

Role of 12% ferulic acid peel in the treatment of constitutional type of periorbital melanosis - A comparative study of clinical efficacy and safety with 15% lactic acid peel

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How to citation this article: Dr. Yasmin Hana S, Dr. Mohana Rao TS, Dr. V Lakshmi Sarojini, “Role of 12% ferulic acid peel in the treatment of constitutional type of periorbital melanosis - A comparative study of clinical efficacy and safety with 15% lactic acid peel”, IJMACR-January - 2023, Volume – 6, Issue - 1, P. No. 263 – 270.

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Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Background: Periorbital melanosis is a common problem affecting all races and genders, yet the studies regarding this entity are limited. Constitutional type of periorbital melanosis is the commonest type of POM seen among Indian patients. Few treatment options including chemical peels are being tried presently.

Aims and objectives: To compare the response of ferulic acid peel and lactic acid peel in the treatment of constitutional type of periorbital melanosis and thereby assess the relevance of chemical peeling for the treatment of the same.

Materials and methods: Prospective observational study from January 2021 to August 2022 was conducted

at Department of DVL, Guntur Medical College. 30 patients with constitutional type of periorbital melanosis were selected and half members were treated with 15% Ferulic acid peel and the other half were treated with 12% Lactic acid peel and the response was assessed using POH grading, physician and patient global assessment and patient global tolerance.

Results: Among 30 cases, 5 were males and 25 were females. Age range was 19-48 years with the mean age being 28 years. Significant improvement was noted in both the groups. Excellent response was noted among the ferulic peel group followed by lactic acid peel group. When side effects were compared, ferulic peel had least number side effects. The side effects were mild enough

to not necessitate the cessation of therapy.

Conclusion: The treatment options for periorbital melanosis is challenging pertaining to its resistance to treatment. Upcoming chemical peels like ferulic acid peel will help in the treatment of constitutional type of POM to a large extent.

Keywords: Periorbital melanosis, chemical peels, ferulic acid, lactic acid, Infraorbital dark circles

Introduction

Periorbital melanosis is defined as bilateral, uniform, round macules, particularly in the infraorbital region. It is one of the most common aesthetic conditions seen in dermatology outpatient department, yet unexplored(1). It usually affects the inferior aspect of the eye, but the entire circumference of periorbital area may be involved. Periorbital hyperpigmentation is most common in females with a usual age of onset between 16 – 25 years. Periorbital melanosis is caused by various exogenous and endogenous factors. The causative factors include heredity, excessive pigmentation, post inflammatory hyperpigmentation secondary to atopic dermatitis, allergic contact dermatitis, periorbital edema, excessive vascularity, skin laxity and resultant shadowing and tear trough(2). When no cause is apparent, it is addressed as idiopathic cutaneous hyperchromia of the orbital region (ICHOR)(3).

It has limited reliable treatment options out of which topical therapy remains the mainstay. Topical applications include depigmenting (bleaching) agents, chemical peeling, carboxytherapy, laser therapies, injectable fillers, dermabrasion, and autologous fat transplantation are the few types of available treatments(4). Chemical peeling is an easy, safe and cost-effective modality for the treatment of periorbital melanosis and studies regarding the efficacy and safety

of chemical peels help the patients tremendously, especially in the Indian scenario, as the other cosmetic procedures mentioned above are too expensive.

Lactic acid (LA) is an alpha hydroxyl acid causing a stratum corneum desquamation with an excellent moisturizing effect. Ferulic peel (FA) peel is a new modality and acts as a depigmenting agent due to its property to inhibit tyrosinase enzyme which is a rate-limiting enzyme in melanogenic pathway(1). However, there are only very few studies comparing efficacy and safety of established peels for periorbital melanosis like lactic acid peel with upcoming chemical peels like ferulic acid peel. Thus, this study was undertaken to evaluate the same.

Materials and methods

This study was conducted in the Department of DVL; Guntur medical college, Guntur, Andhra Pradesh. Thirty patients including males and females with constitutional type of Periorbital melanosis were enrolled in the study for 12 weeks following the application of inclusion and exclusion criteria from January 2021 to August 2022. The patients presenting with constitutional type of periorbital melanosis were counselled regarding the study and consent was taken before enrolling them.

Demographic data and detailed history were taken. General and cutaneous examinations were done for the patients. Patients were ordered routine blood investigation which included Complete blood count with hemoglobin estimation, Liver function test, Renal function test and Random blood sugar to look for any systemic disease at the first visit. Patients were also instructed to use sunscreen regularly before and after the treatment.

The patients were allocated into two groups of fifteen each on an alternate OP basis. Patients in LA group and

FA group underwent 15% Lactic acid peel and 12% Ferulic acid peel treatment respectively every three weeks (totaling three sessions; i.e., at 0 weeks, 3 weeks and 6 weeks) and the final evaluation was done at the end of 12 weeks and study was terminated for that patient. The evaluation was done using POM grading, physician objective assessment, patient global assessment and patient global tolerance.

Statistical analysis

All the statistical calculations were performed using IBM SPSS 24.0. Comparison of variables between 2 groups were done using T test for normally distributed continuous variables and in cases of non-parametric variables Mann Whitney test was used. Chi square test was used to analyse the relation between continuous variables. In all the tests mentioned above, a “p” value less than 0.05 was considered to be statistically significant.

Results

Baseline characteristics of patients

A total of 30 patients participated in the study with 5 male patients and 25 female patients. Female predominance was noticed in both study groups. Most common age group was 21-30 years (50%) followed by 31 -40 (23.3% and 18-20 years (20%). In LA group (Lactic acid peel group), the mean age was 29 and in FA group (Ferulic acid peel group), mean age was 27 years. The difference between the mean age of the 2 groups were statistically insignificant with P value 0.214.

When gender distributions of both groups were compared, there was no significant difference. Mean duration of POM among the two groups were also statistically insignificant (0.468). The baseline POH grading of the patients among both groups were comparable (P value 0.624). Hence, the two groups in

the study were comparable in terms of age, gender, duration of POM and baseline POM grades.

Efficacy and safety evaluation

Ranu et al's POM grading was used for the assessment (5):

Grade 0 – Skin comparable to other facial skin areas

Grade 1- Faint pigmentation of infraorbital fold

Grade 2 – Pigmentation more pronounced

Grade 3 – Deep dark colour, all four lids involved

Grade 4- Pigmentation spreading beyond infraorbital fold

The changes in grades were assessed accordingly and was compared using photographs also as ethics clearance for collection and storage of photographs were taken. Physician objective assessment was done as follows:

Poor – 0-25%

Fair – 26- 50%

Good – 51-75%

Excellent – 76 – 100%

Patient global assessment and patient global tolerance was assessed as poor, fair, good and excellent.

At the end of treatment sessions, significant improvement was seen in both the study groups. Improvement of POH greater than 50% was seen in 20% of patients in LA group whereas it was 66.7% in FA group. When final POM grades were compared between the groups, there was a statistically significant difference between the two groups.

In LA group, 53.3% of patients had one grade improvement, 20% had 2 grade improvement after peeling.

In FA group, 40% of the patients had 1 grade improvement, 40% of the patients had 2 grade

improvement and 13.3% of the patients had 3 grade improvement of POM after ferulic acid peeling.

Table 3 shows physician objective assessment, patient global assessment and patient global tolerance. When physician objective assessment between the two groups were compared, there was statistically significant difference between the two groups with ferulic acid peel producing better result (P value 0.016). 53.3% of patients in LA group had fair response, 13.3% had good improvement and 6.7% patient had excellent improvement. In the FA group, 26.7% had fair improvement, 40% had good improvement and 26.7% had excellent improvement following treatment.

Similarly, when patient's global assessment was compared between the two groups, there was a statistically significant improvement of POM in FA group when compared to LA group (P value 0.005). In LA group, 20% of patients assessed the response as poor, 46.7% assessed the response as fair, 26.7% assessed it as good and 6.7% marked it as excellent.

In FA group, 6.7% of patients assessed the response as poor, 6.7% patients marked the response as fair, 46.7% marked good response and 40% marked excellent response.

When the safety and tolerability of both peels were put into question, 66.7% FA group showed excellent tolerance and only 4 patients had side effects whereas in LA group, only 26.7% showed excellent response. Side effects due to both the peels were mild and transient and did not warrant for the cessation of therapy. Maximum side effects were shown by lactic acid peel followed by ferulic acid peel.

The common side effects noted were burning sensation, pruritus and dryness. No erythema, post inflammatory

hyper or hypopigmentation were noticed. There was no statistically significant difference in terms of side effects (P value 0.056) but clinically there was a noticeable difference between the two groups. When Patient's global tolerance between the two groups were compared, there was a statistically significant difference (P value 0.029) with ferulic acid peeling tolerated particularly well than lactic acid peel.

Image 1 (A) shows periorbital melanosis at baseline in 12% Ferulic acid peel group

(B) shows periorbital melanosis after treatment in 12% Ferulic acid peel group

Image 2 (A) shows periorbital melanosis at baseline in 15% Lactic acid peel group.

(B) shows periorbital melanosis after treatment in 15% Lactic acid peel group

Figure 1



A – Before treatment

B – After treatment

Figure 2



A – Before treatment

B – After treatment

Table 1: showing the baseline grades of the two groups before the treatment.

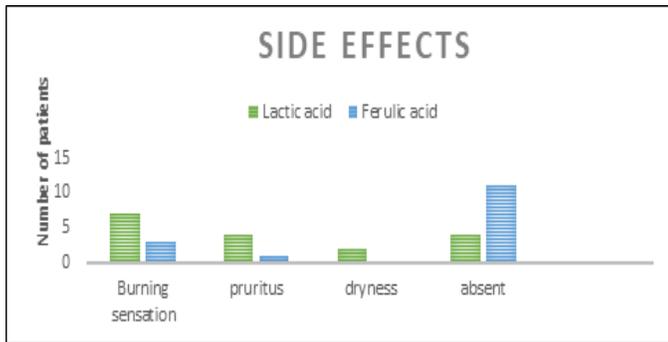
Baseline grade	Group I- 15% Lactic Acid Peel			Group II- 12% Ferulic Acid Peel		P value
	Grade 1	1	6.7%	2	13.3%	
Grade 2	4	26.7%	4	26.7%		
Grade 3	6	40.0%	6	40.0%		
Grade 4	4	26.7%	3	20.0%		

Table 2: showing final grades of the two groups following the treatment.

Final pom grades	Group I15% Lactic Acid Peel			Group II- 12% Ferulic Acid Peel		P value
	Grade 0	1	6.7%	3	20.0%	
Grade 1	4	26.7%	9	60.0%		
Grade 2	7	46.7%	2	13.3%		
Grade 3	1	6.7%	1	6.7%		
Grade 4	2	13.3%	0	0%		

Table 3: comparing physician objective assessment, patient global assessment and patient global tolerance of the two groups.

Physician objective Assessment	Group I15% Lactic Acid Peel			Group II- 12% Ferulic Acid Peel		P value
	Poor	4	26.7%	1	6.7%	
Fair	8	53.3%	4	26.7%		
Good	2	13.3%	6	40.0%		
Excellent	1	6.7%	4	26.7%		
Patient global Assessment	Group I- 15% Lactic Acid Peel			Group II- 12% Ferulic Acid Peel		P value
	Poor	3	20.0%	1	6.7%	
Fair	7	46.7%	1	6.7%		
Good	4	26.7%	7	46.7%		
Excellent	1	6.7%	6	40.0%		
Patient global tolerance	Group I- 15% Lactic Acid Peel			Group II- 12% Ferulic Acid Peel		P value
	Poor	3	20.0%	0	0.0%	
Fair	0	0.0%	0	0.0%		
Good	8	53.3%	5	33.3%		
Excellent	4	26.7%	10	66.7%		



Graph 1

Discussion

One of the most common but understudied causes of aesthetic disfigurement in Indian patients is Periorbital melanosis. This facial presentation can be loosely defined in a number of ways, but generally speaking, it is a vague entity and there is limited literature about this entity. It significantly lowers a person's quality of life and makes them appear worn out and lifeless, particularly in women. Periorbital melanosis influences people of a wide range of age group, all genders and races(5).

In the present study of 30 patients, 15 (50%) patients belonged to 21-30 age group which constituted the majority and followed by 31-40 years, the reason for this age group being them being more apprehensive about their looks. The range was 19 - 48 years and the overall mean age was 28 years, standard deviation being 8 which is in accordance to a study by Verschoore M et al where the average age of their study group was 28 years old, with a range of 14 to 48 years which is in accordance to this study(6).

In this study, the male to female ratio was 1:5 with significant preponderance in females which is in accordance to previous studies(7-9). One reason for this female predominance may be that they are more conscious about the external appearance and consult doctors earlier when compared to male counterpart.

Majority of patients had less than 5 years duration of POM as patients tend to seek advice earlier in the disease owing to the disfiguring look it gives to the face. This is in accordance to previous studies(8,9).

Both the study groups had good clinical improvement following the chemical peeling. Clinical improvement for POM was maximum in Ferulic peel group followed by lactic acid group. In the study by Dayal et al, 46.66% of FA group patients experienced POH improvement of greater than 50%, compared to only 23.33% of LA group patients which is similar to the finding in our study(1) where improvement greater than 50% was seen in 20% of patients in LA group whereas it was 66.7% in FA group. The proportion of patients in grades 1 and 2 to grades 3 and 4 before and after treatment of the total study population was significantly different, which was 11:19 prior to treatment, whereas it shifted to 11:2 following the treatment. When the overall final grades between the two groups were compared, there was significant difference with ferulic peel having better efficacy than lactic peel as shown by the P value (0.023). According to Dayal et al, even though ferulic acid peeling produced better results compared to lactic peel there was no statistically significant difference whereas in our study, there was statistically significant difference with ferulic acid peel resulting in better response when Physician's objective assessment was taken into account. According to the patients of LA group, 6.7% of them marked as excellent response and 26.7% assessed it as good meanwhile in FA group, 46.7% marked good response and 40% marked excellent response. Also, as far as side effects were concerned, ferulic acid group was tolerated very well and had very few side effects when compared with lactic peel group. The side effects were very minimal and included burning sensation,

dryness and pruritus. The clinical improvement was visible from 6th weeks onwards in both the groups.

Ferulic acid acts by scavenging free radicals, binding transition metals like iron and copper, and preventing lipid peroxidation(10). Melanocytic proliferation and melanogenesis are stymied by its action on tyrosinase. Ferulic acid applied locally penetrates the skin deeply in both dissociated and non-dissociated forms, regardless of pH (acidic or neutral)(10,11). Ferulic acid provides adequate photoprotection by deeper penetration into the skin. Ferulic acid also stimulates wound healing and accelerates angiogenesis(12). The multiple actions of ferulic acid peel makes it a novel, efficacious peel in the treatment of constitutional type of periorbital melanos.

Lactic acid (2 hydroxy propanoic acid) is a mild alpha hydroxy acid (AHA) and is formed naturally in derived from sour milk, bilberries, yogurt and tomato juice(13). AHAs like lactic acid applied topically in lower concentrations reduces stratum corneum adhesion and this causes accelerated cell loss and exfoliation. At higher concentrations these may cause epidermolysis. A thickened papillary dermis, increased collagen synthesis, elevated hyaluronic acid levels, and an increased number and quality of elastic fibre tissues are among the dermal effects of AHA(14). When compared to lactic acid peel, ferulic acid peel shows better result which may be because of having the largest molecular weight among AHAs, end result being slower penetration and need for repeated application.

This study is one of the few studies regarding usage of ferulic acid peel and also regarding its use in constitutional type of POM. The limitations of the study include the study being conducted in a single tertiary care Centre with a small sample size of 30 and also the follow up time was limited. So, studies with larger

sample size and long term follow up will help in substantiating the findings of the present study.

Conclusion

Since eyes are a prominent part of facial structure, any type of dyschromia affecting eyes cause a significant cosmetic concern for the patient. Periorbital hyperpigmentation is a common complaint in all races, gender and age group. It is a multifactorial disorder involving lifestyle and genetics factors. The major risk factors include eye strain, sleep deprivation, stress, sun exposure, obesity etc. Constitutional type of POM is hugely linked to family history. Despite of the ubiquity of the disease, no successful treatment has been established for POM. So, a treatment modality that is easily available, affordable, effective and safe is a must. Chemical peels are being widely used successfully nowadays for several dermatological conditions and is being tried as a mode of treatment for POM. Ferulic peel is an emerging peel with good potential in the treatment of POM but studies are limited regarding its efficacy and safety. So, in this study we did a comparison of 15% lactic peel and 12% ferulic peel in terms of efficacy and safety for POM, both the peels produced good responses at the end of study. The clinical efficacy of 12% ferulic acid was superior to 15% Lactic acid peel and resulted in marked improvement of POM. In addition to the response following the treatment which was our aim, we also noticed improvement in texture of skin and decrease in uneven pigmentation. Ferulic peel also produced very few side effects when compared with lactic peel thus making ferulic peel one of the best cost effective and safe treatment for POM.

Ethical approval: Approval for the study was obtained from Institutional Ethics Committee, Guntur Medical College, Guntur, AP, India.

Consent

Written and informed consent was obtained from all participants of the study.

List of abbreviations

POM – Periorbital melanosis, POH- Periorbital Hyperpigmentation, LA group – Lactic acid peel group, FA group – Ferulic acid peel group, AHA- Alpha hydroxy acids, ICHOR-Idiopathic cutaneous hyperchromia of the orbital region

Acknowledgement

I express my sincere gratitude to the Department of DVL, Guntur medical college for their help throughout the study.

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