

Comparative Efficacy of 35% Glycolic Acid Peel vs. Jessner Peel as an Adjuvant to Topical Triple Combination (2% Hydroquinone, 0.025% Tretinoin, 0.01% Fluocinolone Acetonide) Therapy in Melasma Females Cases

AVANI MODI, SWETA PARMAR,
and YOGESH MARFATIYA

*Gmers Medical College, Vadnagar, Gujarat, India (A.M., S.P.),
Department of Skin and V.D.,
Gmers Medical College, Vadnagar 384355, Gujarat, India
Department of Skin & V.D., Medical College
and S.S.G. Hospital Vadodara 390001, Gujarat, India*

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Synopsis

Melasma is a common, acquired, circumscribed hypermelanosis of sun-exposed skin. It presents as symmetric, hyperpigmented macules having irregular, serrated, and geographic borders. Compare the efficacy of 35% glycolic acid (GA) peel vs. Jessner peel (JP) as an adjuvant to topical triple combination (2% Hydroquinone, 0.025% tretinoin, 0.01% Fluocinolone acetonide) therapy in Melasma in females. Sixty cases of Melasma attending Skin-VD OPD, Baroda Medical College from September 1, 2016 to July 30, 2017 were enrolled. Among them, 12% cases had history of menstrual irregularity, 5% cases had past history of oral contraceptive (OC) pill intake, and 10% cases had history of working outdoors. Most common pattern of melasma was centrofacial 32 cases (53%) which was followed by malar pattern in 27 cases (47%) and mandibular pattern in one case (2%). Fifty cases who completed study were evaluated for comparative efficacy of GA peel versus JP as an adjuvant to topical triple combination therapy. Average reduction in Melasma Area and Severity Index (MASI) score in cases treated with GA peel group was 58.56% with Jessner peel group was 59.12%. In GA peel group, 84% cases had moderate to good improvement, whereas in JP group 92% cases had moderate to good improvement. According to present study, safety and efficacy profile of 35% GA peel vs. JP was almost same. Both can be used as an adjuvant to topical triple combination therapy of 2% hydroquinone, 0.025% tretinoin, and 0.01% fluocinolone acetonide in females suffering from melasma. We recommend that it will be safer for the pregnant women to get the GA peel rather than the treatment containing hydroquinone and tretinoin since the activity/performance is very similar.

INTRODUCTION

Melasma is an acquired, circumscribed, pigmentary disorder characterized by more or less symmetrically distributed and medium to dark brown macules with defined geographic

Address all correspondence to Sweta Parmar at drswetaparmar@gmail.com

borders affecting the sun-exposed area, particularly to forehead, cheeks, temples, and upper lip. It is more commonly seen in females than in males (1,2).

Incidence

- 50–70% of pregnant women
- 8–29% of women on oral contraceptive (OC) pills (3,4)

Hydroquinone (HQ) and triple combination creams (TCCs) remain the gold standard of treatment. There have been concerns about the side effects and long-term safety of HQ; hence the need to develop alternate treatment options.

No single therapeutic modality is sufficient to achieve total clearance of pigmentation in melasma and maintenance of response. Therefore, therapies need to be combined to optimize the outcome.

AIMS AND OBJECTIVES

To compare the efficacy of 35% glycolic acid (GA) peel vs. Jessner peel (JP) as an adjuvant to topical triple combination (2% Hydroquinone, 0.025% tretinoin, and 0.01% Fluocinolone acetonide) therapy in Melasma females cases.

To determine the efficacy in terms of

1. Decrease in Melasma Area and Severity Index (MASI) Score
2. Presence of any ADR

MATERIALS AND METHODS

The study was carried out in the department of Skin-VD, Medical College Baroda, after approval of the Institutional Ethics Committee for Human Research, Medical College Baroda & SSG Hospital, Vadodara (16/12/2016), GUJARAT, INDIA.

Study Design: Interventional Randomized clinical study

Sample Size and Study Population: A total of 60 clinically diagnosed patients of Melasma attending the Skin-VD OPD from September 1, 2016, to June 30, 2017, were enrolled as per the inclusion and exclusion criteria.

Inclusion criteria:

- Women (menstruating*) of 20–50 age group with melasma having malar, centrofacial, and/or mandibular pattern melasma.

*Regular menstruation definition (23–39 days and for 2 to 7 days and 25 to 39 mL)

Exclusion criteria:

- Pregnant or nursing women,
- Women on contraceptive pills at the time of the study or in the past 6 months.
- Patients on any concurrent therapy,
- Patients with hypersensitivity to the formulations, concurrent illnesses,
- None of the patients had used topical steroids or hydroquinone 2 weeks before study entry and systemic steroids for 1 month.
- Any chronic medical illness

Method of study: All the eligible cases attending skin VD OPD, S.S.G. Hospital, Medical College Baroda during the study period (September 1, 2016, to June 30, 2017) was included for the study with a written consent.

- **Detailed history** including age, sex, duration of the disease, number of the lesions, history of medication, and so on, was taken.
- **Clinical examination** included both general and dermatological examinations.
- MASI* score calculation was done.
- All cases was given standardized treatment.
- Photographic and clinical assessment was carried out at 0, 2, 6, 10, 14 weeks.
- Treatment was given according to protocol.*
- Patient with odd sr no. (1, 3, 5, ...) was given 35% GA peel.
- Patient with even sr no. (2, 4, 6,) was given JP (14% salicylic acid, 14% lactic acid, and 14% resorcinol in 95% ethanol).

Cutaneous and systemic examination were done and documented in preset proforma.

Morning—sunscreen cream (SPF sunscreen (Octyl Methoxycinnamate 7.5+ Vitamin E Acetate 0.5% W/W+Overa-Spf Aloe Vera Extract 10)

- **At night**—Triple combination (2% hydroquinone, 0.025% tretinoin, 0.01% fluocinolone acetonide)
- **Peeling**—Intermittent peeling either 35% GA peel or JP as per protocol

Pretreatment MASI score noted and pretreatment photograph were taken.

RESULTS AND DISCUSSION

Sixty cases of Melasma attending Skin-VD OPD, Baroda Medical College from September 1, 2016, to June 30, 2017, were enrolled.

Out of 60 cases, 50 cases had completed the treatment as per protocol (14 weeks) while 10 cases had left the study after 6 weeks of enrolment.

The data has been analyzed and the results produced are as follows.

- In the present study, the youngest case enrolled was 26 years old and eldest was 46 years old. (Table I)
- Highest number (total 19) of cases were found in the age group of 36–40 years.
- 60% cases were in 31–40 year age group.

In a large global survey with 324 melasma women, the mean age of melasma cases was 34 years (range 14–65 years) (5).

Table I
Melasma in Female: Age at Presentation

Age Group (in years)	Total (<i>n</i> = 60)	Percentage (100%)
26–30	13	21
31–35	17	28
36–40	19	32
41–45	10	17
46–50	01	2

Table II
Melasma in Female: Duration at Time of Enrollment

Duration	Number of Cases (<i>n</i> = 60)	Percentage Cases (%)
< 6 months	2	3
6 month to 1 year	17	28
1–5 year	27	45
> 5 year	14	23

Table III
Melasma: Triggering Factors

Triggering Factors	Number of Cases (<i>n</i> = 60)	Percentage Cases (%)
Past history of OC pill	3	5
History of cosmetic product application	4	7
History of sun exposure (Outdoor work)	6	10
History of thyroid abnormality	2	3
History of menstrual irregularity	7	12

OC: oral contraceptive.

Table IV
Melasma in Female: Clinical Types

Type of Melisma	Cases (<i>n</i> = 60)	
	No.	%
Centrofacial (Cf)	32	53%
Malar (M)	27	45%
Mandibular (Mn)	1	2%

Table V
Baseline MASI Score (*n* = 50)

MASI Score	GA Peel (<i>n</i> = 25)	Jessner peel (<i>n</i> = 25)	Total (50 cases)
≤5	—	—	—
5–10	5	5	10
10–15	8	7	15
15–20	7	7	14
>20	5	6	11

GA: glycolic acid; MASI Melasma Area and Severity Index.

In Brazil, it was found that most of the female cases (> 50%) developed melasma between the second and fourth decades of life (20–35 years of age) (6).

In India and Singapore, the average ages of disease onset were higher: 30 and 38 years, respectively (7,8).

In the present study, 45% of cases had history of melasma for the duration ranging from 1 to 5 years at the time of enrollment. Only 3% cases presented within 6 months of onset. (Table II)

Table VI
Pre- and Posttreatment MASI Score (A) Glycolic Acid Peel Group ($n = 25$)

No.	MASI Score			Difference	Improvement in Percentage (%)
	Baseline	6 week	14 week		
1	18	16	10.8	7.2	54
2	24.4	20.3	12.6	11.8	48
3	21.9	17.8	7.9	14	64
4	12.7	10	5	7.7	62
5	10.8	7.9	3	7.8	72
6	19.8	14.8	10.8	9	46
7	8.2	7.5	7	1.2	15
8	9	8.7	2.8	6.2	69
9	14.8	12.6	5.1	9.7	66
10	12	8.7	5.2	6.8	57
11	21.6	17.4	7.4	14.2	66
12	19.2	12.6	8.7	10.5	55
13	23.1	19.8	6.2	16.9	73
14	17.4	12.8	5.7	11.7	67
15	13.9	10	5	8.9	64
16	6.3	5	3	3.3	52
17	12.6	8.7	4.9	7.7	61
18	6.6	5	1.6	5	76
19	16.6	13.2	8.7	7.9	48
20	17.4	14.2	6.2	11.2	64
21	7.8	5.1	3.2	4.6	59
22	21.9	19.2	8.2	13.7	63
23	17.4	12.6	7.4	10	57
24	13.2	8.7	6.2	7	58
25	14.7	6.8	5	9.7	66

MASI: Melasma Area and Severity Index.

Hormonal factors (menstrual irregularities and OC pills) and outdoor occupation were commonly reported as triggering factors. Out of 60 cases 12% cases had history of menstrual irregularity, 5% cases had past history of taking OC pill and 10% cases had history of outdoor work. As per Tamega Ade A et al. study of facial melasma in Brazilian women, the most commonly reported trigger factors were pregnancy (36.4%), contraceptive pills (16.2%) and intense sun exposure (27.2%) (6). (Table III)

In present study, 13% (eight cases) cases had positive family history (first-degree relatives) of melasma.

In a study involving 324 cases in nine centers around the world, it was observed that 48% of individuals with melasma reported family history of at least one relative with this dermatosis and, among those, 97% were in first-degree relatives (5).

In Brazil, among the 302 cases had been studied, 56% of cases shown positive family history, particularly, in cases with darker skin types (African American) (7).

Conversely, low positivity of family history in India (33%) and Singapore (10%) suggests that the development of the disease may have epigenetic hormonal control, as well as the influence of environmental stimuli, such as ultraviolet (UV) radiation (7–9).

Table VII
Pre- and Posttreatment MASI Score (B) Jessner Peel Group ($n = 25$)

No.	MASI Score			Difference	Improvement in Percentage (%)
	Baseline	6 week	14 week		
1	13.2	10.2	4.4	8.8	66
2	22.5	17.4	11.1	11.4	51
3	20.1	18.2	16.8	3.3	16
4	13.9	10.8	6.4	7.5	54
5	16.8	9.7	6.8	10	60
6	21	7.6	5.1	15.9	76
7	10.9	7.6	3.7	7.2	66
8	11.7	5.6	4.8	6.9	59
9	16.8	10.8	9.7	7.1	42
10	7.6	5	2.7	4.9	64
11	12.6	10.8	6	6.6	52
12	18.5	17.2	5	13.5	73
13	10	4.4	3.9	6.1	61
14	15.6	10.8	5.1	10.5	67
15	25	12.2	10	15	60
16	7.9	5.6	3.7	4.2	53
17	20.2	17.3	8.5	11.7	58
18	19.4	10.8	8.3	11.1	57
19	8	5.1	3.4	4.6	58
20	12	10	4.8	7.2	60
21	8.3	5.6	2.3	6	72
22	15.9	13.8	5.8	10.1	58
23	23.1	18.9	6.8	16.3	71
24	16.8	12.5	8.3	8.5	51
25	14.4	10.2	3.7	10.7	74

MASI: Melasma Area and Severity Index.

Table VIII
Improvement in MASI Score (%) ($n = 50$)

Improvement	GA Peel Group No. of Cases ($n = 25$)	Jessner Peel Group No. of Cases ($n = 25$)
Excellent (>90%)	—	—
Good (>75–90%)	1 (4%)	1 (4%)
Moderate (>50–75%)	20 (80%)	22 (88%)
Inadequate (<50%)	4	2

GA: glycolic acid; MASI: Melasma Area and Severity Index.

In the present study, the most common pattern of melasma was centrofacial, in 32 cases (53%), which was followed by malar pattern, in 27 cases (47%), and mandibular pattern, in one case (2%). (Table IV)

According to Sanchez N.P. et al., centrofacial pattern is the most common pattern (affecting 63% of all cases) followed by malar pattern (21%) and mandibular pattern (16%) (7).

- Fifty melasma cases completed the study (14 weeks) were evaluated for comparative efficacy and adverse cutaneous side effect of GA peel versus JP as an adjuvant to topical triple combination therapy.

Table IX
Pre- and Posttreatment Average MASI Score: at the 0 Week (i.e. Baseline) and at the 14 Week (i.e. End of Treatment)

Peel Group	Average MASI score		Percentage Improvement (%)
	Pretreatment	Posttreatment	
Glycolic acid peel ($n = 25$)	14.37	6.32	58.56
Jessner peel ($n = 25$)	15.68	6.28	59.12

MASI: Melasma Area and Severity Index.

Table X
Adverse Cutaneous Side Effects ($n = 50$)

Type of side effects	Glycolic acid peel ($n = 25$)	Jessner peel ($n = 25$)	Total
Erythema	6	14	20
Burning	4	6	10
Pigmentation	3	2	5
Dry skin	1	2	3

In GA peel group, average baseline score was 14.37; after 6 week score was reduced to 12.12 and at the end of treatment (14 weeks), it was further reduced to an average score of 6.32. There was a significant difference between baseline and at the end of treatment MASI score. (Tables V, VI)

Statistical analysis: Paired t -test was applied.

1. For baseline and 6 weeks MASI score: Extremely statistically significant difference was found between the two groups; $p < 0.0001$
2. For baseline and 14 weeks MASI score: Extremely statistically significant difference was found between the two groups; $p < 0.0001$

(Statistical significance at the level of 95% confidence interval)

Average reduction in MASI score in cases with GA peel group = 58.56% (Figures 1, 2, 3, 4)

In JP group, the average baseline score was 15.68, after 6 week score was reduced to 8.5, and at the end of treatment (14 week), it was further reduced to average score of 6.28. (Figures 5, 6, 7, 8). There was a significant difference between baseline and at the end of treatment MASI score. (Table VII)

Statistical analysis: Paired t -test was applied.

- For baseline and 6 weeks MASI score: Extremely statistically significant difference was found between the two groups; $p < 0.0001$
- For baseline and 14 weeks MASI score: Extremely statistically significant difference was found between the two groups; $p < 0.0001$

(Statistical significance at the level of 95% confidence interval)

Average reduction in MASI score in cases with JP group = 59.12%

In GA peel group, 84% cases had moderate to good improvement, whereas in JP group 92% cases had moderate to good improvement. (Table VIII)

Pre treatment



Figure 1. Pretreatment glycolic acid peel.

Post treatment



Figure 2. Posttreatment glycolic acid peel.

Pre treatment



Figure 3. Pretreatment glycolic acid peel.

Post treatment



Figure 4. Posttreatment glycolic acid peel.

Pre treatment



Figure 5. Pretreatment Jessner peel.

Post treatment



Figure 6. Posttreatment Jessner peel.

Pre treatment



Figure 7. Pretreatment Jessner peel.

Post treatment



Figure 8. Posttreatment Jessner peel.

Statistical analysis (according to chi-square test):

There is no significant difference found in results between the two groups. Both the treatments have similar effects on MASI score reduction. The p value is > 0.05 at 95% confidence level.

In GA peel group, average reduction in MASI score from 14.37 at baseline to 6.32 at 14 weeks (end of treatment), that is, 58.56%.

In JP group, average reduction in MASI score from 15.68 at baseline to 6.28 at 14 weeks (end of treatment), that is, 59.12%. (Table IX)

There is no significant difference in improvement.

Statistical analysis (according to chi-square test)

The p value is > 0.05 at 95% confidence level. It means that there is no significant difference between the two groups. Both the treatments have similar effects on MASI score reduction. None is superior to other according to statistical analysis.

Erythema was the most common cutaneous side effect seen in 20 cases. It was followed by burning in 10 cases, hyperpigmentation in five cases and dry skin in three cases.

Erythema was seen in 14 cases of JP group and six cases of GA peel group.

Burning was present in six cases of JP group and four cases of GA peel group.

Hyperpigmentation was seen in three cases of JP group and two cases of GA peel group.

Dry skin was present in one case of JP group and two cases of GA peel group. (Table X)

Statistical analysis (according to chi-square test)

There is no significant difference between the two groups. The study also infers that side effects are similar in both the methods. The p value is > 0.05 at 95% confidence level.

Cutaneous side effects were seen in 25 cases out of 50 cases. It was more with JP group (17 cases) as compared to 35% GA peel group (eight cases). But it was not statistically significant.

MELASMA AREA AND SEVERITY INDEX SCORE

MASI score is developed by Kimbrough-green et al. for the assessment of the melasma. The severity of melasma in each of the four regions (forehead, right malar region, left malar region, and chin) is assessed based on the total area involved (A), darkness (D), and homogeneity (H).

A numerical value assigned for the corresponding percentage area involved (A) is as follows:

- 0 = no involvement
- 1 = <10% involvement
- 2 = 10–29% involvement
- 3 = 30–49% involvement
- 4 = 50–69% involvement
- 5 = 70–89% involvement
- 6 = 90–100% involvement

The **darkness of melasma (D)** is compared to the normal skin and graded on the scale of 0–4 as follows:

- 0 = normal skin color without evidence of hyperpigmentation
- 1 = barely visible hyperpigmentation
- 2 = mild hyperpigmentation
- 3 = moderate hyperpigmentation
- 4 = severe hyperpigmentation

Homogeneity of the hyperpigmentation (H) is also graded on the scale of 0–4 as follows:

- 0 = normal skin color without evidence of hyperpigmentation
- 1 = specks of involvement
- 2 = small patchy areas of involvement < 1.5 cm diameter
- 3 = patches of involvement > 2 cm diameter
- 4 = uniform skin involvement without any clear areas

To calculate the MASI score, the sum of the severity grade for darkness (D) and homogeneity (H) is multiplied by the numerical value of the area (A) involved and by the percentage of the four facial areas (10–30%).

$$\text{MASI} = 0.3(\text{Df} + \text{Hf})\text{Af} + 0.3(\text{Drm} + \text{Hrm})\text{Arm} + 0.3(\text{Dlm} + \text{Hlm})\text{Alm} + 0.1(\text{Dc} + \text{Hc})\text{Ac}$$

(f = forehead, mr = right malar, ml = left malar, c = chin)

- Subjects were queried at each visit about the effect of drug and signs of improvement.
- Adverse event: nature and type of event was recorded in the proforma.
- Finally, all findings were analyzed statistically, and attempt was made to compare the results of the present study.

TREATMENT PROTOCOL

Evaluation, MASI score, test pre peel either **GA** (Odd No.) or **JP** (Even No.)

TC application **alternate night** for 1 week

Then **daily** at night for 1 week, to stop TC before 1 day of next visit



Evaluation, MASI score

Add peel either **GA** (Odd No.) or **JP** (Even No.)

Restart TC on next day.

Stop TC before 1 day of next visit.



Evaluation, MASI score

Do peel according to previous peel

Restart TC on next day.

Stop TC before 1 day of next visit.



Evaluation, MASI score.

Do peel according to previous peel.

Restart TC on next day.



Stop all treatment.

Continue sunscreen in day time.

Observation period—**2 Months**

Recurrence

- After two months of observation period, out of 50 cases who completed treatment, five cases came with recurrence. Among them, 12% cases were in GA peel group and 8% cases were in JP group.

CONCLUSION

According to present study, safety and efficacy profile of 35% GA peel versus JP was almost same. Both can be used as an adjuvant to topical triple combination therapy of 2% hydroquinone, 0.025% tretinoin, and 0.01% fluocinolone acetonide in females suffering from melasma.

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