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Original Article

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Safety and Efficacy of 20% Azelaic Acid Vs 4% Hydroquinone in Melasma: A Comparative Study in A Tertiary Care Hospital

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Abstract

Introduction: Melasma is an irregular brown or greyish-brown symmetric facial hyper melanosis, causing significant cosmetic concern and psychological morbidity with loss of self-esteem. ***Objectives:*** In spite of multiple treatment options, melasma seems to be a re-calcitrant as well as recurrent disease to treat. We tried to compare the treatment results with 4% hydroquinone and 20% azelaic acid. ***Results:*** The present study investigated safety and efficacy of two drugs 4% hydroquinone and 20% Azelaic Acid by measuring MASI score and dermatoscopic finding. 60 patients were randomized into two treatment groups. One group were treated with 4% hydroquinone and other group with 20% azelaic acid for 4 months. Every month patients were evaluated by MASI score and dermatoscopy. ***Conclusion:*** The study revealed that 4% hydroquinone was more efficacious than 20% azelaic acid in terms of pigment clearance, however, considering the short duration of the study, long term adverse effect of the drugs cannot be monitored.

Keywords: ***Melasma, hydroquinone, azelaic acid, MASI, Dermatoscope.***

Introduction

Melasma is symmetrical hyperpigmentation over face causing cosmetic and psychological concern for the patients. The reported prevalence of melasma is variable and is based on the population group studied. It ranges from 8.8% to 19.9% in south Indian populations [1]. It may affect any age group starting from puberty. Pregnency and intake of Oral Contraceptive Pills may lead to early age of onset [2]. Females are more affected than males. Up to 10% of melasma cases occur in male [3]. Exact cause of melasma is yet to be known. It is thought to be a multifactorial causations[4] like genetic[5], UV Radiations [5], pregnancy[5] oral contraceptive pills [6]. Facial melasma has been classified as Centro facial(63%), Malar(21%) Mandibular (16%) [7], Depending upon the location of melanin, melasma classified as:[8] Epidermal type Dermal type and Mixed type. Severity has been classified by MASI score which ranges from 0 to 48[9] Patients counselling and protection from sun exposure by broad spectrum sunscreen, umbrella, broad-brimmed hat are very important part in management part [10]. Treatment option includes topical depigmenting agents like hydroquinone, azelaic acid, glycolic acid, kojic acid, niacinamide alone or in combination. Other options like chemical peels, oral tranexamic acids, laser and light based therapies are available [11]. When choosing a treatment regimen, it is important to recognize extent and the severity of the disease with the patient's own perception of his or her disease. In most treatments, the duration of a treatment is restricted because of the cumulative toxicity and in some instance, treatment efficacy may diminish with time (tachyphylaxis)[12] and rebound hyperpigmentation after stoppage of treatment [13].

Methods

Study design

This is a prospective interventional study. 60 patients with melasma, who presented our department from March 2021 to April 2022 were included, divided in two groups after meeting the eligibility criteria for the study.

Patients aged more than 18 years who were willing to participate in the study and not taken any treatment for melasma in last 6 months, were included.

Patients who were non-compliant, patients with active infection on face, pregnant and lactating mothers, history of malignancy, facial acanthosis nigricans, known allergy to hydroquinone and azelaic acid, were exclude from the study.

An institutional ethics committee permission was taken. An informed consent from each patient was taken before their participation in the study.

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Demographic profile like age, gender, religion and residence were noted. A detailed history regarding age at onset, duration and progression of melasma taken and baseline MASI score was calculated. Patients were divided in two groups. All odd numbered patients were started with 4% hydroquinone cream and all even numbered patients was started with 20% azelaic acid cream, daily once application at night on the affected areas.

MASI score was calculated and dermoscopic findings were noted every 1month intervals for a period of 4 months. Reduction in MASI score and side effects were noted in each follow up. Presence or absence of the following parameters on dermoscopic examination on every monthly visit were noted i.e: Diffuse light to dark pigmentation, Multiple brown dots, Granules and globules, Arcuate and annular structures, sparing of perifollicular region, telangiectasia, pseudo reticular network

Statistical analysis

The statistical software SPSS version 20 and Medcalc were used for the analysis. Categorical variables are expressed as Number of patients and percentage of patients and compared across the groups using Pearson's Chi Square test for Independence of Attributes. Continuous variables are expressed as Mean and Standard Deviation. An alpha level of 5% has been taken, i.e. if any p value is less than 0.05 it has been considered as significant. Data was represented by various tables, graphs, diagrams etc

Result and Analysis

Total 60 patients of melasma were included in the study [**Table 1**], out of them 10 (16.6%) were male patients and 50 (83.3%) were female. The mean age was 38.28years (SD +/- 8.37) with a range from 21 to 57 years.

Table 1: Demographic Profile of study subjects

Gender	Male	10
	Female	40
Religion	Hindu	38
	Muslim	22
Marital Status	Married	52
	Unmarried	8
Residence	Urban	22
	Rural	38

Table 2: Reduction of Melasma Severity Index (MASI) Score at different time intervals after initiation of treatment and the patients of the two groups

Reduction of MASI Score	At 1 Month		At 2 Month		At 3 Month		At 4 Month	
	4% Hydro	20% Azelaic	4% Hydro	20% Azelaic	4% Hydro	20% Azelaic	4% Hydro	20% Azelaic
<50%	30(50%)	30 (50%)	30 (50%)	30 (50%)	26 (48.1%)	28 (51.9%)	17 (41.5%)	24(58.5%)
50% - 75%	0(0%)	0(0%)	0(0%)	0(0%)	4(66.7%)	2(33.3%)	13(68.4%)	6 (31.6%)
>75%	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	0 (0%)
TOTAL	30	30	30	30	30	30	30	30
Chi-square	0.01		0.01		0.74		6.04	
p-value	0.99 NS		0.99 NS		0.38 NS		*0.04 S*	

The reduction of MASI score is not statistically significant in both the group [**Table-2**]

As there is no good reduction of MASI Score (>75%), so further comparisons were done on the basis of mild (<50%) and moderate (50% to 75%) reduction of MASI Score [**Figure-1,2,3**]

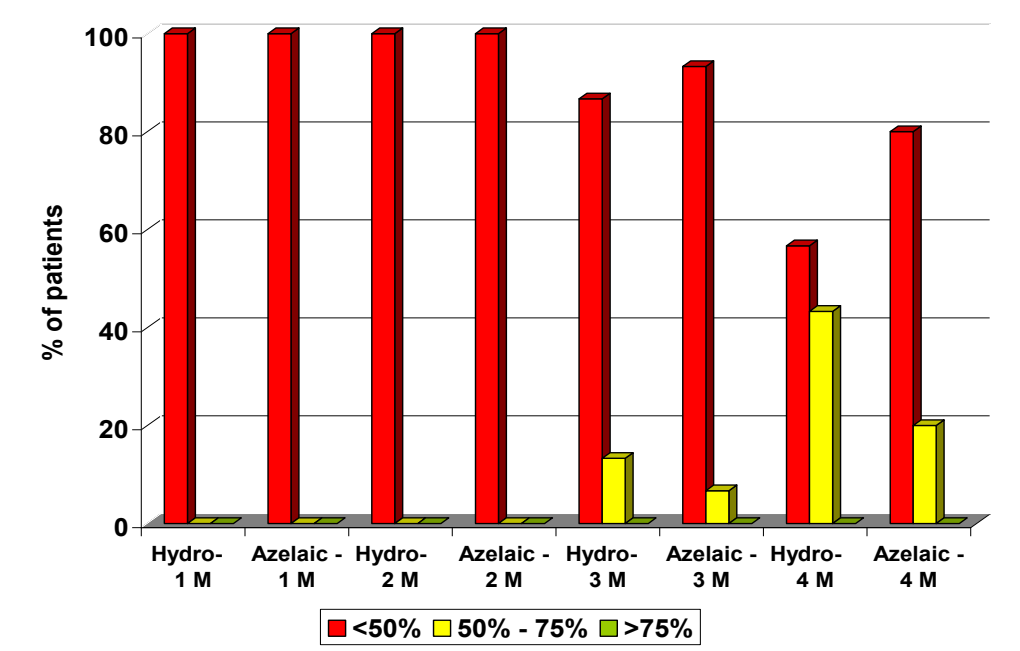

Figure 1: Comparison of efficacy on the basis of reduction in MASI score

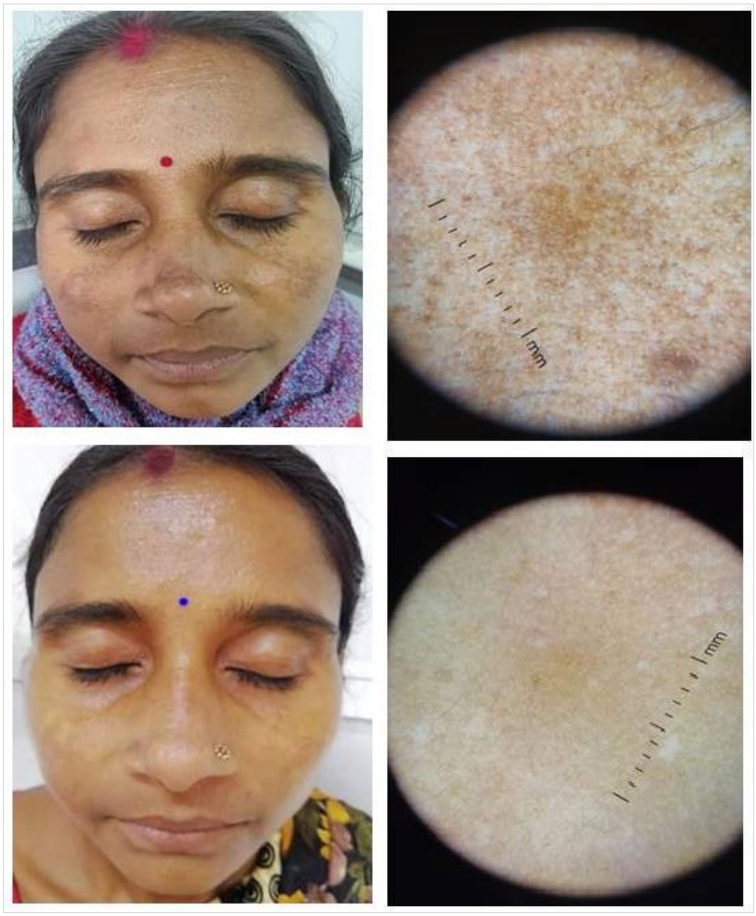

Figure 2: Clinical and Dermoscopic Photo: Before and after 4 Months of Treatment with 4% Hydroquinone

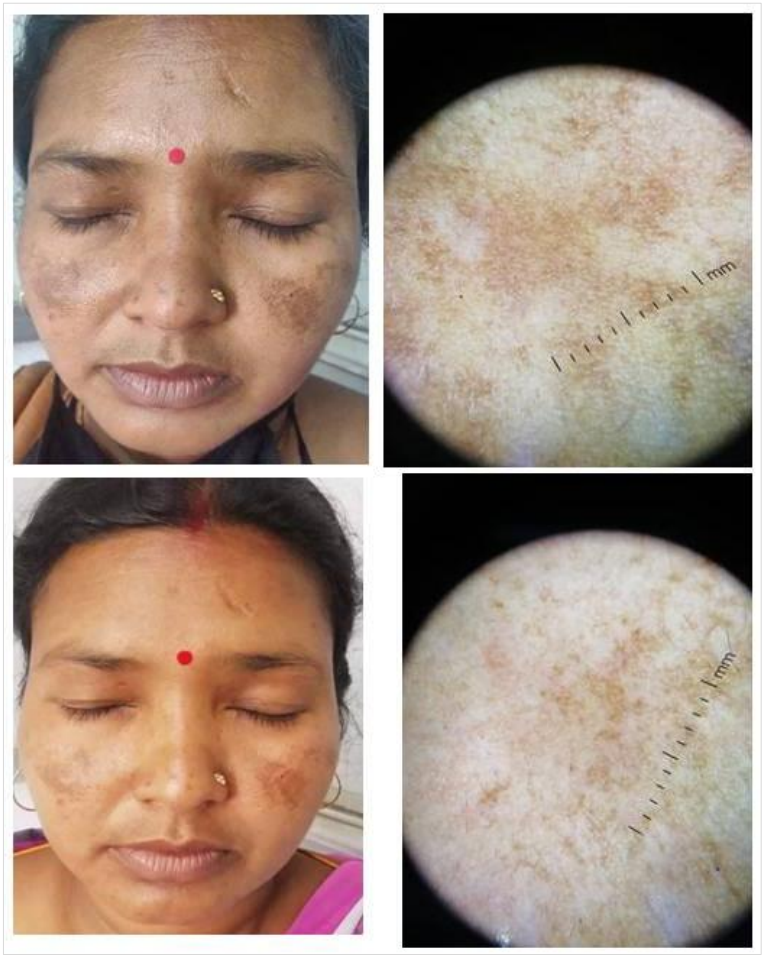

Figure 3: Clinical and Dermoscopic Photo: Before and After 4 Months Treatment with 20% Azelaic Acid

Discussion

The present study, an institutional based comparative interventional study attempted to know about efficacy and safety of 4% hydroquinone and 20% azelaic acid melasma patients. In this study, Prevalence of melasma was found to be 40.2 per 1000 patients among all patients attending Dermatology OPD during the study period. In another study conducted in south-east Asia the prevalence of melasma was found to be 29.8 per 1000 patient seeking dermatology consultation [14]. The mean age of patients was found to be 38.28 years (SD +/- 8.371) with a range from 21 to 57 years. Age of the patients (years) in the study by SARKAR R et al is between 19 to 53 years and mean age was 33.5(SD +/- 11.345) [15]. Krupa Shankar et al estimated the mean age to be 37.2 ± 9.3 [16]. 23 patients (38.3%) belong to 31 to 40 years age category and least number 6 patients (10%) belong to 51 to 60 years category. The 31 to 40 years age group patient are mostly affected. Oral contraceptive pills may be one of the causes. In a study maximum number (31.4%) of sample belonged to 20 to 45 years of age [17]. Melasma is more common in female population. Male patients constitute 16.6%% and female patients 83.33% of study population Among the study population hindu population 63.3% and 36.7% muslim population.

Urban population constitutes 36.7 % of study population and rural 63.3%. Further, large sample sized epidemiological study may be required to assess whether any lifestyle factors associated with urbanization is influencing incidence and prevalence of melasma; thus, influencing prevalence of melasma.

In the present study, 7 out of 60 (11.7%) of the cases were highly educated and none were illiterate. So, education may be an important factor that increases the health seeking behaviour of the society. Majority of study subjects were clerical (33.3%) and semi-skilled (23.3%) workers. Professionals were 3.3%. As our study has low sample size for an epidemiological study, many correlations regarding this aspect came as insignificant by chi square test.

In this study 86.7% population were married and 13.3% population were unmarried. As melasma is mainly cosmetics concern but here we see most the sample were married may be due to contraceptive practices like oral contraceptive pills. Out of 50 female populations 21 females (35%) were taking oral contraceptive pills. In a study Sharad J et al, 23 female population (8.6%) out of 266 female sample population were taking oral contraceptive pills [18].

Duration of the disease at presentation 2.25 years(SD +/- 0.932), whereas in study of Somani V K et al the average duration of presentation was 3 years [19].

15% of the population were on regular medications (other than for hypertension, diabetes mellitus or thyroid disorder) whereas in a study, 19.8% patient was on other medications [20]. In this tudy 23.3% patients used to use facial cosmetics. Among the study population 33.3% were engaged in outdoor work among the males 80% were outdoor worker. In study 55.5% patients has history of sun exposure. In this study we found that 83.3% of the total population had a progressive melasma when presented to us for treatment. Out of these 89.4% patients were outdoor worker which indicates associations between these two factors. Among the study populations, 30% patients (mainly from rural areas) had taken treatment for melasma at least 6 months before presenting to us in the form of either over the counter or from quack and it was mainly triple combination (19%) In a study by Mysore V R et al 42% study population take treatment before [21]. In the study we got 33.3% positive family history; similar prevalence was seen in two other studies [22].

In our study we got 21.7% obese; 38.3% overweight and rest 40% within normal BMI and mean MASI scores were 19.4+/- 4.8; 19.3+/- 19.3 ;19.1 +/- 4.4 respectively. Normal weighing people mainly belongs to rural population. It is very important to differentiate facial acanthosis nigricans from melasma. In this study mostly the patients had centrofacial melasma(60%) followed by malar and mandibular. In another study centrofacial melasma was on much more higher side(72.3%) followed by malar(18.7%) and mandibular(9%) [23].

MASI score and dermoscopic finding as clinical to assess the outcome of the therapy in both the intervening group. Though MASI is subjective assessment tool but being the primary investigator there will not be any inter-assessor difference. MASI score ranges from 0 to 48. In the present study baseline mean MASI score in female was 20.2 +/- 4.7(SD) and in male was 14.8 +/- 3.1(SD) and in 4% hydroquinone group baseline mean MASI score was 19.5 +/- 4.9(SD) and in 20 % azelaic acid group it was 19 +/- 5(SD) with no significant difference between them (p=0.335). In a study. The mean MASI score before treatment was 7.2 ± 3.2 in the hydroquinone group and 7.6 ± 3.5 in the azelaic acid group [24].

During initial 3 visit the reduction of MASI score is not statistically significant in both the groups :1st follow up P=0.99, Chi-square = 0.1; 2nd follow up P=0.99, Chi-square= 0.01; 3rd flow up P=0.38, Chi-square=0.74 and in final 4th follow up P=0.04, Chi-square=6.04. In this study 4% hydroquinone was 6 times more effective than 20% azelaic acid though the results were not significant.

There were no significant associations between reduction of MASI score and age distribution of the patients(P=0.48); gender of the patients (P=0.48); intake of OCPs(P=0.28); using cosmetics on face(P=0.54); Outdoor work((P=0.58); Duration of the disease(P=0.73); treatment taken before 6 months(P=0.09); Positive family history(P=0.06); BMI(P=0.63).

All the patients underwent dermoscopically to see whet her the findings present or not at every follow up

Findings of reduction rate of every dermoscopic features is higher in 4% hydroquinone group at every follow up but is not significant as compared to 20% azelaic acid group except diffuse light to dark brown pigmentation (P=0.0096) in which the reduction rate is significant. No side effect was observed during and during follow-up after treatments among the patients of the two groups.

Limitations

Sample size is small. The study has been done in a single centre. As patient satisfaction is Subjective, possibility of bias is present. The duration of the study is 4 months for each case, long term adverse effect of the drugs cannot be monitored.

Conclusion

Prevalence of melasma was found to be 40.2 per 1000 patients. Centrofacial was most common pattern consists 60% of study population. Mean duration of melasma was found to be 2.25 years.33.3% of study population were involved in outdoor work.23.3% of study population used to use facial cosmetics.30% of study population taken treatment before 6 month. Progressive melasma in case of 83.3% study population .35% female study population used to take Oral Contraception Pills.21.7% population were over-weight. Both 4% Hydroquinone and 20% Azelaic Acid are effective for treatment of melasma.4% Hydroquinone acts faster than 20% Azelaic Acid. No serious adverse effect was found during our study.

Declarations

Acknowledgements

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Consent of Patient

The authors certify that they have obtained all appropriate patient consent.

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Nil

Conflicts of Interest

There is no conflict of interest.

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