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Comparative Study On The Efficacy Of Topical 20% Azelaic Acid And 4% Hydroquinone In Epidermal Melasma

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ABSTRACT
Background:Melasma is a common acquired condition of symmetric hyperppigmentation, typically occurring on the face. Objective: To compare the efficacy of topical 20% Azelaic acid and 4% Hydroquinone in the treatment of epidermal melasma.To observe for side effects in both study groups. Methods: in this study, data was collected from 100 patients with 50 patients each in Group A (treated with 20% Azelaic acid) and Group B (treated with 4% Hydroquinone).Results: The mean MASI values were calculated for both groups using independent samples t test. This was done to compare the efficacy of 20% Azelaic acid and 4% Hydroquinone. There was decrease in mean MASI values each month with treatment in both groups. The mean baseline MASI score (i.e, before treatment) was 14.886±5.5483 for Group A (20% Azelaic acid) and 15.486±7.6463 for Group B (4% Hydroquinone). At the end of 1st month, the mean MASI score reached 12.240±5.0364 for Group A and 13.224±6.6994 for Group B. At the end of 2nd month, the mean MASI score became 8.364±3.9678 for Group A and 9.210±5.0905 for Group B. At the end of 3rd month, the mean MASI value was observed to be 5.700±2.9338 for Group A and 6.096±3.4025 for Group B. When the mean MASI values of Group A and Group B were compared and there was no significant difference in the treatment efficacy between the two groups. But the mean values of Group B (4% Hydroquinone), calculated at the end of each month, were found to be little higher compared to Group A (20% Azelaic acid).Conclusion: It can be concluded that in this study, even though not statistically significant, Group B (4% Hydroquinone) had better therapeutic response than Group A (20% Azelaic acid) in the treatment of Melasma

INTRODUCTION

Melasma is a common, acquired and chronic disorder of hypermelanosis with symmetrical distribution, affecting the sun-exposed areas mainly the face, where it involves the forehead, cheeks, upper lip and chin.1 It manifests as light to dark brown patches of hyperpigmentation.2,3Melasma also has cosmetological significance with crucial impact on physical appearance of an individual,especially females, leading to emotional disturbances and psychosocial stress which in turn affects their quality of life.4

Management of melasma is very challenging, mainly because it needs long term treatment and proper follow up. Identification and avoidance of aggravating factors is very important to prevent recurrence.1 Systemic diseases should also be treated if present. Patient compliance is an important factor in treatment because drop outs can occur due to the long term treatment plan. This can be controlled to an extent by proper counseling of the patients. The possibility of recurrence of the lesion should also be made aware to the patient, and the importance of sun protection along with the use of proper sunscreen should be made clear, because this will prevent relapse to an extent. Treatment options include broad-spectrum sunscreens, topical depigmenting

agents, chemical peels, lasers, dermabrasion, microdermabrasion and camouflage.5Topical depigmenting agents remain the mainstay of treatment.

Here in this study, efficacy of topical 20% azelaic acid and 4% hydroquinone are compared for the treatment of epidermal melasma.

AIMS AND OBJECTIVES

To compare the efficacy of topical 20% Azelaic acid and 4% Hydroquinone in the treatment of epidermal melisma and to observe for side effects in both study groups.

MATERIALS AND METHODS

This study was conducted among patients with epidermal melasma, who came to the out-patient department of Dermatology Venereology and Leprology of Meenakshi Medical College Hospital and Research Institute, Enathur, Kanchipuram.Data was collected from 100 patients with 50 patients each in Group A (treated with 20% Azelaic acid) and Group B (treated with 4% Hydroquinone).

STUDY DESIGN:

Prospective study

METHODOLOGY

Patients who came to the Dermatology out-patient department with epidermal melasma were taken up for the study. Epidermal melasma was diagnosed clinically and by using Wood's Lamp examination. After getting written informed consent, detailed history was taken and patients were thoroughly evaluated.

Patients were randomly divided into two groups - Group A and Group B. Group A patients received topical 20% Azelaic acid cream and Group B patients received topical 4% Hydroquinone cream. Patients were evaluated at the end of every month for a total period of 3 months for each patient. They were assessed monthly based on MASI (Melasma Area and Severity Index) score and clinical photographs

RESULTS

The study population was 100 patients with epidermal melasma attending the dermatology out-patient department of Meenakshi Medical College Hospital and Research Institute, Enathur, Kanchipuram. They were divided into 2 groups of 50 patients each. Group A was treated with 20% Azelaic acid and Group B with 4% Hydroquinone. The treatment given was not discontinued by any of the patients.

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COMPARISON OF MASI SCORES AND TREATMENT RESPONSES BETWEEN THE TWO GROUPS

The mean difference value of Group A before treatment and 1st month of treatment was slightly more than that of Group B (Group A=2.646, Group B=2.262), indicating that better treatment response was seen with 20% Azelaic acid at the end of 1st month of treatment (though not statistically significant). The mean difference of Group A between 1st and 2nd months of treatment was less compared to that of Group B (Group A=3.876, Group B=4.014), stating that therapeutic efficacy was better with 4% Hydroquinone at the end of 2nd month of treatment (not statistically significant). The mean difference of Group A between 2nd and 3rd months of treatment was also less than that of Group B (Group A=2.664, Group B=3.114), indicating that treatment response was better with 4% Hydroquinone at the end of 3rd month (not statistically significant) (Table 12, Table 13).

The mean MASI values were calculated for both groups using independent samples t test. This was done to compare the efficacy of 20% Azelaic acid and 4% Hydroquinone. There was decrease in mean MASI values each month with treatment in both groups. The mean baseline MASI score (i.e, before treatment) was 14.886±5.5483 for Group A (20% Azelaic acid) and 15.486±7.6463 for Group B (4% Hydroquinone). At the end of 1st month, the mean MASI score reached 12.240±5.0364 for Group A and 13.224±6.6994 for Group B. At the end of 2nd month, the mean MASI score became 8.364±3.9678 for Group A and 9.210±5.0905 for Group B. At the end of 3rd month, the mean MASI value was observed to be 5.700±2.9338 for Group A and 6.096±3.4025 for Group B. When the mean MASI values of Group A and Group B were compared and there was no significant difference in the treatment efficacy between the two groups. But the mean values of Group B (4% Hydroquinone), calculated at the end of each month, were found to be little higher compared to Group A (20% Azelaic acid). Thus it can be concluded that in this study, even though not statistically significant, Group B (4% Hydroquinone) had better therapeutic response than Group A (20% Azelaic acid) in the treatment of melasma (Table 14)

TABLE 14: COMPARISON OF MASI SCORES BETWEEN BOTH STUDY GROUPS

MASI Score	Treatment Given	N	Mean	Std. Deviation	Std. Error Mean	Independent t test value	p value	
Before Treatment	Azelaic acid 20%	50	14.886	5.5483	.7846	6.766	.654	NS
	Hydroquinone 4%	50	15.486	7.6463	1.0814		.654	
Ist Month of	Azelaic acid 20%	50	12.240	5.0364	.7123	4.801	.408	NS

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Treatment	Hydroquinone 4%	50	13.224	6.6994	.9474		.409	
2nd Month of Treatment	Azelaic acid 20%	50	8.364	3.9678	.5611	4.075	.356	NS
	Hydroquinone 4%	50	9.210	5.0905	.7199		.356	
3rd Month of Treatment	Azelaic acid 20%	50	5.700	2.9338	.4149	1.003	.535	NS
	Hydroquinone 4%	50	6.096	3.4025	.4812		.535	

NS - Not Significant

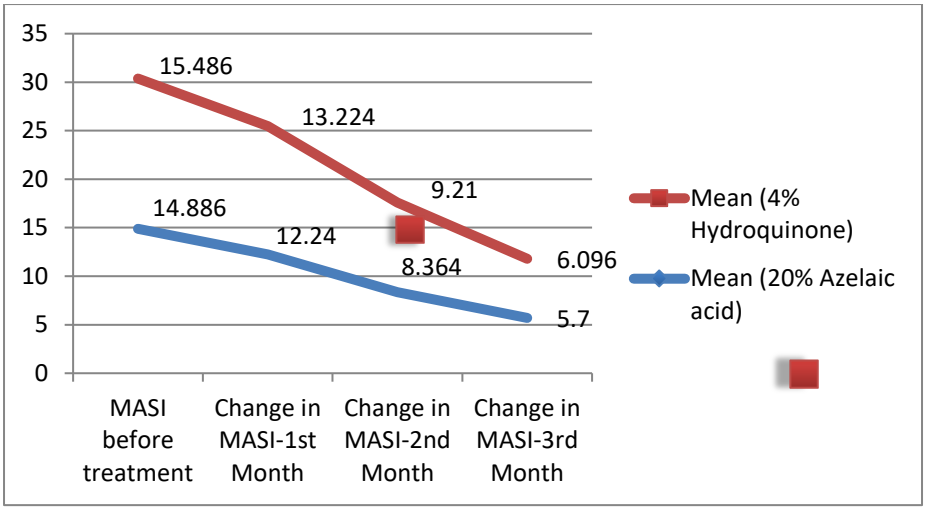

FIGURE 21: COMPARISON OF MEAN MASI SCORES BETWEEN GROUP A AND GROUP B

SIDE EFFECT PROFILE

In the present study, the side effects were minimal. Burning was seen in 2 patients treated with 4% Hydroquinone during 1st month of treatment. Erythema was also observed in another 2 patients treated with 4% Hydroquinone during 1st month of treatment. Itching was found in 1 patient treated with 20% Azelaic acid during 1st month of treatment. Dryness was also observed in another 1 patient treated with 20% Azelaic acid during 1st month of treatment (Table 15).

These adverse effects were not severe. Burning, erythema and dryness were managed with emollients. Antihistamine was prescribed to relieve itching. These adverse effects were not observed during 2nd and 3rdmonths of the study period.

TABLE 15: SIDE EFFECT PROFILE IN BOTH STUDY GROUPS

Side Effects	Treatment Given	Total	Onset of Side

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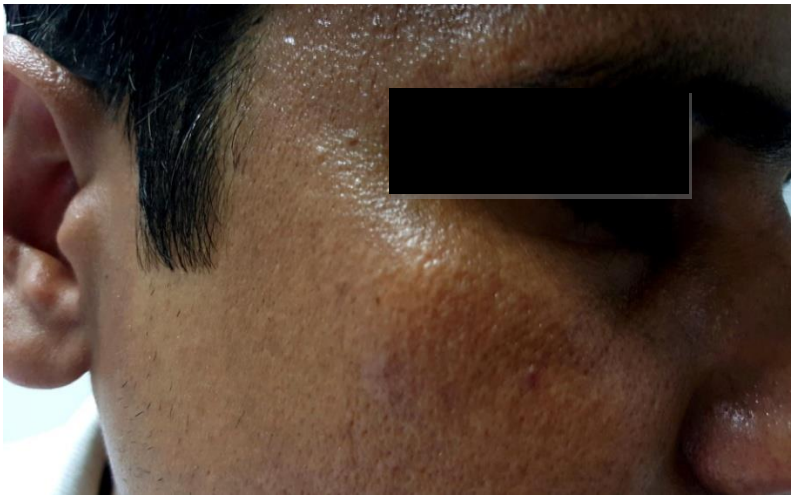
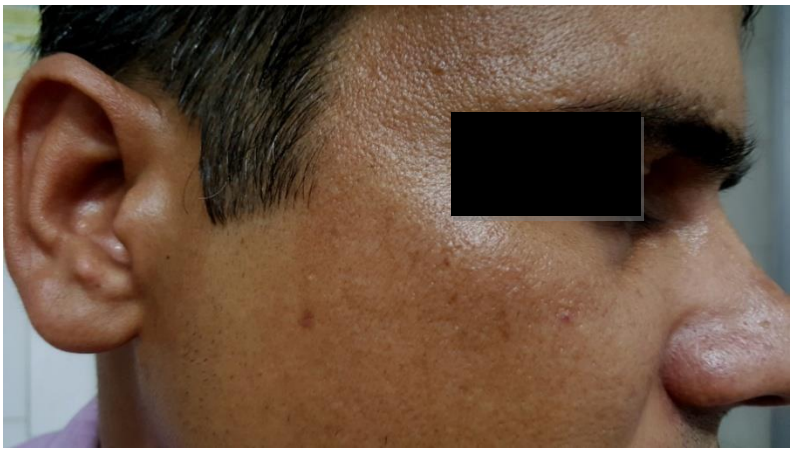
	20% Azelaic acid	4% Hydroquinone	(Nos.)	Effects
	Nos.	Nos.		
Burning	0	2	2	1st month of treatment
Erythema	0	2	2	1st month of treatment
Itching	1	0	1	1st month of treatment
Dryness	1	0	1	1st month of treatment
Nil	48	46	94	
Total	50	50	100	

20% AZELAIC ACID



BEFORE TREATMENT



AFTER TREATMENT

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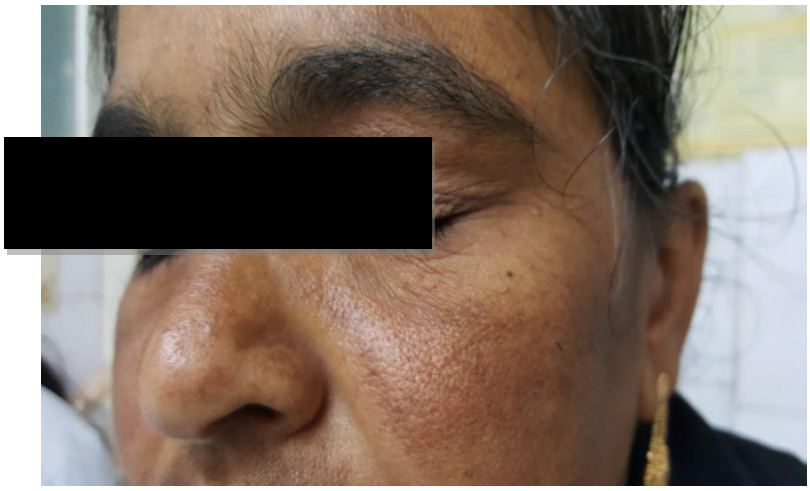
4% HYDROQUINONE



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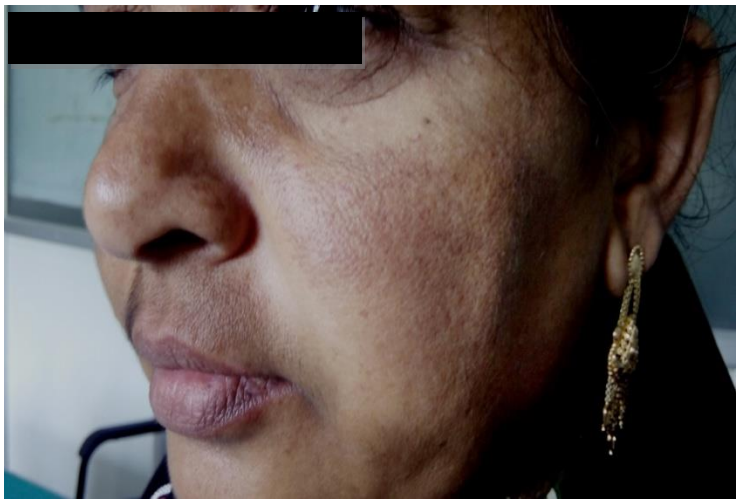

AFTER TREATMENT

DISCUSSION

While evaluating the therapeutic response of 20% Azelaic acid and 4% Hydroquinone within their respective groups, both of them were found to be effective in the treatment of melasma. For both the groups, the mean difference of the MASI scores before treatment and at the end of each month of treatment was statistically highly significant.

While comparing the treatment response between the two groups using mean values and mean difference values of MASI scores, it was found that the therapeutic efficacy was comparable in both the groups (not statistically significant), though 4% Hydroquinone (Group B) was slightly more effective in reducing melasma than 20% Azelaic acid (Group A). None of the patients discontinued the treatment.

Side effects were minimal and mild in both the groups, however slightly more adverse reactions were seen with 4% Hydroquinone. But these were observed only during 1st month of treatment.

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COMPARISON OF MASI SCORES OF BOTH GROUPS:

The mean values of MASI score were calculated to compare the efficacy of 20% Azelaic acid and 4% Hydroquinone. In our study, the mean baseline MASI score (i.e, before treatment) was 14.886±5.5483 for Group A (20% Azelaic acid) and 15.486±7.6463 for Group B (4% Hydroquinone). The mean MASI score reached 12.240±5.0364 for Azelaic acid group and 13.224±6.6994 for Hydroquinone group, at the end of 1st month. At the end of 2nd month, the mean MASI score was 8.364±3.9678 for Azelaic acid group and 9.210±5.0905 for Hydroquinone group. The mean MASI score became 5.700±2.9338 for Azelaic acid group and 6.096±3.4025 for Hydroquinone group,at the end of 3rd month. Mean MASI values reduced each month with treatment in both the groups.There was no statistically significant difference between the therapeutic efficacy of both the groups. But even though not statistically significant, 4% Hydroquinone had slightly better therapeutic effect than 20% Azelaic acid in the treatment of melasma.

This can be compared with a similar study done by Susan Farshi among Iranian females with melasma for a 2 month period for each patient. But in that study, the patients were asked to apply the depigmenting agent (Azelaic acid 20% or Hydroquinone 4%) twice daily and a broad spectrum sunscreen during daytime. Here the mean baseline MASI score for Azelaic acid group was 7.6±3.5 and for Hydroquinone group was 7.2±3.2. The mean MASI score became 6.3±3.4 for Azelaic acid and 6.7±3.4 for Hydroquinone at the end of 1st month. By the end of 2nd month, mean MASI score was found to be 3.8±2.8 for Azelaic acid and 6.2±3.6 for Hydroquinone. So it was concluded that 20% Azelaic acid applied twice daily was more effective in the treatment of melasma than 4% Hydroquinone applied twice daily, along with broad spectrum sunscreen.6

In another study by Balina and Graupe, 20% Azelaiczcid and 4% Hydroquinone were found to have similar therapeutic efficacy.7 Efficacy of azelaic acid 20% was found to be superior to Hydroquinone 2% in a study done by Verallo-Rowell VM, et al.8Kakita, et al, reported that a combination of 20% Azelaic acid and 15-20% Glycolic acid were equally effective as 4% Hydroquinone in the treatment of melasma.9

SIDE EFFECTS

In this study, adverse effects were less in both the study groups, but comparatively more side effects were noted in Group B (4% Hydroquinone). The adverse reactions which appeared in both the groups were mild.

2 patients experienced burning only during the 1st month of treatment with 4% Hydroquinone and another 2 patients in the same group had erythema only during the 1st month of treatment. In a study done by Balina and Graupe, allergic contact dermatitis was seen with 4%

hydroquinone.7SepidehTehrani, et al observed that 35% Iranian female patients had burning and stinging following treatment with 4% hydroquinone.10
Among patients treated with 20% Azelaic acid, 1 patient developed itching and another 1 patient had dryness. Both of these were observed only during the 1st month of treatment. Balina and Graupe observed that local irritation was common with 20% azelaic acid.7

So Azelaic acid can be used as an alternative to Hydroquinone asmelasma requires long term treatment and Azelaic acid does not have risk of long term side effects like exogenous ochronosis.

CONCLUSION

On evaluating the efficacy of both the drugs in their respective treatment groups, both showed a significant reduction inmelasma. On comparing, there was no significant difference in their therapeutic efficacy but 4% Hydroquinone was slightly better than 20% Azelaic acid in reducing melasma. Side effects were minimal and mild in both the groups, though slightly more incidence of adverse reactions were observed with 4% Hydroquinone. Hence 20% Azelaic acid can be used in par with the gold standard Hydroquinone, without compromising the efficacy and duration of response, while eliminating the risk of exogenous ochronosis (long term side effect of Hydroquinone).

In this study, the sample size was small and cannot be extrapolated to the general population. The study period was short. Hence we could not document the recurrence following treatment and also the long term side effects. To assess these, a larger study population has to be chosen and the study should be done for a longer period.

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