A comparative study between the efficacy of 35% glycolic acid peel and triple combination cream in the treatment of melasma

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Abstract

Introduction: Melasma is an acquired symmetric hypermelanosis characterized by irregular light to greyish brown macules on sun exposed skin, usually face. It is more seen in women and is more prevalent in individuals with skin type IV, V and VI. The exact etiology of melasma is not known therefore various treatment modalities have been employed. These include topical depigmenting agents like hydroquinone, azelaic acid, retinoids, chemical peels, low and high fluence lasers, yet none have proven to being fully beneficial in our study, we aim at comparing the therapeutic efficacy of 35% glycolic peel and triple combination cream in the treatment of melasma.

Materials and Methods: It is a hospital based study. 60 diagnosed cases of melasma were randomly enrolled equally to two groups P and Q. Group P patients given serial 35% Glycolic acid peel and group Q patients given Triple combination cream to be applied topically once at night daily. Followed up on 4th, 8th and 12th week. At each visit clinical response to treatment was calculated using MASI score.

Results: At 4th, 8th and 12th week post treatment evaluation, Triple combination cream had an overall superiority to serial 35% glycolic acid peel as a topical hypopigmenting agent.

Conclusion: The results of the study show that Triple combination cream is a better hypopigmenting agent with rapid rate of clinical improvement when compared to 35% glycolic acid peel.

Keywords: Melasma, Triple combination cream, 35% Glycolic acid peel.

Introduction

Melasma is a common hyperpigmentary disorder known for a considerable time. It not only causes a tremendous emotional and psychosocial distress but also plays a major role in affecting the quality of life.[1-3] Individuals with melasma have been described as enduring great emotional suffering.[4] The condition is particularly disturbing to patients because of its location on the face.[5] In a study using proven instruments developed particularly to measure health-related quality of life in melasma, three life areas most affected by the condition were social life, recreation and leisure, and emotional well-being.[6]

It is particularly discomfort to women from cultures favouring impeccable skin i.e. in some Asian cultures facial pigment abnormalities are related with bad fortune.[7] In Latin cultures, pigmentary irregularities are considered disfiguring, and have been associated with ill health or poor nutrition.[8]

Melasma is an acquired symmetric hypermelanosis characterized by uneven light to grayish-brown macules on sun exposed skin with a propensity for face.[9] Women of child bearing age are commonly affected than men. Both men and women with the disease have same clinical and histological features.[10] All races may be affected by melasma but usually seen among individuals of skin types IV to VI, especially in women of Hispanics, Orientals and Indo-Chinese origin who are exposed to high intensity UV radiations. One of the most common pigmentary disorder in India, but exact population based incidence not been recorded yet.[12] Clinically three patterns of melasma are observed: centro facial (63%), malar (21%) and mandibular (16%).[13]

Melasma can be divided into 3 types, they are epidermal, dermal and mixed based on visible light, Wood's light examination and skin histology. The epidermal type has increased melanin mainly in the basal and suprabasal epidermis. Macules are high lightened when examined through Wood's lamp. The dermal type has melanin-laden macrophages in the perivascular distribution in the superficial and deep dermis. There is no Wood's lamp accentuation in dermal type. The mixed type has elements of both epidermal and dermal and there is accentuation of the epidermal component through Wood's lamp. A fourth type known as Wood's light in apparent is also illustrated.[14]

Depending on natural history of the lesions, melasma can be classified into transient and persistent types.[15] The transient type fades away within one year of cessation of hormonal stimulus like pregnancy or usage of oral contraceptive pills. The persistent type continues to be present more than one year irrespective to the hormonal stimulus and is caused by the action of UV rays and other factors.

While the exact etiology of melasma remains unknown, several risk factors are incriminated including exposure to UV radiation and visible light, genetic influences, pregnancy, use of oral contraceptives, estrogen and progesterone therapy, diethyl-stilbesterol, use of certain cosmetics and

endocrine factors associated with mild ovarian dysfunction in women and testicular resistance in men. The thyroid dysfunction and medications including anticonvulsants and photosensitizing agents have also been implicated.[16-21]

The treatment of melasma has been a challenge due to the non-availability of a universally effective agent. The majority of existing treatments temporally fades the melasma but the condition usually recurs. The principles of therapy include avoidance of exposure to sunlight, inhibition of the activity of melanocytes, inhibition of synthesis of melanin, removal of melanin and disruption & dispersion of melanin granules.[22] The standard treatment for melasma includes elimination of any possible risk factors coupled with use of a sunscreen and hypopigmenting agents like hydroquinone, azelaic acid, kojic acid often in combination with other therapies such as retinoids, topical corticosteroids and chemical peeling using alpha hydroxyl acids. Hydroquinone has well established efficacy against hyperpigmentation but can also lighten normal skin and can cause harmful reactions.[9,23] Chemical peeling is based on skin healing pattern seen with chemical burns. This method of skin rejuvenation has been in mode for long, though in less polished ways. Cleopatra centuries ago used sour milk for facial rejuvenation. Since then a number of chemicals have been used as peeling agents, out of which the most productive ones are the alpha hydroxyl acids. These have been shown to regulate stratum corneum barrier function, improved photodamaged skin and fine wrinkles on face.[24,25]

Glycolic acid is one of the most commonly used and adaptable peeling agent and a member of alpha hydroxy acids. It has been found used in a variety of skin disorders including disorders of keratinization like xerosis, icthyosis, commoner skin pigmentary changes like post inflammatory hyperepigmentation, melasma, acne, wrinkles, warts, actinic seborrhoeic keratosis and skin rejuvenation.[26] Glycolic acid can be seen in higher concentrations in chemical peels used in dermatology clinics. It is a versatile peeling agent. It alters dermal collagen and matrix through fibroblast modulation and also has an antioxidant action, thus offering photoprotection.

Hydroquinone is the prototype depigmenting agent used in melasma that exerts its effect by inhibiting tyrosinase, the rate limiting enzyme in melanin synthesis.[27,28] This prototype drug is combined with many agents including retinoids and topical steroids to increase its efficacy in causing a pigment dilution in melasma.[29] Topical steroids have also been used in melasma either alone[30,31] or in combination with hydroquinone and retinoids.[28] Kligman's formula is a combination therapy in the management of melasma that has been in use for more than two decades.[3] This original formula employed a mild steroid dexamethasone 0.1%) in combination with 0.1% tretinoin, and 5% hydroquinone in a cream base.

Materials and Methods

This is a hospital based, prospective randomized study. Duration of the study is one year from January 2016 to December 2016. The study is conducted at Dermatology opd of a private medical college. The study was approved by the Institute's Review Board and Ethics Committee. 60 diagnosed cases of melasma is randomly enrolled equally into two equal groups P and Q. Patients would be diagnosed on the basis of morphology (symmetrical, circumscribed brown to grey hypermelanosis). Group P patients received serial 35% Glycolic acid peels and Group Q patients received triple combination cream (4% hydroquinone, 0.05% Tretinoin and 0.1% mometasone furoate cream) once daily application at night. Patients were reviewed on 4th, 8th and 12th week and response to treatment was calculated using MASI score. Statistical analysis was carried out using the statistical software SPSS 17.0. Inclusion criteria are, clinically diagnosed cases of melasma with age group 18 years and above and previously untreated cases. The exclusion criteria are, patients on oral contraceptive pills or hormone replacement therapy, pregnant women and lactating mothers, patients with any systemic illness or endocrinological disease, history of sensitivity to 35% glycolic acid peel and non consenting patients. Photograph at the beginning and at the end of the treatment was taken for documentation. All patients were advised sun protection and to use sunscreen lotion for outdoor activities during the study period. A detailed history was taken in each case with particular reference to the aetiological factors. A thorough general physical examination of each patient was done with the informed and written consent of the patient. A systemic examination was done to rule out any systemic illness and a detailed cutaneous examination was carried out. A battery of haematological and biochemical investigations were carried out in every case in the study. Complete hemogram, liver function tests, kidney function tests, blood sugar–fasting/post prandial, lipid profile, serum electrolytes, urine–routine/microscopy, stool-microscopy were done. The pattern of melasma was noted. Clinical pattern of melasma, pattern of sun exposure, comparison within the groups, effectiveness within the groups and side effects are recorded. Data obtained are presented as percentages.

Results

A total number of 60 patients with facial melasma attending the outpatient Department of Dermatology, Venereology and Leprosy of our Medical college and Hospital, who fulfilled inclusion and exclusion criteria were studied during the year 2016.

Table 1: Clinical pattern of melasma in each study group

		Glycolic acid Peel	Triple combination cream	Total
Pattern	Centro facial	5 (16.7%)	6 (20.0%)	11 (18.3%)
	Malar	22 (73.3%)	20 (66.7%)	42 (70.0%)
	Mandibular	3 (10.0%)	4 (13.3%)	7 (11.7%)
Total		30 (100.0%)	30 (100.0%)	60 (100.0%)

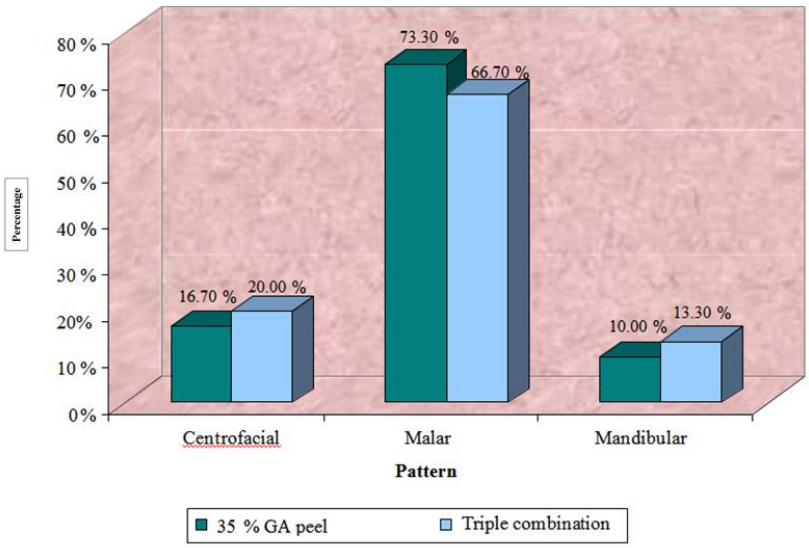

Fig. 1: Clinical Pattern of melasma in each study group

A centro facial pattern was observed in 11 patients (18.3%), 42 patients (70%) had a malar distribution of lesions and 7 patients (11.7%) had a mandibular pattern of melasma. The distribution of these various clinical patterns among the two regimen was uniform statistically.

Table 2: Pattern of sun exposure in both the study groups

		35% Glycolic peel	Triple combination cream	Total
Sun exposure	< 1 hr	5 (16.67%)	7 (23.33%)	12 (20%)
	1-2 hrs	10 (33.33%)	12(40%)	22 (36.67%)
	> 2 hrs	15 (50%)	11 (36.67%)	26 (43.33%)
Total		30 (100.0%)	30 (100.0%)	60 (100.0%)

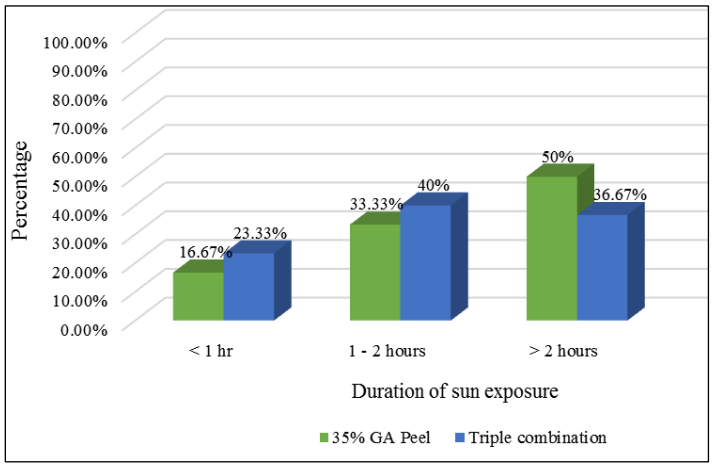

Fig. 2: Pattern of sun exposure in both the study groups

The effect of duration of sun exposure in the 35% Glycolic acid peel group and Triple combination cream group was significant.

Table 3: Effectiveness within the group

	MASI score	N	Minimum	Maximum	Mean	Std. Deviation	Median	Anova F	P value
35% Glycolic acid peel	Week 0 Week 4 Week 8 Week 12	30 30 30 30	2.4 2.1 2.1 1.8	23.4 23.4 21.6 21.0	11.177 10.547 9.527 8.773	6.4817 6.5585 5.9767 5.6743	10.600 9.600 8.550 7.350	27.4	p<0.001 HS
Triple combination cream	Week 0 Week 4 Week 8 Week 12	30 30 30 30	1.2 2.4 1.2 0.6	38.4 35.4 27.0 18.3	15.613 12.180 8.060 4.334	9.6626 8.2989 6.2829 3.5709	12.750 9.900 6.600 3.900	52.303	p<0.001 HS

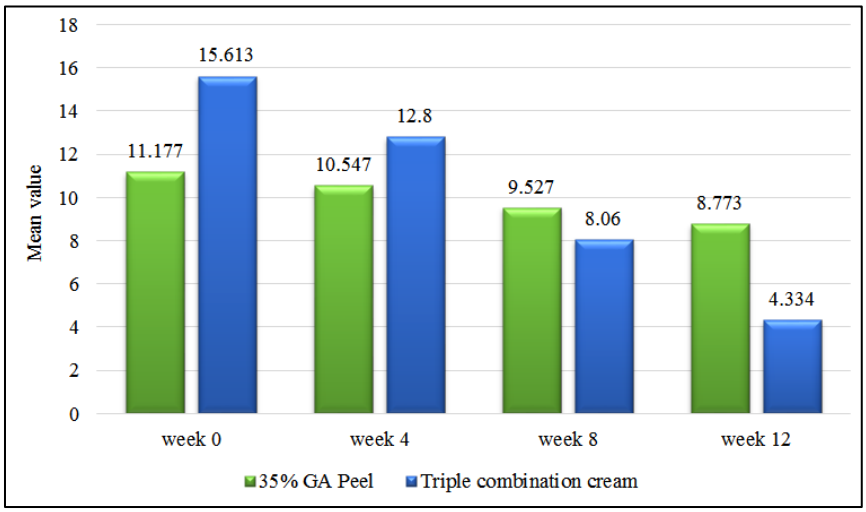

Fig. 3: Effectiveness within the group

Table 4: Pairwise comparison

	(I) factor1	(J) factor I	Mean Difference (I-J)	Std. Error	p	
35% Glycolic acid peel	Week 0 MASI	Week 4 MASI Week 8 MASI Week 12 MASI	.630 1.650* 2.403*	.256 .340 .412	.121 P<0.001 P<0.001	NS HS HS
	Week 12 MASI	Week 0 MASI Week 4 MASI Week 8 MASI	-2.403* -1.773* -.753*	.412 .268 .178	P<0.001 P<0.001 .001	HS HS HS
Triple combination cream	Week 0 MASI	Week 4 MASI Week 8 MASI Week 12 MASI	3.521* 7.741* 11.652*	.664 .981 1.462	P<0.001 P<0.001 P<0.001	HS HS HS
	Week 12 MASI	Week 0 MASI Week 4 MASI Week 8 MASI	-11.652* -8.131* -3.910*	1.462 1.207 .729	P<0.001 P<0.001 P<0.001	HS HS HS

Based on estimated marginal means *. The mean difference is significant at the 0.05 level.

Table 5: Comparison between the groups

		N	Minimum	Maximum	Mean	Std. Deviation	Median	Z value*	P value
Change in MASI (week 0-4)	35% GA peel	30	.0	6.0	.630	1.4037	4.276	4.276	P<0.001, HS
	Triple combination cream	30	-1.2	12.7	3.433	3.5450	5.074		
Change in	35% GA peel	30	.0	8.4	1.650	1.8636	.900	5.074	P<0.001,

MASI week 0-8)	Triple combination cream	30	-1.2	18.3	7.553	5.2897[a]	6.150		HS
Change in MASI (week 0- 12)	35% GA peel	30	.0	9.3	2.403	2.2541	1.500	5.371	P<0.001, HS
	Triple combination cream	30	-1.2	33.6	11.423	7.8362	9.600		

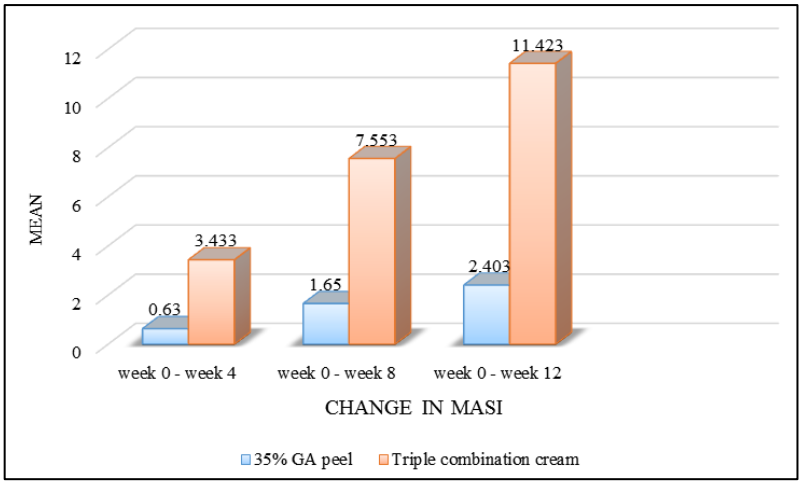

Fig. 4: Comparison between the groups

Patients who received 35% glycolic acid there was no significant change from week 0 to 4 weeks (p=0.121) but there was significant decrease from week 0 to 8weeks (p<0.001). Also there was significant change from week 0 to 12 weeks (ANOVA F=27.4, p=<0.001).

Patients who received triple combination there was significant decrease from week 0 to 4weeks (p<0.001), there was significant decrease from week 0 to week 8 (p<0.001). And also, there was significant decrease from week 0 to 12 weeks (ANOVA F=52.303, p=<0.001).

In comparison between the two groups, at 4th week 35% glycolic acid (mean 0.630±1.403) showed less effect than triple combination cream (mean 3.433 ± 3.54).

At 8th week, compared to 35% glycolic acid (mean 1.650±1.863) triple combination showed better effect (mean 7.553±5.289).

Similarly, at 12th week, triple combination showed better effect (mean 11.423±7.836) compared to 35% glycolic acid (mean 2.403±2.254).

So, at the end of treatment triple combination cream showed better efficacy than 35% glycolic acid peel.

Table 6: Side effects

		35% Glycolic acid peel	**Triple combination cream**	**Total**
Side effect	Absent	28 (93.33%)	28 (93.3%)	56 (93.33%)
	Present	2 (6.67%)	2 (6.67%)	4 (6.67%)
Total		30 (100%)	30 (100%)	60 (100%)

χ^2=0.001, p=0.999, NS

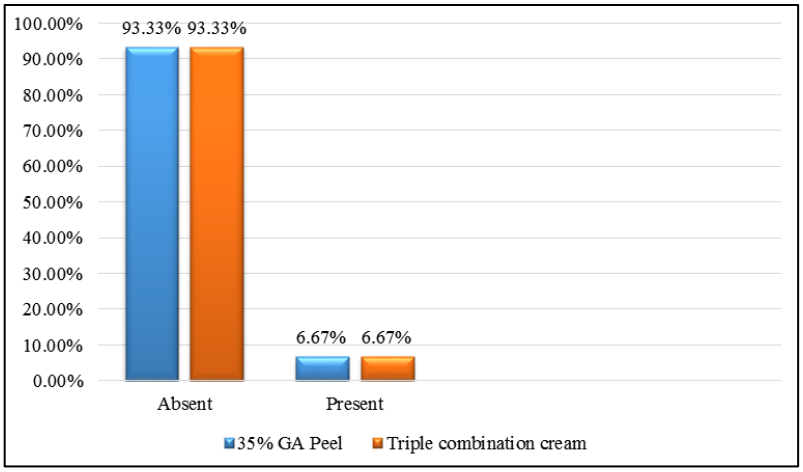

Fig. 5: Side effects

Side effects were noted in 1 patient receiving 35% glycolic acid peel (3.3%) and 2 patients receiving triple combination cream (6.7%).

Triple Combination Cream

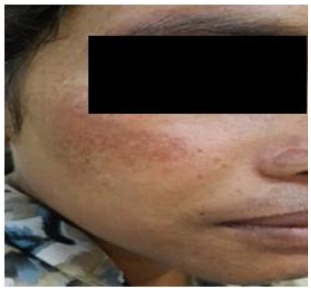

Fig. 1: Pre-treatment photograph (malar type)

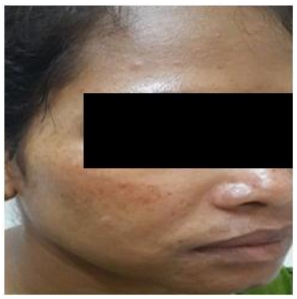

Fig. 2: Post-treatment photograph

Triple Combination Cream

Fig. 3: Pre-treatment photograph (malar type)

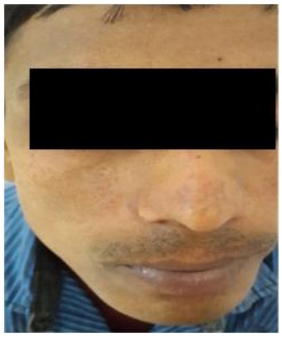

Fig. 4: Post-treatment photograph

35 % Glycolic Acid Peel

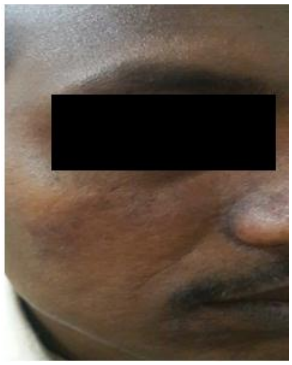

Fig. 5: Pre-treatment photograph (malar type)

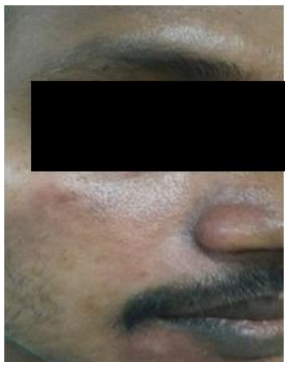

Fig. 6: Post-treatment photograph

35% Glycolic Acid Peel

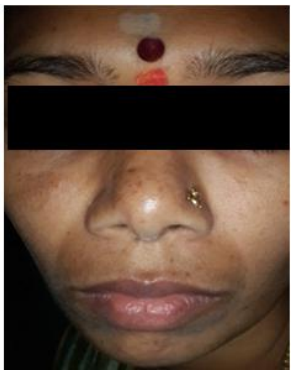

Fig. 7: Pre-treatment photograph (malar with centro facial type)

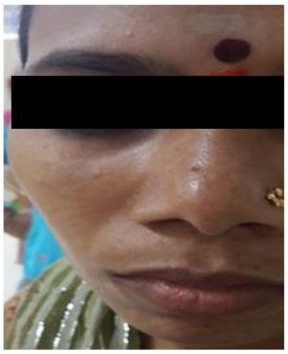

Fig. 8: Post-treatment photograph

Discussion

60 patients with facial melasma attended the out patient department of Dermatology, Venereology and Leprosy in the Medical College and Hospital, Mangalore were included in the study.

Melasma is a common condition that develops uniquely on the exposed areas of the face. The basic mechanisms involved in the pathogenesis of this disorder is still not known. Despite the use of large number of treatment modalities available, the treatment of melasma is often unsuccessful and disappointing and is still a challenge.

Melasma occurs in middle aged adults and is more commonly seen in females.

Mean age of onset in this study is 38.85 years. This was similar to the study done by Vazquez et al.[10] A study by Griffiths CEM et al showed an average age of 30 years at onset.[35] The female preponderance is attributed mainly to hormonal factors. Our study showed a higher number of female cases, M:F::1:4.5. This was also similar to the studies done by Nanda et al showing male to female ratio of 1:4.22.11

Malar pattern was the commonest in this study, occurring in 70% of patients, followed by centrofacial in 18.3% of cases and mandibular in 11.7% of cases. This is similar to the study by Lim et al[38] and Chan R where majority of patients had malar pattern. A study by Vazquez et al showed equal occurrence of centrofacial and malar pattern (41.1%) and mandibular pattern was the least common (11.1%).[10] Studies done by R.Sarkar et al[10] and Vazquez[10] concluded that centrofacial was the commonest pattern in males (48.39% & 44.1% respectively). Similarly Griffiths CEM et al showed that centrofacial was the predominant pattern of involvement.[35]

Similar to other studies, all our patients had history of sun exposure. However the duration varied. 20% patients had < 1hour of sun exposure, 36.67% patients had 1-2 hours of sun exposure, and 43.33% patients had > 2 hours of sun exposure. According to our study sun exposure had a significant association with occurrence of melasma. Approximately 80% of our patients gave history of ≥2 hours of sun exposure. Griffiths CEM, in their study showed that sunlight was an exacerbating factor in 98% cases.[35]

There is a significant link between a positive family history and occurrence of melasma in our patients. 70% of patients gave a positive family history of melasma.

In the study by Griffiths CEM et al, 47% patients gave a positive family history of first degree relative being affected.[35] Vazquez M et al showed 70.4% occurrence of positive family history which was similar to our study.[10]

90% of patients denied the use of any kind of cosmetics and only 10% used cosmetics. Majority of these included over the counter (OTC) available fairness creams, winter cold creams, depigmenting agents, mustard oil and coconut oil. In contrast, a study by Sanchez et al, nearly all patients with melasma reported using cosmetics.[14] No specific ingredient in the cosmetic preparation has been implicated.

There was no history of an underlying systemic disorder in any of our patients.

Comparing the effectivity of 35% glycolic acid peel and Triple combination cream it was seen that at 4th, 8th and 12th week of post treatment evaluation of MASI from 0 week, the mean change in MASI following application of 35% glycolic acid peel was less than that of Triple combination cream, which was statistically highly significant (0.630, 1.650, 2.403 and 3.433, 7.533, 11.423 respectively, $p<0.001$). This is in contrast to the study done by Sarkar et al, on 40 Indian patients who were divided into two equal groups of 20 each where one of was treated with a combination of serial Glycolic acid peels combined with Triple combination cream and a second group treated with only Kligman's triple combination cream.[37] The results showed a significant decrease in the MASI score from 0 to 12 weeks in both groups ($P <.001$). The group receiving the glycolic acid peels showed a more rapid and greater improvement, with statistically significant results ($P <.001$). In this study 35% glycolic acid peel was not used alone.

At 4th week, the mean change in MASI was 3.433 for the Triple combination cream group and 0.630 for

the 35% glycolic peel group which was statistically highly significant (p=<0.001). The mean difference was highly significant for the Triple combination cream group (p<0.001) and not significant for the 35% glycolic acid peel group. This shows that Triple combination cream acts faster and more effectively than 35% glycolic acid peel. This was similar to a multicentric safety study performed over 12 month period on patients affected with moderate to severe melasma. By month twelve, the melasma was resolved or almost resolved in 80 percent of the subjects.[14] Torok. et al also reported the efficacy of Triple combination creams in the treatment of melasma.[36]

At 8th weeks, the mean change in MASI was 7.553 for the Triple combination cream group and 1.650 for the glycolic acid peel group which was statistically highly significant (p=0.001). This shows that Triple combination cream was more effective than 35% GA peel at 8 weeks.

At the end of 12 weeks post treatment period, Triple combination cream proved to be superior to 35% glycolic acid peel with respect to mean reduction in MASI (11.423 vs 2.403, p=<0.001 which was highly significant). This indicates that Triple combination cream is a better topical agent in the treatment of melasma when compared to 35% glycolic acid peel and also, Triple combination acts faster than 35% glycolic acid peel.

In the two groups included in our study, only 2 patients in each group had side effects which were mild. Patients receiving 35% glycolic acid peel complained of mild erythema, burning and stinging sensation. 2 patients receiving Triple combination cream had mild erythema. Similar to patients in the study done by Sarkar et al where 35% glycolic acid peel was associated with mild erythema, burning and stinging sensation.[37] Multiple studies have shown side effects with long term use of Triple combination creams associated with the steroid component of the cream like atrophy, hypopigmentation, telangiectasia but none of these side effects were observed in any of our patients who were on 12 week long treatment with Triple combination cream.

Conclusion

The results of this study shows that both Triple combination cream and 35% glycolic acid peel are effective topical agents in the treatment of melasma. Triple combination cream is a better topical hypopigmenting agent with rapid rate of clinical improvement. The side effects of both the agents were not significant.

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