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1% RETINOIC ACID PEEL IN TREATMENT OF MELASMA: PEEL FOR THE DARK SKINED? An Interventional Study.

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Abstract:

Melasma is a common disorder of hyperpigmentation, which has a severe impact on the quality of life. Inspite of tremendous research, the treatment remains frustrating both to the patient and the treating physician. Peels are a well-known modality of treatment for melasma, having shown promising results in many clinical trials. Dark skin types (Fitzpatrick types IV to VI) are especially difficult to treat owing to the increased risk of post-inflammatory hyperpigmentation (PIH). Although a number of new agents have come up, there is little published evidence supporting their use in day-to -day practice.

AIMS: To determine the efficacy of 1% Retinoic acid peeling in the treatment of melasma. To assess the degree of improvement in pigmentation objectively using Melasma Area and Severity Index at baseline and after 12 weeks of treatment with 1% retinoic acid peel and to compare the side effects associated with the modality.

Objective: Because there is a paucity of studies evaluating the efficacy and safety of 1% tretinoin peel in the treatment of melasma in dark-skinned Asian population, we conducted a pilot study to evaluate the efficacy and side effects of this potentially new peeling agent in the treatment of melasma patients.

Methods: Thirty patients of melasma, after written consent, were taken up for an open pilot study of 12 weeks. One percent tretinoin peel was applied on full face at three weekly intervals. The results were evaluated by using the modified Melasma Area and Severity Index and with photographs at baseline and 6 and 12 weeks

Results: A significant decrease in the modified Melasma Area and Severity Index from baseline to 6 weeks and then from 6 to 12 weeks was observed ($p<0.001$). Side effects were minimal and 1% tretinoin peel appeared to be well tolerated by the patients.

Conclusion: It was concluded from the present trial that serial 1% tretinoin peel is a well tolerated and as effective a therapy for melasma in dark-skinned individuals as a standard and well-tried chemical peel.

Introduction

Melasma is an acquired disorder of hyperpigmentation characterised by blotchy, light-to-dark brown macules distributed symmetrically on the sun-exposed parts of the body. It is seen in Fitzpatrick skin types IV-VI. The disorder has a severe impact on the quality of life, causing deep psychological and social stress. Despite tremendous research into the etiology, pathogenesis and possible treatment options for melasma, the disease remains a therapeutic challenge to dermatologists, and a definitive modality of treatment is still a distant reality. [1,2]

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. Current treatment modalities include kojic acid, azelaic acid, arbutin, ascorbic acid, chemical peels and lasers. Newer formulations that are being tried include tranexamic acid (TA), rucinol (4-n-butylresorcinol), oligopeptides silymarin and orchid extracts. Various botanical extracts that have been tried in melasma are grape seed extract, pycnogenol, aloesin, green tea extracts, coffee berry, soy, and licorice extract [3].

Various lasers like Green light: Flashlamp-pumped PDL (510 nm), frequency doubled Q switched neodymium: Yttrium aluminium garnet-532 nm (QS Nd: YAG), Red light: Q switched ruby (694 nm), Q switched alexandrite (755 nm), Near-infrared: QS Nd: YAG (1064 nm) have been tried to treat melasma. Although good efficacy has been seen with this technique, side effects have also been reported. These include hypopigmentation, depigmentation, rebound hyperpigmentation, physical urticaria, acneiform eruption, petechiae, and herpes simplex reactivation [4].

Chemical Peels for Melasma

Chemical peeling is the application of a chemical agent to the skin, which causes the controlled destruction of a part or of the entire epidermis, with or without the dermis, leading to exfoliation and removal of superficial lesions, followed by the regeneration of new epidermal and dermal tissues [4]. Well-known modality of treatment for melasma. Peels have proved to be useful agents for melasma both as a sole treatment as well as an adjunct to other topical therapies.

Chemical Peels for Melasma in Dark Skin

Although a wide variety of agents are available for chemical peels, the choice becomes relatively limited when you are treating a patient with a Fitzpatrick skin type IV or above [5]. This is because the deep chemical peels cannot be used in dark-skinned patients owing to the risk of prolonged hyperpigmentation. [6,7]. Even medium-depth peels need to be used with extreme caution. A list of agents which can be used for peeling in darker skin types is summarised below

Table 1: Peeling agents for dark skin

Very superficial and superficial peels (epidermis to upper papillary dermis)
Trichloroacetic acid 10-30%
Glycolic acid solution 30-70%
Salicylic acid 20-30%
Jessner's solution
Tretinoi 1-5%
Medium-depth peels (epidermis to upper reticular dermis)
Trichloroacetic acid 35-50%
Trichloroacetic acid 35%+glycolic gel 70%
Jessner's solution+trichloroacetic acid 35%
88% phenol unoccluded
Solid CO_2+trichloroacetic acid 35%

*(In accordance with the Mark Rubin classification), CO_2: Carbon dioxide

Furthermore, chemical peels are generally used to treat only the epidermal and mixed forms of melasma, as an attempt to treat the deeper variant often leads to unwanted complications like hypertrophic scarring and permanent depigmentation.

Various Studies have been done on chemical peeling in melasma patient with dark skin

Grimes et all (1999) conducted a study on 6 patients in melasma with 20-30% salicyclic acid and found moderate improvement in 66% patients.

Javahri et all (2001) conducted a study on 25 Indian patients with 50% glycolic acid and found 45% improvement in epidermal melasma and 27% in mixed type.

Sharique et all (2005) conducted a study on 20 Indian patients with 92% lactic acid and found significant improvement.

TRETINOIN PEEL

Topical Tretinoin is widely used for the treatment of melasma as an over-the-counter lightening agent. It is also one of the constituents of Kingman regimen used for treatment of melasma, wherein 5-10% tretinoin is applied as slow release peel and and helps to eliminate epidermal pigment, reduces photodamage and improves skin texture. It is beneficial as patients are already primed with topical tretinoin or Kingman's regimen. In few studies(Khunger et all) Tretinoin peels were found to be of equal efficacy of glycolic acid in treatment of melasma in dark skinned patients . Due to paucity of studies on tretinoin peels as a treatment modality in melasma we have conducted this study.

Materials and Methods

An Open label prospective interventional study to evaluate the efficacy of 1% tretinoin peel in treatment of melasma in dark skinned patients was conducted at tertiary centre. Total of 30 patients of melasma of any type (epidermal, dermal, mixed), attending the outpatient skin department of Tertiary Centre , having Fitzpatrick's skin type IV and V were enrolled in the study, after ethical approval and informed consent. Pregnant and lactating women, patients with active infection, having keloidal tendencies, photosensitive dermatoses and those taking drugs known to cause facial hyper melanosis and those treated with medium depth and deep peels were excluded from the study. Demographic profile, complete history and examination of the patients were documented in a prescribed predesigned performa. Type of melasma was noted using Wood's lamp. Baseline melasma area and severity index (MASI) scoring was done. Before each session, patients were advised to wash the area with bland soap and water. 1% Retinoic acid peel was applied to full face and left for 4 hours. Peel was to be washed with after 4 hours and patients were instructed to apply Sunscreen every morning before going outdoor in between the sessions. Total 3 sessions were done. Patients were evaluated using Modified melasma area severity index scoring (MASI) and photographs were taken before each peel and 4 weeks after the last session. Efficacy was assessed 4 weeks after the last session. A 4- grade scale was use to assess the efficacy

Table 2:

poor	<25% improvement
moderate	25-50% improvement
good	>50% improvement
excellent	75% improvement

The degree of tolerability to the peel and side effects, if any, were recorded. Data was pooled in Microsoft excel 2016 and analyzed statsticaly.

Results

Total 30 cases, 18(60%) were females and 12 (40%) were males. Age of patients ranged from 18-44 years with mean

age of 28.88 ± 6.02 years. The maximum numbers of patients were in age group 26-30 (36%). The mean duration of melasma was 3.36 ± 1.59 years, and majority (25, 83% patients) had it for duration of 5 years. 13 (43%) patients were housewives and the rest were students, shopkeeper, computer assistants, teacher, stenotypist and salesman.

26 (86%) patients had type IV skin and 4 (13%) were with type V skin. 12(41%) patients had mixed type of melasma and 16(53%) patients presented with epidermal and 2(6%) patients of dermal melasma was included in the study . 22(73%) centrofacial , 6(20%) malar and only 2(6%) had mandibular type of melasma.

Baseline MASI score ranges from 11-20 with Mean MASI Score 10.82. The mean MASI score at the end of treatment at 12 weeks was 5.2 with majority of patients (68%) in MASI score range of 1-10. In this study, the mean of percentage reduction of MASI score was 49%

6(20%) had excellent response (>75% reduction in MASI). All had Epidermal type of melasma.

12 (40%) patients were recorded with good response i.e. 50-75% reduction in MASI score at the end of 12 weeks. Out of which 6 were Epidermal and 6 were Mixed

8(26%) patients showed moderate response (25-49% reduction in MASI score), Out of which 4 were Epidermal and 4 were of Mixed Melasma and only 4(13%) patients came out with poor response. Out of which 2 were Dermal and 2 were mixed.

The peel was well tolerated in all except one patient who showed worsening of acne.

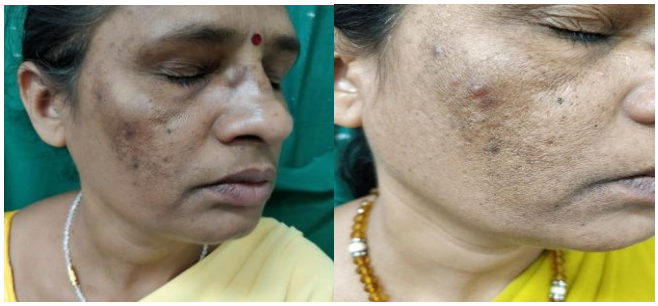

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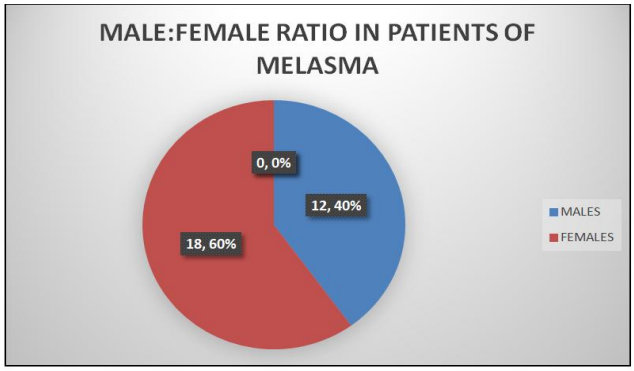
Table 3:

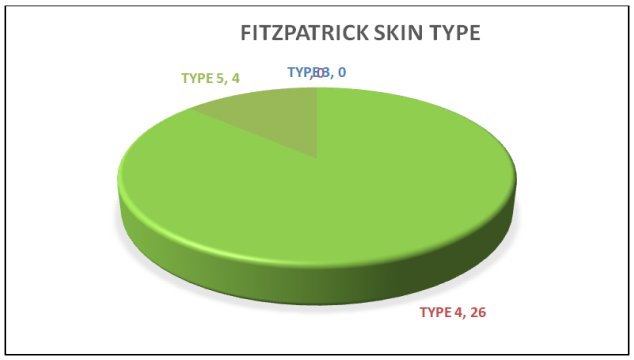
TYPE OF MELASMA BASED ON HPE	PATIENTS
EPIDERMAL	16
MIXED	12
DERMAL	2

Table 4:

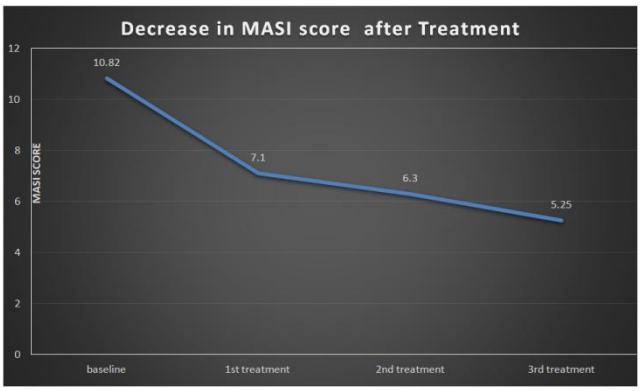
TYPE OF MELASMA BASED ON FACIAL DISTRUBITION	NO. OF PATIENTS
CENTROFACIAL	22
MALAR	6
MANDIBULAR	2



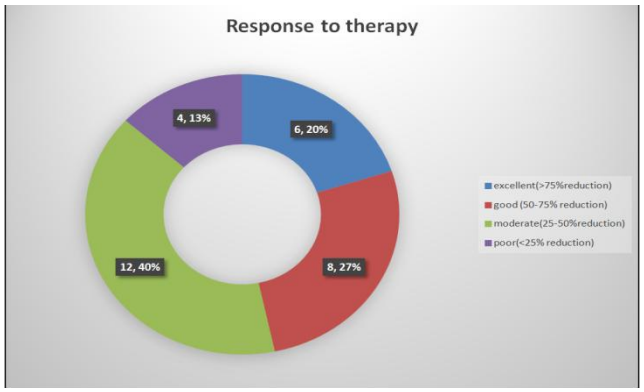
Graph 1: MALE: FEMALE RATIO IN ENROLLED PATIENTS



Graph 2: FITZPATRICK SKIN TYPE RATIO IN ENROLLED PATIENTS



Graph 3: Mean decrease in MASI score after treatment



Graph 4: Response to treatment in melasma patients

Discussion

Tretinoin peels

The liposoluble vitamin A is essential to the human body and only available in the diet. Its molecule is an alcohol and therefore is called "retinol". It is absorbed by the small intestine, stored in the liver as retinyl esters (palmitate and ethyl propionate), or converted to active metabolites such as tretinoin. Tretinoin activates three nuclear retinoic acid receptors (RAR-alpha, RAR-beta and RAR-gamma). The retinoic acid receptors (RARs) bind to regulatory regions in DNA called retinoic acid response elements (RAREs) or target sequences, and activate many gene transcriptions [8,9]. Topical tretinoin is used for the treatment of various dermatoses such as acne, melasma, scars, skin aging and non-melanoma skin cancer.

Chemical peels not only improve skin appearance but also cause histologic changes such as improvement of epidermal atrophy and atypia, as well as deposition of new subepidermal collagen. (10,11)

Cuce etall first tried Tretinoin peel in fair skinned followed by khunger etall who tried 1% retinoic acid in dark skinned.

In 2001, a case series with 15 participants investigated clinical and histologic modifications of the skin after five sessions of tretinoin peeling. The procedures were performed twice a month in concentrations of 1-5%. The study showed good clinical and histologic results applying the peel with 6 to 8 hours in contact to the skin in patients with skin types I to IV, with a quick achievement of lightening of melasma in photoaged skin over 2.5 weeks. (12)

In 2004, one study demonstrated that 1% tretinoin peel was probably as effective in the reduction of the pigmentation in melasma in dark-skinned patients as the standard peel, using 70% glycolic acid .(13)

Topical retinoic acid applied daily to the skin produces modifications in the epidermis with dispersion of melanin (14,15). It is possible that tretinoin peel, which is classified as a superficial peel, can induce the same modifications with the advantage of being faster and less cumbersome for the treatment of patients with melasma (15,16). In addition, 1% tretinoin peel provided the results in a relatively shorter period, that is, 12 weeks as opposed to the daily treatment with 0.1% tretinoin cream, which required 24 weeks to achieve the same outcomes (17,18) . In comparison with 70% glycolic acid peel, the 1% tretinoin peel was less irritating and therefore better tolerated (19). As for effectiveness, both treatments reduced pigmentation, with no difference between the agents. Additionally it is essential to investigate the ideal concentration, vehicle and standardization of application (range and number) for a particular treatment. For this purpose it is necessary more controlled, randomized and comparative studies between the gold standard tretinoin cream treatment versus its use as a peeling agent.

Conclusion

It is concluded that 1% tretinoin peeling is effective in the treatment of melasma in patients with Fitzpatrick's skin type IV and V. It is safe and well-tolerated with very few side effects. Tretinoin peeling is effective in patients with epidermal and mixed melasma having type IV skin as compared to patients with dermal melasma and type V skin. Increasing the number of peeling sessions may result in more effective clearance of melanin pigment. Priming or preparing the skin prior to the peel is a useful adjunctive measure which not only enhances the effect of peeling but also decreases the risk of post inflammatory hyperpigmentation. Although the treatment of melasma in dark skin is frustrating and challenging, cautions and judicious use of tretinoin peeling and combining it with other treatment modalities may give better cosmetic outcome

References

1. Sheth VM, Pandya AG. Melasma: A comprehensive update: Part I. J Am Acad Dermatol. 2011;65:689–97.
2. Ball Arefiev KL, Hantash BM. Advances in the Treatment of Melasma: A Review of the Recent Literature. Dermatol Surg. 2012;38:971–84.
3. Melasma update Rashmi Sarkar1, Pooja Arora2, Vijay Kumar Garg, Sidharth Sonthalia, Narendra Gokhale
4. Department of Dermatology, Maulana Azad Medical College and Lok Nayak Hospital, New Delhi, India
5. Department of Dermatology, Hamdard Institute of Medical Sciences and Research, Jamia Hamdard, New Delhi, India 3 Skin Clinic, Skinnocence, Sushant Lok, Gurgaon, Haryana, India 4 Skin Clinic, Sklinic, Indore, Madhya Pradesh, India
6. Roenigk RK, Brodland DG. A primer of facial chemical peel. Dermatol Clin. 1993;11:349-59.

7. Nelson BR, Fader DJ, Gillard M, Majmudar G, Johnson TM. Pilot histologic and ultrastructural study of the effects of medium-depth chemical facial peels on dermal collagen in patients with actinically damaged skin. J Am Acad Dermatol. 1995;32:472-8.

8. Cucé LC, Bertino MC, Scattone L, Birkenhauer MC. Tretinoin peeling. Dermatol Surg. 2001;27:12-4

9. Khunger N, Sarkar R, Jain RK. Tretinoin peels versus glycolic acid peels in the treatment Grimes PE. Melasma: etiologic and therapeutic considerations. Arch Dermatol. 1995;131:1453-7.

10. Tur E, Hohl D, Jetten A, Panizzon R, Frenk E. Modifications of late epidermal differentiation in photoaged skin treated with topical retinoic acid cream. Dermatology. 1995;191:124-8.

11. Grimes PE. Melasma: etiologic and therapeutic considerations. Arch Dermatol. 1995;131:1453-7. Cucé LC, Bertino MC, Scattone L, Birkenhauer MC. Tretinoin peeling. Dermatol Surg. 2001;27:12-4.

12. Rubin ME. Manual of Chemical Peels: Superficial and Medium Depth. Philadelphia: Lipincott, 1995. p.17-25.

13. Kimbrough-Green CK, Griffiths CE, Finkel LJ, Hamilton TA, Bulengo-Ransby SM, Ellis CN, et al. Topical retinoic acid (tretinoin) for melasma in black patients - a vehicle-controlled clinical trial. Arch Dermatol. 1994 Jun;130:727-33.

14. Lawrence N, Cox SE, Brody HJ. Treatment of melasma with Jessner's solution versus glycolic acid: a comparison of clinical efficacy and evaluation of the predictive ability of Wood's light examination. J Am Acad Dermatol. 1997;36:589-93.