6 months of therapy; lesions were reduced in size by 50% or more compared with their pretreatment state. In the present study there was no complete resolution of the clinical lesion, but 8 out of 15 patients had marked remission of the clinical lesion. In the present study, as there was no complete remission of the lesion at the end of 12th week, patients were reluctant to the follow up visits that led to the discontinuation of the study at the end of 3 months. In the present study out of 8 erosive forms of OLP, 7 patients showed remission of clinical lesion similar to the findings noted by Eisen D [12], where 9 out of 10 erosive forms showed remission of the lesions after 6 months HCQ therapy where in using global evaluation scale, almost complete or complete improvement was noted in five patients, three patients showed marked improvement, and one patient improved moderately.

The present study was further in accordance with study done by Ishrat B et al. [21] where patients were randomly divided into 2 equal groups. Group A was given hydroxychloroquine 400 mg daily and group B was given griseofulvin 500 mg daily for a period of 6 months. In group A complete response was seen in 7 (17.5%) and moderate improvement was seen in 21 (52.5%) and in group B complete response was seen in 2 (5%) and moderate improvement was seen in 15 (37.5%).

On intergroup comparison of the present study, at the end of 2nd week there was no change in mean score of size of the clinical lesion. At the end of 4th week an Independent Sample T test was computed to assess the difference observed in the Mean of Difference obtained in both the groups. Systemic Group showed a mean change of 0.533 score after 4 weeks while Topical Group showed a change of only 0.133. this showed that systemic group showed better remission in the size of clinical lesions as compared to topical group and this difference was observed statistically too, with a p value of <0.05. At the end of 6th and 12th week, an Independent Sample T test was computed to assess the difference observed in the Mean of Difference obtained in both the groups. Systemic Group showed a mean change of 0.933 score after 6th and 12th week while Topical Group showed a change of only 0.133. This showed that systemic group showed better remission in size of clinical lesion as compared to topical group and this difference was observed statistically too, with a p value of <0.05. It was also observed that erosive forms of OLP healed better when compared to other forms of OLP with HCQ therapy which was in accordance with Bendas ER [12] and Eisen D [8]. And there was significant difference between the clinical scores of OLP before treatment and at the end of treatment in Group B (Systemic) but no complete remission of the lesions was observed that can be attributed to pharmacokinetics of drug and patient compliance. Whereas there was no significant decrease between the clinical scores of OLP before and at the end of treatment in the Group A (topical group) as this can be attributed to delayed pharmacokinetics, poor penetrability of drug and poor patient compliance.

Conclusion

From the present study it can be concluded that systemic HCQ therapy is better than topical HCQ therapy, the efficacy of the drug is moderate and relatively delayed, that can be attributed to the pharmacokinetics of the drug. Furthermore, it is primarily effective in erosive forms of Oral Lichen Planus rather than other forms. Although it is not advised for first line of therapy it can be used as an adjunctive therapy in the management of OLP.

References

1. Nico MM, Fernandes JD, Lourenço SV. Lichen Planus Affecting the Lips. *Journal of Clinical and Experimental Dermatology Research.* 2015; **6**: 306.

2. Raghavendra K, Nagaratna DV, Ankit S. Therapeutic Management of Oral Lichen Planus: A Review for the Clinicians. *World Journal of Dentistry.* 2011; **2**: 249-253.

3. Glick M (2015) Burkets Oral Medicine (12thedn). PMPH, USA.

4. Roopashree MR, Gondhalekar RV, Shashikanth MC, George J, Thippeswamy SH, et al. Pathogenesis of oral lichen planus – a review. *Journal of Oral Pathology and Medicine.* 2010; **39**: 729-734.

5. Anita DM, Ravindra RK, Pranali KW, Safia SS, Meena K. Demographic and clinical profile of oral lichen planus: A retrospective study. *Contemporary Clinical Dentistry.* 2013; **4**: 181-185.

6. Ingafou M, Leao JC, Porter SR, Scully C. Oral lichen planus: A retrospective study of 690 British patients. *Oral Disorders.* 2006; **12**: 463-468.

7. Laeijendecker R, Van Joost T, Tank B, Oranje AP, Neumann HA. Oral lichen planus in childhood. *Pediatric Dermatology.* 2005; **22**: 299-304.

8. Eisen D. Hydroxychloroquine sulfate (Plaquenil) improves oral lichen planus: An open trial. *Journal of the American Academy of Dermatology.* 1993; **28**: 609-612.

9. Benzvi I, Kivity S, Langevitz P, Shoenfeld Y. From malaria to autoimmunity. *Clinical Reviews in Allergy and Immunology.* 2012; **42**: 145-153.

10. Petri M. Use of hydroxychloroquine to prevent thrombosis in systemic lupus erythematosus and in antiphospholipid antibody positive patients. *Current Rheumatology.* 2011; **13**: 77-80.

11. Shereen Abdel MA, Enas Ahmed E, Rasha AEA. A Comparative Study between Intralesional Low Molecular Weight Chitosan and Triamcinolone Acetonide for Treatment of Erosive-Atrophic Oral Lichen Planus. *Journal of American Science.* 2011; **7**: 338-345.

12. Ehab RB, Abdullah H, Mohamed HM El-Komy, Kassem MAA. Hydroxychloroquine niosomes: A new trend in topical management of oral lichen planus. *International Journal of Pharmaceutics.* 2013; **458**: 287-295.

13. Ingafou M, Lodi G, Oslen, Porter SR. Oral lichen planus is not associated with IgG circulating antibodies to epithelial antigen. *Oral Surgery, Oral Medicine, Oral Pathology.* 1997; **84**: 175-178.

14. Silverman S, Gorsky M, Lozada-Nur F. A prospective follow-up study of 570 patients with oral lichen planus: Persistence, remission, and malignant association. *Oral Surgery, Oral Medicine, Oral Pathology.* 1985; **60**: 30-34.

15. Al-Hashimi I, Schifter M, Lockhart PB, Wray D, Brennan M, et al. Oral lichen planus and oral lichenoid lesions: diagnostic and therapeutic considerations. *Oral surgery, oral medicine, oral pathology, oral radiology, and endodontics.* 2007; **103**: S25.e1-12.

16. Boyd AS, Neldner KH. Continuing medical education Lichen planus. *Journal of the American Academy of Dermatology.* 1991; **25**: 593-619.

17. Huber MA. Oral lichen planus. *Quintessence International.* 2004; **35**: 731-752.

18. McCarthy PL, Shklar G (1980) Diseases of the Oral Mucosa (2ndedn), Febiger, Philadelphia, USA.

19. Regezi JA, Scuibba JJ (1999) Oral pathology: clinical - pathological correlations (1stedn) WB Saunders, Philadelphia, USA.

20. Sehgal VN. Natural history or oral lichen planus. *Indian Journal of Dermatology, Venereology and Leprology.* 1974; **40**: 204-207.

21. Ishrat Bhuiyan, Wahab MA, Ahammed Ali, Abida Sultana, Rahmat Ullah Siddique, et al. Comparative efficacy of hydroxychloroquine and griseofulvin in the treatment of lichen planus. *Journal of Pakistan Association of Dermatologists.* 2016; **20**: 79 -83.