ORIGINAL ARTICLE

Serial Glycolic Acid Peels Verses Topical Adapalene Gel in the Treatment of Melasma

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ABSTRACT

Objective: The study aimed to access the efficacy and safety of serial glycolic acid peels verses topical adapalene gel in melasma.

Study Design: Prospective, randomized trial.

Place and Duration: Department of Dermatology, Isra University, Hyderabad, during May 2014 - December 2014.

Material & Methods: Sixty patients with melasma were enrolled in this prospective, randomized trial, and divided into two groups; the Group A received chemical peels of serial glycolic acid peels. The Group B received topical adapalene gel at night. The clinical improvement was assessed with the Melasma Area Severity Index (MASI) at baseline and every six weeks during the 30-week treatment period, the observations were analysed and results were tabulated.

Results: The results showed a prominent decrease in MASI scores at the end of the treatment in both groups, the results were better in the Group A receiving chemical peels ($P = 0.048$). All patients tolerated the topical agents well with minimal irritation observed in the first few weeks of the therapy.

Conclusion: Study suggests that treatment with serial glycolic acid peels should be considered as an effective and safe therapy in melasma.

Key words: Adapalene, Chemical peel, Glycolic acid, Melasma.

INTRODUCTION:

Melasma is a common, acquired hyper-pigmentary condition manifests as irregular tan to dark brown macules and patches in sun-exposed areas involving the face especially the cheeks and less commonly the neck, hand and the forearm[1]. The condition seen most commonly on the face of women with Fitzpatrick skin types iv-vi[2]. The pathogenesis of melasma is not fully understood but, the reported predisposing factors are sunlight exposure, pregnancy, oral contraceptive and hormone replacement therapies, cosmetics, inflammatory processes of the skin, photo-sensitizing drugs and genetic influences[3,4].

Melasma is much more common in women than men (9:1). Currently different treatment modalities are used for melasma but, the first line of treatment for melasma is sun block, sun block should contain zinc and titanium, which have peaks of absorption in the UVA and UVB range, respectively, and an SPF of at least 45, although 60 is preferable. Sun block should be reapplied during the day to maximize its coverage and should also be used on cloudy days. The other treatment modalities include chemical peels, laser therapies and topical agents including azelaic acid, hydroquinone, kojic acid and retinoic acids.[5] Superficial chemical peels with glycolic acid, trichloroacetic acid (TCA) and Jessner's solution have been introduced as a treatment option in melasma, primarily acting as removing melanin from the epidermis[6]. A recent study indicated an additive inhibitory effect of glycolic acid on

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melanin synthesis through tyrosinase activity in melanocytes[7].

Adapalene is a synthetic napthoic acid derivative with potent retinoic acid receptor activity. Adapalene has been documented to be a safe and efficacious monotherapy in the treatment of melasma, with a lower potential for skin-irritation compared with topical tretinoin.[8] In recent studies combined treatment methods such as glycolic acid peels combined with Kligman's formula (i.e. 5% hydroquinone, 0.05% tretinoin and 1% hydrocortisone acetate) have yielded better results compared with topical agents used alone.[8]

In this study we compared the efficacy and safety of serial glycolic acid peels, and topical adapalene gel in the treatment of melasma.

MATERIAL & METHODS:

The study designed as a randomized, prospective study. The study group consisted of 60 women patients, aged between 25-50 years attending out patient department of Isra University Hospital. The inclusion criteria required a diagnosis of epidermal melasma confirmed by wood's lamp examination that was resistant to conventional therapies. The exclusion criteria included topical treatment with in 3 months, dermal and mixed melasma, pregnancy, recent delivery, oral contraceptive and hormone replacement therapies, keloidal tendencies and history of hypersensitivity to chemical peels.

Patients gave written informed consent before enrolment. The patients who were randomly allocated in to two groups, comprising 30 patients in each group, but during the study period 18 cases were drop out due to unrelated reasons and finally there were 24 patients in Group A and 18 patients in Group B. The Group A received a total of six glycolic acid peels every 6 weeks, during a 30-week treatment period. The Group B applied only topical adapalene gel at night during a 30 week treatment period. All patients were instructed to use broad-spectrum sunscreens to entire face every 3 hour during the day time. Before each peel, the face was cleansed with neutral ph soap. The initial chemical peel was performed with 20% glycolic acid solution. Higher concentrations of glycolic acid solutions (i.e. 20%, 50% and 70%) were applied in every other chemical peel course, respectively (0^{th} and 6^{th} week 20%, 12^{th} and 18^{th} week 50%, 24^{th} and 30^{th} week 70%), (Table-1). The duration of each peel session was 2-3 min, depending on patient tolerance and degree of erythema. The solution is applied with cotton to the entire face and neutralized with saline soaked gauze at the end point, followed by rinsing with cool water. Patients used sunscreens until the next session.

Clinical assessments were performed by the same investigator every 6 weeks during the 30-week treatment period. Evaluations of Melasma Area Severity Index (MASI) scores were done at baseline and every 6 weeks during the 30-week period. The MASI is an index designed to quantify the severity of melasma during therapy, determined by Kimbrough-Green *et al.* [9] According to the MASI score, the face is divided into four anatomical areas: (F) frontal; (MR) right malar; (ML) left malar; and (C) chin. These correspond to 30, 30, 30 and 10% of the total face area, respectively. The area of involvement in each of these was given a numerical value of 06: (0) no involvement; (1), 09%; (2) 10-29%; (3) 30-49%; (4) 50-69%; (5) 70-89%; (6) 90-100%. Other parameters were: (D) darkness, on a scale of 0 (absent) to 4 (maximum); and (H) homogeneity of hyperpigmentation from 0 (minimum) to 4 (maximum). The values were added to calculate the MASI score according to the formulation of Kimbrough-Green *et al.*:[9] MASI = 0.3 (Darkness of frontal region (DF) + Homogeneity of frontal region (HF)) Area of frontal region (AF) + 0.3 (Darkness of right malar region (DMR) + Homogeneity of right malar region (HMR)) Area of right malar region (AMR)+0.3 (Darkness of left malar region (DML) + Homogeneity of left malar region (HML) Area of left malar region (AML)+0.1 (Darkness of chin (DC)+ Homogeneity of chin (HC)) Area of chin (AC). The results were analysed statistically using the Wilcoxon signed rank *t*-test for unpaired samples and MannWhitney tests. Significance was defined as $P < 0.05$.

Skin irritation and adverse effects were observed every 6 weeks during the 30-week treatment period. Degrees of erythema, blister, peeling, crust, hyperpigmentation and hypopigmentation were assessed in each chemical peel session. Skin irritation findings secondary to adapalene gel including erythema, burning, stinging and desquamation were also noted in a similar manner.

RESULTS:

A total of 60 cases were enrolled in the study, 18 cases were dropped and remaining forty two patients completed 30 weeks of treatment: The mean age was 35 years (range, 25-50 years) in the Group A, and 34 years (range, 25-50 years) in the Group B. The mean MASI scores (baseline) with Group A was 13 and with Group B was 14. Statistical analysis showed no significant difference with respect to age and baseline mean MASI scores between the two groups (Table -2)

A significant decrease in MASI scores was obtained in both groups at the completion of the study. The mean MASI Scores (6th week) with Group A was 11.6 and with Group B 11.8, mean MASI scores at (12th week) with Group A was 10.2 and with Group B 9.5, mean MASI scores at 18th week with Group A was 4.1 and with Group B 6.9, mean MASI scores at (24th week) with Group A was 3 and with Group B 5, mean MASI scores at (30th week) with Group A was 2.3 and with Group B 4.2. (Table-3). In the Group A, a percentage change of 83.08% in mean MASI scores was observed, compared with a 69.34% decrease in the Group B ($P = 0.001$ and $P = 0.005$, respectively). Although the improvement was better in the Group A at 12 ($P = 0.013$), 9 ($P = 0.035$) and 30 weeks ($P = 0.048$) of treatments.

Signs of mild erythema, itching, burning and stinging were observed in few patients, no allergic reactions, scarring or infection was observed in either group.

DISCUSSION:

Chemical compounds with depigmenting activity are used in dermatology and cosmetics for a long time. In melasma, the enhanced risk of developing postinflammatory hyperpigmentation restricts the use of medium-depth or deeper chemical peels, in most cases.[9,10]

Table-1 Concentrations of glycolic acid solution on each chemical peel session

Weeks	Glycolic Acid Concentration (%)
0	20%
6	20%
12	50%
18	50%
24	70%
30	70%

Table-2: Demographic Features of Patients

Variable	Group A	Group B	P Value
Mean Age	35	34	0.814
Mean Masi Scores (baseline)	13.65	14	0.949

The mode of action of glycolic acid peels mainly depends on facilitating the removal of melanized keratinocytes, leading to melanin pigment loss and acceleration of skin turnover. At high concentration, glycolic acid diminishes corneo-cyte adhesion in the upper layers of the epidermis, causing an epidermolytic effect that may hasten the removal of excessive melanin pigment.[11] A decade old study showed that topical application of glycolic acid at concentrations of 50% had resulted in decrease of melanin deposits in the epidermis as well as acceleration of desquamation.[5]

In the study by Usuki et al., glycolic acid was shown to inhibit melanin formation in a dose-dependent manner, through direct inhibition of tyrosinase enzyme activity in cultured melanoma cells.[2]

Table-3: Mean Melasma Area Severity Index (MASI) Scores over 30 Week Treatment Period

Period	Baseline	6th Week	12th Week	18th Week	24th Week	30th Week
Group A	13	11.6	10.2	4.1	3.0	2.3
Group B	14	11.8	9.5	6.9	5.0	4.2

Some authors suggested that glycolic acid is a week peeling agent and requires concentrations of 50-70% to achieve a desired improvement.[12] Our clinical trial supports this opinion, with a statisti-cally better result in the Group A, compared with the Group B at 18, 24 and 30 weeks. A clinical trial, in which no additional effects were obtained with a combined regimen, including 20% & 30% glyco-lic acid peels with topical 4% hydroquinone cream, compared with topical hydroquinone alone also suggests the need to use higher concentrations of glycolic acid for a synergistic effect at this point.[13] Statistically, differences in the clinical scores between the two groups in terms of P-values were more pronounced at 18 weeks, corres-ponding to the time we carried out 50% glycolic acid peels, then at 24 and 30 weeks, the time that we completed the treatment with 70% glycolic acid peels. These findings suggest that a final concentration of 50% glycolic acid may be ideal for serial glycolic acid peels in the treatment of melasma, thus higher concentrations may diminish the clinical results probably as a result of the enhanced risk of postinflammatory hyper-pigmentation. In a recent clinical trial, a combined therapy using serial glycolic acid chemical peels and Kligman's formula (5% hydro-quinone, 0.05% tretinoin and 1% hydro-cortisone acetate) was compared with topical Kligman's formula in the treatment of melasma; at the end of the 21-week treatment period, a 79.99% decrease in MASI scores was obtained in the glycolic acid peel group, compared with a 63.14% decrease in the group applying Kligman's formula only.[7] Our results were similar with a 83.08% and 69.34% decline in MASI scores at the final follow up, in the Group A (receiving glycolic acid peel) and Group B (receiving only topical adapalene gel), respectively.

The exact mechanism of topical retinoids in the lightening of melasma is unclear, although skin turnover acceleration and enhancing the efficacy of bleaching agents should be the modes of action. Topical tretinoin alone has been shown to be effective in a 10-month, vehicle-controlled clinical trial in melasma.[9] In another study, combined therapy with topical tretinoin and azelaic acid yields better results in comparison with glycolic acid alone.[8] Adapalene is a synthetic retinoid with an established clinical efficacy against melasma and solar lentigines and good local tolerabilities.[2] In the present study, topical 0.1% adapalene gel has been well tolerated with minimal irritancy.

CONCLUSION:

We conclude that serial glycolic acid peels has a beneficial effect on melasma, with minimum adverse effects. Our results suggest that the serial chemical peels with a final concentration of 50% glycolic acid should provide better improvement in melasma.

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