



To Compare the Clinical Efficacy and Safety Of 20% Mandelic Acid Peel Versus 20% Arginine Peel in the Treatment of Peri-Orbital Hyperpigmentation - A Prospective Randomised Controlled Trial

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Abstract

Background: Periorbital hyperpigmentation (POH) is a very common, yet unexplored aesthetic condition. Topical therapy is mainstay of treatment which includes chemical peels. **Objective:** To compare the clinical efficacy and safety of 20% Mandelic acid peel versus 20% Arginine peel in the treatment of constitutional type of peri-orbital hyperpigmentation. **Method:** 24 patients of constitutional POH were enrolled for 12 weeks. They were divided into two groups of 12 each. In 1st group 20% Arginine peel and 2nd group 20% Mandelic peel sessions were performed at 3 weekly intervals. Clinical improvement was assessed objectively using POH grading, physician's and patient's global assessment, and patient's global tolerance. **Results:** Significant improvement in periorbital hyperpigmentation was noted in both the groups. Physician's and patient's global assessment was excellent with mandelic peel as compared to arginine peel. The incidence of side effects in the form of erythema and itching was maximum with mandelic peel and least with Arginine peel, which did not necessitate cessation of therapy. **Conclusion:** Mandelic peel showed the better results among the two peels; however, Arginine peel emerged as a safe and effective modality for the treatment of POH.

Keywords: Arginine Peel; Chemical Peeling; Mandelic Peel; Periorbital Hyperpigmentation

Introduction

Periorbital hyperpigmentation (POH), commonly referred to as dark circles, infraorbital pigmentation, or periorbital melanosis, is characterised by bilateral, symmetrical darkening of the skin surrounding the eyes. It primarily affects the lower eyelids but may also extend to the upper eyelids, eyebrows, cheeks, temples, and nasal root (Sheth *et al.*, 2014; Hang & Lim, 2025; Badran *et al.*, 2025).

This condition is particularly prevalent in individuals of Asian descent and is recognised as a growing cosmetic concern. Studies indicate that POH most commonly affects individuals between 16 and 25 years of age (47.5%) and is significantly more frequent in women (81%), especially among homemakers (45.5%) (Sheth *et al.*, 2014). In India, nearly half of the female population experiences moderate to severe dark circles, with severity increasing with age (Nouveau *et al.*, 2016).

Ranu *et al.* proposed a classification system for periorbital melanosis, identifying five types: constitutional, post-inflammatory hyperpigmentation (PIH), vascular, shadow effect, and miscellaneous causes. Among these, the constitutional variant is the most prevalent, followed by PIH (Dayal *et al.*,

2016). The pathogenesis of POH is multifactorial, involving both intrinsic and extrinsic contributors. While genetics play a key role, external factors such as lack of sleep, fatigue, chronic eye rubbing, UV exposure, allergic reactions, hormonal imbalances, dehydration, poor nutrition, and lifestyle habits like smoking and alcohol intake also contribute (Roh & Chung, 2009; Cymbalista *et al.*, 2012).

Treatment options for POH encompass a range of topical agents and procedural interventions. Topical therapies typically include depigmenting agents such as hydroquinone, kojic acid, arbutin, azelaic acid, tretinoin, and vitamin C. Among procedural modalities, chemical peels, laser therapy, blepharoplasty, and autologous fat transfer have demonstrated varying degrees of efficacy (Raka & Brahmbhatt, 2016).

Chemical peels have gained popularity as a minimally invasive and effective option for treating pigmentation disorders, including POH. These agents promote controlled exfoliation by inducing keratolysis and protein denaturation in the skin, which facilitates the removal of melanin from the epidermis and supports regeneration. Peels targeting the basal layer can significantly reduce pigmentary irregularities (Roberts, 2014).

Based on their depth of penetration, chemical peels are categorised into superficial (limited to the epidermis), medium (reaching the papillary dermis), and deep (extending to the reticular dermis). Superficial and medium-depth peels are frequently used in managing hyperpigmentation, either alone or in combination with topical agents (Khunger & IADVL Task Force, 2008). Alpha hydroxy acids (AHAs) and trichloroacetic acid (TCA) are among the most commonly employed agents in POH treatment. Both mandelic acid and arginine peels belong to the AHA group, with mandelic acid offering superficial to medium-depth effects, while arginine peel is primarily superficial.

AHAs—such as glycolic, lactic, citric, malic, and tartaric acids—are organic acids known for promoting exfoliation by disrupting corneocyte cohesion. They are effective in addressing acne, photodamage, pigmentation, and early signs of aging by enhancing glycosaminoglycan production and increasing skin thickness (Soleymani *et al.*, 2018). Mandelic acid, an AHA derived from bitter almonds, possesses antibacterial and depigmenting properties. It is well-suited for use in darker skin types due to its larger molecular size, which reduces the risk of irritation while promoting collagen synthesis and skin renewal (Dayal *et al.*, 2020).

In a comparative study by Rangarajaiah *et al.*, both 40% lactic acid and 40% mandelic acid peels were evaluated for treating periorbital pigmentation, with no significant difference observed in terms of patient comfort or tolerability (Rangarajaiah, 2023).

Arginine, a naturally occurring amino acid derived from sugar cane, is often combined with lactic acid to form a gentle yet effective peeling agent. It offers the benefits of exfoliation, brightening, and hydration with minimal irritation. Arginine enhances ceramide production, strengthens the skin barrier, evenly distributes melanin, inhibits tyrosinase activity, and provides antioxidant defense (Weissler *et al.*, 2017).

This study aims to comprehensively assess and compare the efficacy and safety of two commonly used chemical peels—mandelic acid and arginine—in the management of periorbital hyperpigmentation.

Methodology

This study was designed as a 12-week, non-blinded, prospective, randomised controlled trial conducted between November 2023 and February 2024 in the Department of Periodontology and Oral Implantology at I.T.S Centre for Dental Studies and Research, Muradnagar, Ghaziabad, Uttar Pradesh, India. Ethical clearance was obtained from the Institutional Ethical Committee, and informed written consent was collected from all participants following a detailed explanation of the procedure.

A total of 24 patients under the age of 18 years presenting with constitutional periorbital melanosis (POM) were enrolled. A comprehensive clinical history was recorded for each participant, including demographic data, personal and family history, presence of atopy, medication use, lifestyle habits, cosmetic application, known triggers (e.g., seasonal variation, allergies, photosensitivity), and any associated pigmentation or systemic disorders such as anemia, gastrointestinal, hepatic, renal, or thyroid conditions.

Exclusion criteria included patients with a history of systemic medication use in the previous year (including hormonal therapy, antiepileptics, antidepressants, or thyroid medications), those on anticoagulant therapy, individuals with coagulopathies, pregnant or lactating women, users of oral contraceptives, and those with a history of keloids, herpes infections, active skin infections, systemic illness, recent dermatologic procedures (within the past 6 months), known allergies, photosensitivity, or unrealistic treatment expectations.

Treatment Protocol

Participants were randomly allocated into two treatment groups (n=12 per group) using a computer-generated randomisation sequence. Group A (Arginine peel group) received 20% arginine peels (Sesderma, Spain), composed of 20% arginine, 20% lactic acid, urea, aloe vera, and allantoin, while Group B (Mandelic peel group) received 20% mandelic acid peels (Sesderma, Spain), containing 20% mandelic acid and 5% thioglycolic acid. Both groups underwent treatment at three-week intervals for a total duration of 12 weeks.

During each session, patients were instructed to keep their eyes closed. The infraorbital region was cleansed using a wipe soaked in an acidified hydroalcoholic solution containing citric acid. Four layers of the designated peel solution were applied to the affected area. The first three layers were each left for 1–2 minutes, while the final layer was retained for approximately 5 minutes. The entire session lasted between 8 and 11 minutes. After the procedure, patients were advised to rinse the area with water and avoid mechanical trauma, sun exposure, and to apply sunscreen regularly and wear protective eyewear.

Outcome Measures and Clinical Assessment

Clinical evaluation of treatment efficacy was performed at baseline and at 3-week intervals (i.e., weeks 3, 6, 9, and 12). Objective assessment was conducted using the grading system for POH proposed by Sheth *et al.* (2014). Additionally, standardised high-resolution digital photographs were taken at each visit.

Two independent dermatologists, blinded to group allocation and not involved in treatment administration, evaluated the degree of pigment reduction based on photographic comparisons. The POH grading scale by Sheth *et al.* was used as follows:

Grade 0: No visible pigmentation, skin tone matches surrounding facial areas

Grade 1: Mild pigmentation limited to the infraorbital fold

Grade 2: Moderate pigmentation with clear contrast

Grade 3: Pronounced darkening involving all four eyelids

Grade 4: Severe pigmentation extending beyond infraorbital areas

Subjective and Global Evaluations:

- **Physician Global Assessment:** Clinical improvement was rated as poor, fair, good, or excellent by the treating physician (Vavouli *et al.*, 2013).
- **Patient Global Assessment:** Each patient self-evaluated their treatment response using the same grading scale (poor, fair, good, excellent) (Vavouli *et al.*, 2013).
- **Treatment Tolerance:** Patient-reported tolerability was recorded and graded similarly to the above parameters (Vavouli *et al.*, 2013).

Any side effects or adverse events encountered during the study period were documented and analysed.

Statistical Analysis

The data was analysed using SPSS software v 23.0. The level of significance was kept at 5%. Demographic and clinical characteristics were presented using descriptive statistics and compared using an independent t-test or chi-square test depending on the nature of the data. A comparison of baseline and 12 weeks POH grading scores in each group was done using Wilcoxon signed rank test.

Comparison of median POH, physician global assessment scale, patient global assessment scale and satisfaction between two groups was performed using Mann Whitney test. Comparison of patient global tolerance at 12 weeks between two groups was done using chi-square test.

Significance of Results

All tests were performed at a 5% level of significance; thus, an association was significant (S) if the P-value was less than 0.05 and nonsignificant (NS) if $p > 0.05$.

Ethical Approval

The Ethical Approval is obtained with reference number ITSCDSR/IIEC/LD/PERIO/2022-25/003 on 20th September 2024.

Results

Table 1: Demographic and Clinical Characteristics of Both the Groups

Variable	Category	Arginine Peel	Mandelic Peel	p-value
Age	--	30.67 ± 10.59	33.25 ± 8.80	0.523
Gender	Female	9 (75%)	6 (50%)	0.400
	Male	3 (25%)	6 (50%)	
Classification	Constitutional type	12 (100%)	12 (100%)	--
Eyelid stretch test	No color change	1 (8.3%)	2 (16.7%)	1.000
	Positive	11 (91.7%)	10 (83.3%)	
Stress	No	9 (75%)	9 (75%)	1.000
	Yes	3 (25%)	3 (25%)	
Haemoglobin (Hb)	--	12.58 ± 1.38	12.58 ± 1.51	1.000

Independent t test; chi-square test

Demographic and Clinical Characteristics:

The demographic and clinical characteristics among the two groups is tabulated in Table 1. The mean age of the subjects of Arginine peel and Mandelic peel was 30.67 ± 10.59 years and 33.25 ± 8.80 years ($p=0.523$). There were 9 females and 3 males in Arginine peel and 6 females and 6 males each in Mandelic peel. The two groups did not differ significantly regarding male and female distribution. Eyelid stretch test was positive in 11 subjects of Arginine peel and 10 subjects of Mandelic peel and there was a non-significant difference between the two groups. To rule out etiological factors, presence of stress and haemoglobin gm% was also assessed amongst patients prior to the procedure. The two groups did not differ significantly in terms of stress. All the subjects of both groups were non-smokers. The two groups did not differ significantly in terms of anemic status.

Table 2: Comparison between Both Groups for Grades of POH at before and after Intervention

POH Grade	Arginine Peel	Mandelic Peel
Baseline		
0	0	0
1	0	0
2	0	2 (16.7%)
3	3 (25%)	2 (16.7%)
4	9 (75%)	8 (66.7%)
Median POH grade	4 (3.25-4)	4 (3-4)
12 weeks		
0	2 (16.7%)	8 (66.7%)
1	9 (75%)	3 (35%)
2	1 (8.3%)	1 (8.3%)
3	0	0
4	0	0
Median POH grade	1 (1-1)	0 (0-1)
p-value	0.001*	0.002*

Mann Wilcoxon signed rank test; * indicates significant difference at $p \leq 0.05$

POH: periorbital hyperpigmentation

There was nonsignificant difference between both groups before starting therapy. On comparing the grades of POH before and after completing treatment, in both groups, there was statistically significant improvement. Furthermore, when evaluating grades of POH in both groups after intervention, a high statistically significant difference in favor of the group treated with mandelic peel was found ($p < 0.001$).

Table 3: Intergroup Comparison of Physician's Global Assessment Scale between Two Groups

Physician's global assessment grading	20% Arginine peel		20% Mandelic peel	
	No. of patients	Percentage(n=12)	No. of patients	Percentage(n=12)
Excellent	2	16.70%	10	83.30%
Good	10	83.30%	2	16.70%
Fair	0	0.00%	0	0.00%
poor	0	0.00%	0	0.00%

At baseline, both the Arginine peel and Mandelic peel groups showed similar results, with 83.3% of participants in the "Poor" category and 16.7% in the "Fair" category, indicating no significant difference ($p=1.000$). Over the following weeks, both groups showed improvement, with a higher percentage of participants moving into the "Good" category. However, there were no statistically significant differences between the two groups at 3, 6, and 9 weeks ($p > 0.05$). By 12 weeks, a significant difference was observed ($p = 0.001$), with the Mandelic peel group showing 83.3% in the "Excellent" category, compared to 16.7% in the Arginine peel group. This indicates that the Mandelic peel was more effective in improving the condition.

Table 4: Intergroup Comparison of Patient Global Assessment Scale between Two Groups

Patient's global assessment grading	20% Arginine peel		20% Mandelic peel	
	No. of patients	Percentage(n=12)	No. of patients	Percentage(n=12)
Excellent	3	25.00%	11	91.70%
Good	9	75.00%	1	8.30%
Fair	0	0.00%	0	0.00%
poor	0	0.00%	0	0.00%

At baseline, both the Arginine peel and Mandelic peel groups showed similar results, with the majority in the "Poor" category (83.3% for Arginine and 75% for Mandelic), and a smaller percentage in the "Fair" category (16.7% for Arginine and 25% for Mandelic), with no significant difference ($p = 0.623$). Over the next 12 weeks, both groups showed improvement, with more participants moving into the "Good" category. However, no significant differences were observed in 3 weeks ($p = 0.576$), 6 weeks ($p = 0.088$), and 9 weeks ($p = 0.284$). By 12 weeks, a significant difference was seen ($p = 0.001$), with the Mandelic peel group showing 91.7% in the "Excellent" category, compared to 25% in the Arginine peel group, indicating that the Mandelic peel was significantly more effective in improving the condition.

Table 5: Comparison of Patient Global Tolerance at 12 Weeks between Two Groups

Group		Erythema/Poor Tolerance	Excellent Tolerance
Arginine peel	n	0	12
	%	0.00%	100.00%
Mandelic peel	n	2	10
	%	16.70%	83.30%

In the Arginine peel group, all participants (100%) had excellent tolerance, while in the Mandelic peel group, 16.7% experienced erythema/poor tolerance, and 83.3% had excellent tolerance. However, the difference was not statistically significant ($p = 0.478$), indicating that both peels were generally well tolerated, with a slight trend toward better tolerance for the Arginine peel.

Table 6: Comparison of Proportionality of Patients and Percentage across Different Satisfaction Levels between Two Groups at 12 Weeks

Group		Slightly satisfied	Satisfied	Very satisfied
Arginine peel	n	4	4	4
	%	33.30%	33.30%	33.30%
Mandelic peel	n	2	2	8
	%	16.70%	16.70%	66.70%

In the Arginine peel group, satisfaction was evenly distributed, with 33.3% of participants reporting being slightly satisfied, satisfied, and very satisfied. In contrast, the Mandelic peel group had a higher percentage (66.7%) of participants in the "very satisfied" category, while fewer reported being slightly satisfied (16.7%) or satisfied (16.7%). However, the difference between the groups was not statistically significant ($p = 0.132$), suggesting that while more participants in the Mandelic peel group reported higher satisfaction, the results were not conclusive.

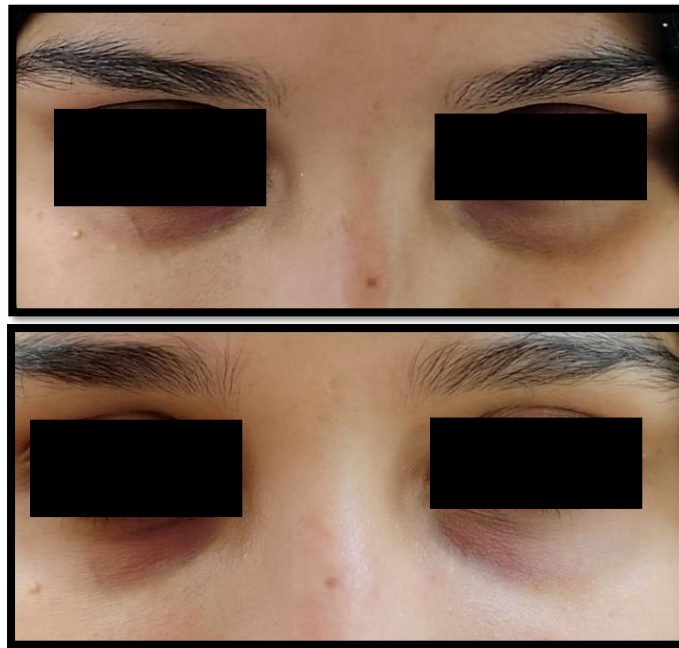


Figure 1: (a) Periorbital Hyperpigmentation Before 20% Arginine Peels. (b) Periorbital Hyperpigmentation After 20% Arginine Peels

Figure 1 depicts the periorbital hyperpigmentation (dark circles) before and after treatment with a 20% Arginine peel. In the first part of the image, the skin around the eyes shows noticeable pigmentation, characteristic of the condition. However, after the 20% Arginine peel treatment, the second part of the image illustrates a marked improvement in the pigmentation, indicating a significant reduction in the intensity of the dark circles and a more even skin tone around the eyes.

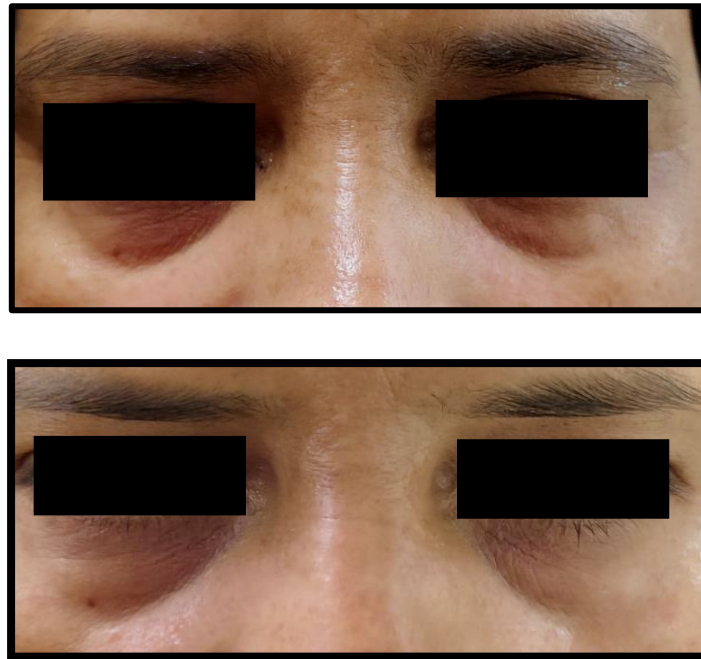


Figure 2: (a) Periorbital Hyperpigmentation Before 20% Mandelic Peels. (b) Periorbital Hyperpigmentation After 20% Mandelic Peels

Figure 2 showcases the effects of the 20% Mandelic peel on periorbital hyperpigmentation. The first image displays the presence of dark circles around the eyes, which is a common aesthetic concern for many individuals. After undergoing the Mandelic peel treatment, the second image shows a visible reduction in the pigmentation, with a clearer and more balanced skin tone, highlighting the effectiveness of the Mandelic peel in treating periorbital hyperpigmentation.

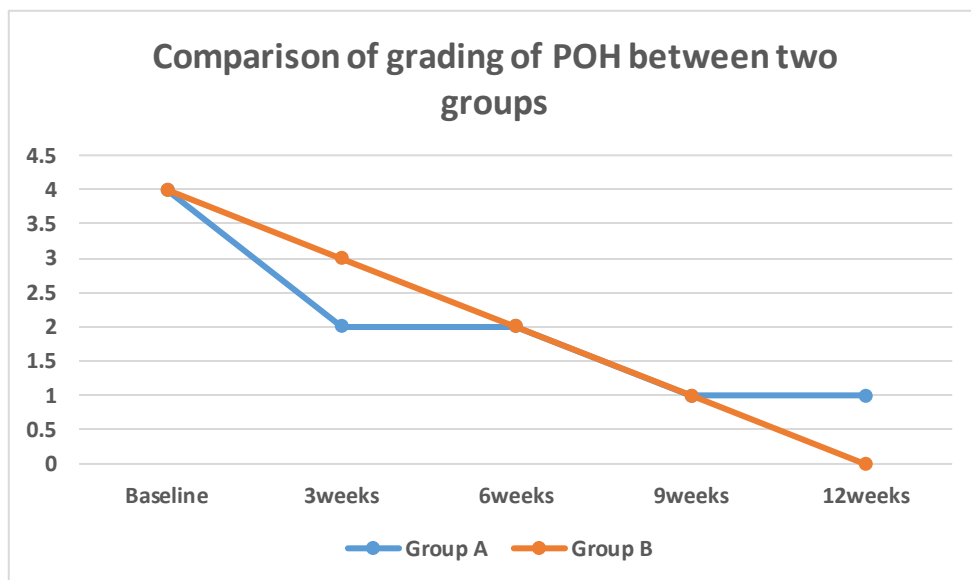


Figure 3: Improvement in Grading of Periorbital Hyperpigmentation

Discussion

Periorbital hyperpigmentation (POH) is a highly prevalent yet under-researched aesthetic concern among Indian individuals. It affects approximately 30% of the Indian population, often imparting a fatigued or unwell appearance (Roh & Chung, 2009; Heidari *et al.*, 2025; Brady & Shah-Desai, 2025). In the present clinical trial, female participants outnumbered males, with a male-to-female ratio of

approximately 5:3. This female predominance aligns with findings by Sheth *et al.* (2014) possibly due to heightened cosmetic awareness and increased consultation rates among women. Most of the enrolled participants in both treatment arms fell within the 18–60-year age group—a demographic most commonly seeking aesthetic treatments. Baseline characteristics, including age distribution, duration of treatment, and initial POH scores, were statistically comparable between both groups (Table 1).

Previous literature, including work by Sheth *et al.* (2014) indicates a strong association between POH and iron-deficiency anemia, with nearly half of the patient's demonstrating anemia. Improvements in POH following anemia correction may be attributed to enhanced tissue oxygenation or the resolution of facial pallor that exacerbates the contrast of pigmentation in the infraorbital region.

In this study, patients treated with the arginine peel demonstrated a significant reduction in POH scores compared to baseline; however, improvements plateaued between weeks 9 and 12. Conversely, the mandelic peel group exhibited continuous and statistically significant improvement across all evaluation points. These findings are in line with a study by Sidiq, Gopalan and Kandasamy (2019) where all groups receiving different peeling agents showed improvement, with glycolic acid (GA) peel showing a faster onset of effect from week 3, while lactic acid (LA) and ferulic acid (FA) peels demonstrated noticeable results starting from week 6. The GA peel group exhibited greater improvement compared to LA and FA groups throughout the study duration (Goyal *et al.*, 2025) (Table 2).

In the current investigation, 66.7% of patients in the mandelic peel group showed excellent improvement, whereas in the arginine peel group, 75% demonstrated good results and 8.3% showed fair outcomes. The differences were statistically significant ($p < 0.001$), as depicted in Figure 3. These outcomes exceed those reported by Vavouli *et al.* (2013) who observed excellent responses in 16.6% of cases, while 40.0% showed good, 36.7% fair, and 6.6% poor outcomes after chemical peeling for infraorbital dark circles.

Physician Global Assessment (PGA) scores further supported the superior efficacy of mandelic peel, with 83.3% of patients rated as having excellent improvement and the remaining 16.7% as good (Table 3). These findings are consistent with Sidiq *et al.* (2019) who reported excellent improvement in 78% of patients using mandelic acid. In the arginine peel group, although significant improvement was observed in week 3 compared to baseline, changes between weeks 3 to 9 and 9 to 12 were not statistically significant. In contrast, the mandelic peel group showed progressive and significant improvement throughout the study period. Unlike our study, Dayal *et al.* (2020) reported no significant differences in PGA scores within treatment groups over time (Table 3).

Regarding the Patient Global Assessment (PGA), mandelic peel again demonstrated superior outcomes, with 91.7% reporting excellent improvement and 8.3% reporting good outcomes. This contrasts favorably with the findings by Vavouli *et al.* (2013) where 23.3% rated the outcome as excellent, 46.7% good, 26.7% fair, and 3.3% poor. In the Arginine group, a statistically significant improvement was noted from baseline to week 3 and from week 3 to week 6; however, changes from week 6 to week 12 were not significant. On the other hand, the mandelic peel group showed consistent improvement at all time points. Again, Sidiq *et al.* (2019) did not find statistically significant changes in patient assessment within their treatment arms (Table 4).

In terms of patient global tolerance, 91.7% of patients rated their experience with the treatment as excellent, while 8.3% rated it as good. This high level of tolerance is comparable to the findings by Vavouli *et al.* (2013) where 46.7% of patients reported excellent tolerance, 30% good, and 23.3% fair. Reported side effects were mild and transient. Among mandelic peel users, there were no reports of burning or tingling; however, 16.7% experienced mild itching, and none reported dryness or erythema (Table 5).

Patient satisfaction was high in both groups. In total, 66.7% of patients were very satisfied with their results, 33.3% expressed satisfaction, and 16.7% were slightly satisfied. These results are consistent with previous findings by Vavouli *et al.* (2013) who reported 63.3% of respondents were very satisfied, 23.3% slightly satisfied, and 13.3% dissatisfied (Table 6).

Limitations

The limitation of this study is the relatively small sample size, which may affect the generalisability of the findings. Future randomised controlled trials with larger cohorts are essential to validate these outcomes. Additionally, comparative studies exploring combination therapies (e.g., peels with topical agents or lasers) may offer insights into more effective and sustained treatment options. Long-term follow-up is also necessary to assess the recurrence of pigmentation and the durability of therapeutic outcomes, ideally over a period of at least 6 to 12 months.

Conclusion

This study demonstrated that both 20% mandelic acid and 20% arginine peels are effective and safe in the management of periorbital hyperpigmentation. Mandelic peel achieved superior clinical improvement, while arginine peel offered excellent tolerability, making both suitable choices depending on patient needs and skin sensitivity. These results support chemical peels as practical and minimally invasive approaches for treating pigmentation disorders.

Looking ahead, future research should emphasise long-term outcomes, recurrence rates, and patient-centered benefits such as quality of life and satisfaction. Comparative studies across diverse skin types and populations are needed to strengthen clinical recommendations. In addition, integrating chemical peels with topical agents, laser-based therapies, or regenerative modalities like platelet-rich plasma may enhance efficacy and durability. The development of novel peeling formulations, including advanced AHA or combination agents, also holds promise for improving treatment outcomes.

Conflict of Interest

The authors affirm that they have no conflicting interests.

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