Original Article

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A Clinical Study of Melasma and the Effect of Different Therapeutic Modalities in its Treatment

Vijetha Rai[1], Sharath Chandra B Athanikar[2], Naveen KN[3], Varadaraj V Pai[4], Tukaram Sori[5]

Author Affiliation:
[1]Assistant Professor, Department of Dermatology, Venereology, Leprology, Srinivas Institute of Medical College and Research Center, Mukka Suratkal Mangalore, Karnataka 574146, India. [2]Professor and Head [3]Associate Professor [5]Consultant, Department of Dermatology, Venereology, Leprology, Sri Dharmasthala Manjunatheshwara College of Medical Sciences and Hospital, Dharwad, Karnataka 580009, India. [4]Associate Professor, Department of Dermatology, Venereology, Leprology, Goa Medical College, Goa 403202, India.

Corresponding Author:
Vijetha Rai, Assistant Professor, Department of Dermatology, Venereology, Leprology, Srinivas Institute of Medical College and Research Center, Mukka Suratkal Mangalore, Karnataka 574146, India.
E-mail: vijju.rai86@gmail.com
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Abstract

Context: Melasma is a common, acquired, symmetric hypermelanosis, characterized by irregular light to dark brown macules and patches commonly involving the cheeks, forehead, upper lip, nose, and chin. *Aims:* To study the clinical patterns of melasma in patients attending skin OPD and To study the effect of different therapeutic methods in treatment of melasma. *Settings and Design:* Prospective cohort. *Materials and methods:* Patients attending OPD were randomly divided into 3 equal groups to be treated with either topical hydroquinone or topical triple combination or chemical peeling. All patients were evaluated before treatment, followed up for 6 months, peel session done at an interval of 1 month and MASI score was calculated every time. *Statistical analysis:* Student t test *Results:* Among 150 patients studied, majority were in the age group of 20-30 yrs [38.7%], females [79%] and belonged to epidermal type [51.33%] of melasma based on woods lamp, centrofacial [74.7%] type of melasma based on clinical findings. There was improvement in the MASI score of all patients in all melasma type [both clinical and woods lamp] irrespective of treatment group and the difference seen was statistically significant in each group [$p<0.05$]. *Conclusion:* Triple combination showed better results compared to glycolic acid peels and hydoquinone with no significant side effects with short contact time. Considering the high prevalence of melasma among people with Indian skin type there is a need to study effect of various modalities of treatment used for the same.

Keywords: Melasma; chemical peeling; hydroquinone; triple combination

Introduction

Skin colour is an important visible sociocultural characteristic of an individual [1]. Hence, any deviation from the normal colour adversely affects the social and emotional well-being of the patient. Melasma is a common pigmentary disorder characterized by almost symmetrically distributed, brown macules with defined geographic border affecting the sun exposed areas [2]. The reported prevalence of melasma ranges from 8.8% among Latino females in the Southern United States to as high as 40% in Southeast Asian populations [3]. The exact incidence in India is not known [2]. An assortment of treatment modalities are available for melasma including topical hypopigmentary agents, chemical peels, lasers, dermabrasion but the response is not overwhelming. Though melasma does not cause any health related problems it has a severe impact on the quality of life. This prompted us to study the clinical patterns of melasma and also to evaluate the effect of various modalities of treatment used for the same.

Subjects and Methods

Patients with melasma who visited the Out Patient Department over the period of one year and had not received any prior treatment were enrolled for the study after ethical clearance. Pregnant ladies, patients on treatment for melasma, patients with known history of allergies to any of topical medication, patients with unrealistic expectations were excluded from study. After obtaining an informed written consent detailed history was taken and clinical examination of all patients was done. All patients were examined under Wood's lamp and were classified into epidermal, dermal, mixed

melasma. The MASI (Melasma Area And Severity Index) score was calculated and color photographs were taken of all patients under standard conditions in natural light [4]. Patients were then randomly divided into 3 groups of 50 each. Group A patients were treated with glycolic acid peels, group B were treated with topical 4% hydroquinone and group C patients were treated with triple combination of hydroquinone 2% + tretinoin 0.025% + momentasone 0.1%. All patients were given sunscreens for daily application after treatment. In group A peeling was done with glycolic acid (GA) peel. 70% glycolic acid was diluted to 20% and 35%. After degreasing, treatment with GA peel was carried out for a period of 20-30 seconds and was left for a definite period of time (first peel: 20% GA for 2 minutes; second peel: 20% GA for 5 minutes; third peel: 35% GA for 2 minutes; fourth peel: 35% GA for 3 minutes; fifth peel: 35% GA for 5 min, separated by 1 month interval) on the individual anatomic units, separately and in a preset sequence. If patient complained of pain or burning sensation peel was terminated early. Peel was terminated by using a neutralizer. Post peel patients were advised to apply sunscreen topically daily every 2 hrs. Patients in group B were given hydroquinone 4% to be applied in the night. The remaining 50 patients were treated with triple combination of 0.025% tretinoin and 0.1% momentasone and 2% hydroquinone for short period (upto 30 min). Melasma severity was scored at baseline, and at each peel session using the Melasma Area and Severity Index (MASI) at an interval of 1 month [4]. The face was divided into four areas: forehead, right malar, left malar, and chin that correspond respectively to 30%, 30%, 30%, and 10% of total face area. The melasma in each of these areas was graded on three variables: percentage of total area involved on a scale from 0 (no involvement) to 6 (90% to 100% involvement); darkness on a scale from 0 (absent) to 4 (severe); homogeneity on a scale of 0 (minimal) to 4 (maximum). The MASI was then calculated by the following equation:

MASI=0.3 (DF+HF) AF+0.3 (DMR+HMR) AMR+0.3(DML + HML) AML + 0.1 (DC + HC) AC where D is darkness, H is homogeneity, A is area, F is forehead, MR is right malar, ML is left malar, C is chin, and the values 0.3, 0.3, 0.3, and 0.1 = respective percentages of total facial area. This grading for each patient was done clinically at every visit.

Statistics

Data collected was imported into Microsoft Excel 2007. Data was analyzed using IBM SPSS 20.0. Student t test was applied.

Results

The study comprised of 119 females and 31 males in the age group of 20 – 70 yrs with a mean age of 34.78 years. Majority had Fitzpatrick's type IV (76%) and V skin (17.33%), and very few had Fitzpatrick's type III skin (6.67%). All the three groups were comparable with no statistically significant difference in the age distribution, skin type, duration of melasma and pattern of melasma. Majority of our patients had epidermal type (51.33%) and mixed (48%) melasma. Only one patient (0.67%) had dermal melasma. Centrofacial melasma was the most common type (74.7%), followed by malar type (25.3%) of melasma. None of the patients had mandibular pattern of melasma. The mean MASI reduction in patients was 50%, 39%, and 66% in groups A, B and C respectively. In all three groups the reduction in MASI was statistically significant. Triple combination showed significantly better results compared to peel and hydroquinone (Figure 1,2,3). The mean MASI

Fig. 1a: Before chemical neel

Fig. 1b: After chemical neel

Fig. 1: Pre and post treatment photograph with chemical peeling

Fig. 2a: Before Hydroquinone

Fig. 2b: After hydroquinone

Fig. 2: Pre and post treatment photograph with hydroquinone

Fig. 3a: Before Triple Combination

Fig. 3b: After Triple Combination

Fig. 3: Pre and post treatment photograph with triple combination

reduction in patients with epidermal melasma was 51%, 40%, 62% in group A,B,C respectively. The difference in the reduction of mean MASI scores of epidermal melasma in the three groups was, however, not statistically significant. (Table 1) Difference in reduction in MASI score between the three treatment modalities was not significant. On the other hand in patients with mixed melasma triple combination and glycolic acid showed significantly better results compared to hydroquinone. Only 1 patient belonged to dermal melasma group and showed 30% reduction in MASI score. The reduction in MASI in different types of clinical melasma is given in Table 2. In centrofacial and malar group triple combination gave significantly better results compared to hydroquinone. The percentage reduction of the mean MASI score in different skin types is given in Table 3. The difference in reduction in MASI score between all the three groups was not significant in people with skin type 3 and 5. In skin type 4 patients treated with triple combination showed better results.

No complications were observed in patients who received hydroquinone. Only 5 (10%) patient treated with triple combination cream experienced slight burning sensation. In chemical peeling group, 1 (5%) patient developed post peel burns. None of the patients suffered worsening of melasma on treatment.

Table 1: Percentage improvement in different types of melasma

	MASI1		MASI 5		n	% improvement	p value
Epidermal	Mean	SD	Mean	SD			
Group a	14.81	11.38	7.259	5.45	27	51%	<0.05
Group b	9.725	5.018	5.877	4.71	23	40%	<0.05
Group c	12.78	4.698	4.891	3.61	23	62%	<0.05
Dermal							
Group c	9.9	0	6.9	0	1		
Mixed							
Group a	10.00	4.299	5.208	3.05	23	48%	<0.05
Group b	13.23	5.407	7.956	4.59	23	40%	<0.05
Group c	12.40	9.077	3.584	4.46	26	71%	<0.05

Table 2: Percentage improvement in different treatment groups in different clinical types of melasma

	MASI 1		**MASI 5**		**n**	**improvement**	**p value**
cf	**Mean**	**SD**	**Mean**	**SD**			
Group a	12.8	9.373	6.4	4.63	39	49%	<0.05
Group b	11.69	6.06	6.93	5.179	32	41%	<0.05
Group c	12.42	7.304	4.468	4.226	41	64%	<0.05
Malar							
Group a	11.75	8.447	5.790	4.602	11	51%	>0.05
Group b	10.71	4.199	6.65	3.950	18	38%	<0.05
Group c	13	7.224	3.266	3.315	9	75%	<0.05

Table 3: Descriptive statistics: Reduction in MASI score in fitzpatrick skin types 3,4,5.

	n	**MASI 1**		**MASI 5**		**% improvement**	**p [1 and 5]**
		mean	**SD**	**mean**	**SD**		
A-3	6	12.27	7	7.05	4.16	42.54%	Not significant
A-4	37	13.53	9.92	6.51	4.91	51.88%	significant
A-5	7	7.97	3.89	4.67	2.97	41.41%	Not significant
B-3	19	10.47	5.46	6.69	4.86	36.10%	significant
B-4	30	11.91	5.54	7	4.79	41.23%	significant
B-5	1	10.8	0	4.5	0	58.33%	Not significant
C-3	10	14.7	9.07	6.63	5.28	54.90%	significant
C-4	37	12.04	6.58	3.53	3.44	70.68%	significant
C-5	3	11.4	9.9	5.2	5.4	54.39%	Not significant

Table 4: Comparison of our study with other studies using hydroquinone

	Solis JN et al. [17]	**Iraji F et al. [18]**	**Rochelle et al. [19]**	**Present study**
No of cases	27 cases	72	30	50 cases
Interval and %hydroquinone	8 weeks 4% hq	6 months 4% hq	12 weeks 4% hq	6 months 4% hq
Reduction in MASI	70%	48.8%	72.2%	39%

Table 5: Comparison of our study with other studies using GA peel

	Rashmi kumari et al. [9]	**Javaheri et al. [22]**	**Sarkar et al. [21]**	**Kar et al. [8]**	**Present study**
%GA and interval	20-35% and 2 weeks	50% 4 weeks	30-40% 3 weeks	35-70% 2 weeks	20-35% 4 weeks
No of caseses and avg no of peel	20 cases 7 peels	23 cases 3 peels	20 cases 6 peels	25 cases 6 peels	50 cases 5 peels
Reduction in MASI	79%	47%	46%	40.44%	50%

Discussion

Melasma is a pigmentary disorder more common in women than in men and occurs most commonly in women of reproductive age. It is found most commonly in women with Fitzpatrick skin phototypes III – V especially in people of East and South-East Asian and Hispanic origin living in areas of intense ultraviolet (UV) light exposure [3,5]. Majority of the patients in our study were in the age group 20-30 years (58 patients), followed closely by 31-40 yrs (57 patients). This was in agreement with other Indian studies [6,7,8]. The mean age of the patients in our study was 34.78 years. In a study by Kumari R. et al. [9] the average age of patients at the onset of melasma was middle age, but Kimbrough-Green et al. [4] reported a much higher age of onset (44 years) in their study of Black patients, whereas in another study in Griffiths et al. the age group was comparable with mean of 30 years [10]. Among the 150 patients included in our study 119 were females and 31 were males. The ratio was 1:3.83. This was in agreement with other Indian studies [7,8,9] and a study done in Western Nepal by Dwari BC et al. [11] The most common pattern of melasma was centrofacial (74.7%) followed by malar pattern (25.3%). This was in agreement with the study by Bansal C et al. [6] and in contrast to studies by Kumari R et al. [9] and Grover et al. [12]. None of the studies reported mandibular type of melasma except a study by Kar et al. [8] which reported 11.6% mandibular pattern. On woods lamp examination, epidermal melasma more common. This was in corroboration with study by Kar et al. [8], Rashmi et al. [9], Sanchez et al. [13] and in contrast with study of Bansal C et al. [6] where mixed was more common. Patients included in our study belonged mainly to skin type 3, 4, 5. Most of our patient belonged to skin type 4 (76%), others belonged to type 5 (17.33%) and type 3 (6.67%). This was in agreement with other studies done in India [6,8]. In the present study 42 patients (28%) had a family history of melasma whereas in study by Bansal et al [6] 55% patients had family history.

A variety of treatment modalities have been tried in melasma including topical hypopigmentary creams, peels and lasers. We studied the response of melasma patients to hydroquinone, triple combination and glycolic acid peels. Hydroquinone is one of the earliest compounds used for the treatment of hyperpigmentation. Its mechanisms of action are inhibition of tyrosinase, inhibition of DNA and RNA synthesis, degradation of melanosomes and destruction of melanocytes. It is commonly used at concentrations ranging from 2% to 5% [14,15]. The most frequently observed reactions are mild skin irritation and sensitization, while chronic use is said to cause exogenous ochronosis [16]. In our study the reduction of MASI score after 5 months was 39% with hydroquinone. This was lesser compared to other studies. In a double blind split face randomized clinical trial of niacinamide versus 4% hydroquinone carried out on 27 patients in Mexico by Solis JN et al. showed average decrease in MASI at the end of 8 weeks for hydroquinone was 70% [17]. In another study conducted on 72 women in Iran by Iraji F et al. comparing 10% zinc sulphonate and 4% hydroquinone in treatment of melasma, the average decrease in MASI at the end of 6 months follow up was 48.8% [18]. In a study by Rochelle et al. where they compared the efficacy of 0.75% KA and 4% hydroquinone, in patients who received 4% HQ average decrease in MASI at the end of 12 weeks was 72.2% [19]. The improvement seen in the present study was lesser compared to other studies. This could be explained by the reduced compliance with sunscreen usage in our set up.

Kligman's formula is one of the most popular combination therapies in the management of melasma. This original formula used dexamethasone 0.1% in combination with 0.1% tretinoin, and 5% hydroquinone [20]. It has been modified in a number of ways over the years to suit different skin types. We used a combination of 0.025% tretinoin, 0.1% momentasone and 2% hydroquinone. Sarkar et al. [21] had compared the efficacy of 20% GA with Kligman's formula in 20 cases of epidermal melasma and had seen a significant reduction (>80%) in MASI scores with GA when compared to plain Kligman's regime. In total contrast to the above study in our study the percentage improvement with triple combination (66%) was more than with GA (50%) and the difference was statistically significant.

Glycolic acid, an alpha hydroxy acid is most commonly used for chemical peeling. It causes a decrease in corneocyte adhesion and epidermolysis [9]. We used glycolic acid in concentrations of 20 and 35%. In our study, results were statistically significant with glycolic acid peel. The average improvement of 50% in mean MASI score was obtained. Many other studies [8,9,21,22] that have used GA in various concentrations in similar skin type patients have shown variable results. In a study done by Kar et al. [8] where they compared the efficacy of low fluence laser, high fluence laser with glycolic acid peels in treatment of melasma the results with six sessions of peel

with glycolic acid were statistically significant. There was an improvement of 40.44% in the mean MASI score. Grover and Reddu [12] had in their experience with GA (10-30%) in various cases showed response, above 60% in more than 90% of cases. Sarkar et al. [21] had compared the efficacy of 20% GA with Kligman's formula in 20 cases of epidermal melasma and had seen a significant reduction (>80%) in MASI scores with GA when compared to plain Kligman's regimen (Table 5).

Complications

No complications were observed in patients who received hydroquinone. Only 5 (10%) patient treated with triple combination cream experienced slight burning sensation. In a study by Taylor SC [23] erythema and desquamation occurred in about half of treated patients. The reduced incidence of side effects in our study could be attributed to the short contact time. (5 min – 30 min). In chemical peeling group, 1 (5%) patient developed post peel burns. In a study by Kar H K et al. [8], 4% patients showed immediate burning and erythema and 1% showed post inflammatory hyperpigmentation.

Conclusion

Treatment of melasma has eluded dermatologists for years. No treatment guarantees full recovery. In our study triple combination showed better results compared to glycolic acid peels and hydoquinone with no significant side effects with short contact time. In all three groups the reduction in MASI was statistically significant.Considering the psychologic and social impact melasma has on the patient, additional research in developing new and effective treatments for melasma is required.

Limitations

Follow up after 5 sitting was not done so recurrence rate could not be assessed.

Key messages

Melasma is an acquired pigmentary disorder wherein numerous treatment modalities have been tried with no one modality being superior. So this is an attempt to find the better treatment among commonly used modalities.

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