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Original Research Article

Comparative Study of Safety and Efficacy of 35% Glycolic Acid Chemical Peel versus Combination of Topical Agents Containing Liposomal 4-n-Butylresorcinol, Kojic Acid and Arbutin in the Management of Melasma

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Conflict of interest: Nil

Abstract:

Background: Melasma is characterized by hyperpigmented macules commonly affecting the malar region, forehead and temple region of face. It is a common disorder of hyperpigmentation with prevalence ranging from 1.5 % to 33.3%. Various treatment options have been evaluated in treatment of melasma, but none have been effective universally.

Aim: To compare the safety and efficacy of 35% Glycolic acid chemical peel versus combination of topical agents containing liposomal 4-n-butylresorcinol, kojic acid and arbutin in the management of melasma.

Method: An analytical interventional study was conducted at Anugraha Narayan Magadha medical college and hospital, Gaya, Bihar. Melasma cases were diagnosed clinically and classified with the help of woods lamp examination. Patients were randomly divided into two groups. The response was assessed and collected data were analyzed and Probability (p) value is calculated at baseline and 12 weeks.

Result: In 35% Glycolic acid chemical peel group average baseline M. MASI was 3.6 which got to 2.5 with a statistically significant P value of 0.004. In group receiving combination of 4nbutylresorcinol, kojic acid and arbutin the M. MASI was 4.1 which got improved to 3.3 with a statistically significant P value of 0.043. No adverse effects were observed in any group.

Limitation: The main limitations of the study were the small sample size and the lack of long term follow up to assess recurrence.

Conclusion: Both 35% Glycolic acid chemical peel and combination of 4nbutylresorcinol, kojic acid and arbutin are safe and effective method to treat melasma. Comparison between two groups was statistically insignificant with a P value of 0.441.

Keywords: Glycolic Acid, Melasma, 4-n-butylresorcinol, Modified MASI, Hyperpigmentation.

Introduction

Melasma is a common disorder of hyperpigmentation. It is characterized by a symmetrical macular pigmentation of sun-exposed areas of the face commonly over malar, forehead, nose region. [1] It typically affects women of reproductive age with Fitzpatrick skin type IV-VI, though men also represent 20.5-25.83% of cases. [2] The overall prevalence varies between 1.5%-33.3percentdepending on population. [2] The understanding of pathophysiology of melasma has undergone a paradigm shift. [4] The exact pathogenesis and cause of melasma are still unknown. Various risk factors are known such as exposure to sunlight, drugs, OCPs, pregnancy, etc. [6]

It is now considered to be a complex interaction involving keratinocytes, melanocytes, fibroblast, vascular endothelial cells with influences from genetic, hormonal and environmental factors. With the aid of in-vivo reflectance confocal microscopy, it has revealed that the distribution of melanophages is heterogeneous suggesting that all melasma are mixed. [4] It has paved the way for several potential targets for its treatment. Various agents acting at different levels like inhibition of melanogenesis pathway, reducing inflammation, inhibiting melanosomal transfer to keratinocytes, restoring the skin barrier have been developed. [4]

Agents like liposomal 4-n-butylresorcinol, arbutin and kojic acid inhibits tyrosinase enzyme and related proteins, thereby inhibiting the process of melanogenesis. [2] On the other hand chemical peeling is a popular method to treat melasma and provides more rapid response to topical therapy. It

creates injury in a controlled manner at a specific skin depth with the aim of stimulating new epidermal growth and collagen redistribution with more evenly distribution of melanin. [6]

Despite all these treatment modalities, none of them is effective universally making treatment of melasma a challenging disorder. [1]

Therefore, the present study was undertaken to compare safety and efficacy between agents targeting the process of melanogenesis and agents targeting skin remodelling and resurfacing in the treatment of melasma.

Methods: An interventional analytical study was performed in a tertiary care hospital setting in Bihar.

A total of 35 patients were enrolled in the study from 1June 2022-30 Nov 2022 and each patient is followed up for a period of three months after taking informed written consent.

A detailed demographic profile and thorough clinical history and examination were done.

Inclusion Criteria: Patients with a clinical diagnosis of melasma.

Exclusion Criteria: Patients on oral contraceptive pills or hormone replacement therapy, pregnant females, lactating mothers, patients with any systemic illness, inflammatory dermatoses, active infection, on any other drug including topical or oral depigmenting agents, any facial resurfacing procedure in last one year were excluded from the study. Clinical photographs were taken using iPhone 12 pro under standard conditions in natural light.

Participants were classified to clinical patterns of melasma into epidermal, dermal and mixed based on wood's lamp examination. Patients with epidermal and mixed melasma are included in the study. In the prepeel programme patients were advised to apply topical sunscreen daily (SPF 30) and emollient (containing ceramides, cholesterol, and free fatty acid) for a period of 2 weeks as per standards of study and were continued throughout study and follow up period.

The first group was treated with 35% glycolic acid chemical peel for a period of 3-5 minute depending on tolerability and minimal erythema.

For the purpose of peeling, the face was divided into anatomical units- left forehead, right forehead, right cheek, left cheek, glabella, nose, and perioral area. After degreasing, treatment with 35% glycolic acid peel was carried out in the respective group for a period of 20-30 seconds and was left for a definite period (3- 5 minutes).

The peel was terminated by the dilutional effect of sodium bicarbonate spray solution in the same sequence as the application.

At 3 weekly intervals the side effects were noted before proceeding to higher duration. The second group was advised to apply combination of 4-n-butylresorcinol, kojic acid, arbutin on the lesion of melasma twice daily single coat, uniformly with the help of cotton.

Improvement was assessed using clinical photographs, modified melasma area and severity index (mMASI-figure1), and any adverse event is noted. The collected data were analysed with IBM SPSS stats for window version 23.0 and mean, standard deviation, independent T test, paired T test were calculated.

The Probability (P) value of less than 0.05 is considered as significant.

Results

Out of 35 patients in the study, 5 patients lost to follow up and were excluded from the study.

8 Male (26%) and 22 female (73%) patients in age group 18-42 years (average 30.7 years with average duration of melasma 3.73+/- 1.65 years.

In total, family history was positive in 11 patients (36.7%) with average duration of outdoor work 1.7 hour and Fitzpatrick skin type 2-5. In 35% glycolic acid group average baseline mMASI was 3.6+/- 1.7 which got improved to 2.5+/- 1.3 after 12 weeks with a statistically significant P value of 0.004

Side effects after peeling were stinging sensation in 12 patients (80%), mild burning in 3 patients (20%) and 0% cracking, 0% moderate to severe pain. No adverse event was noted.

In the group receiving combination of liposomal 4-n-butylresorcinol, kojic acid and arbutin the mMASI score from 4.1+/- 2.2 got improved to 3.3+/-1.6 with a statistically significant P value of 0.043.

No side effects of stinging, burning, pain, dryness were noted. No adverse effects were noted. The average decrease in m MASI score from baseline in both groups was statistically significant.

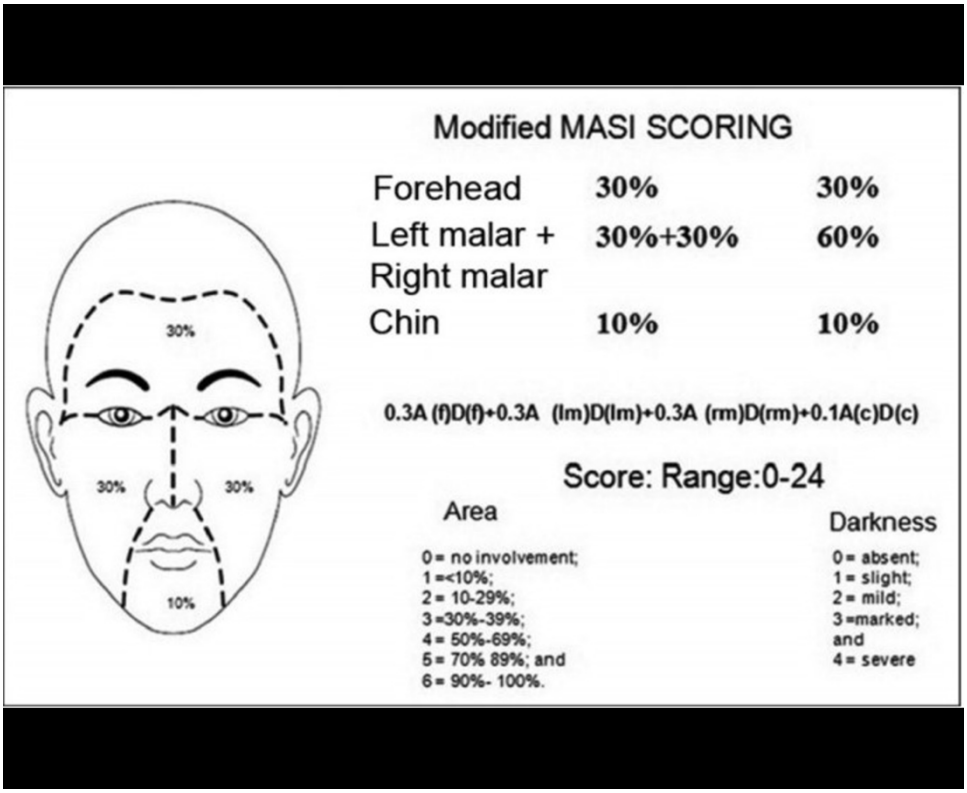

Figure 1: Modified melasma area and severity index (mMASI)

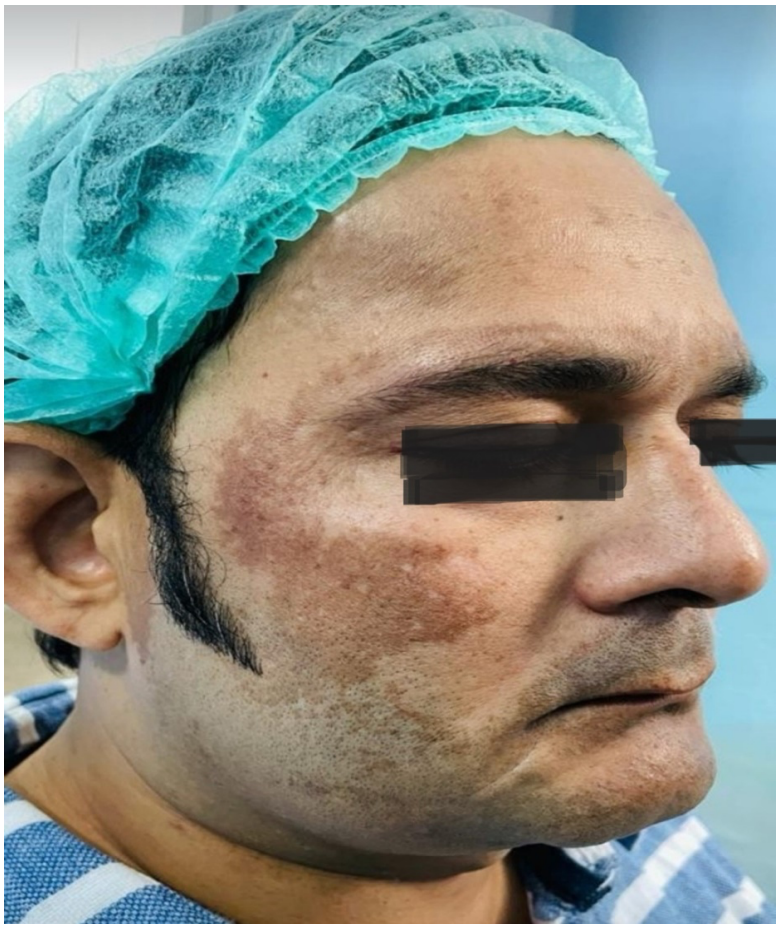

Figure 2(a): Melasma in a 38 year-old-male before treatment

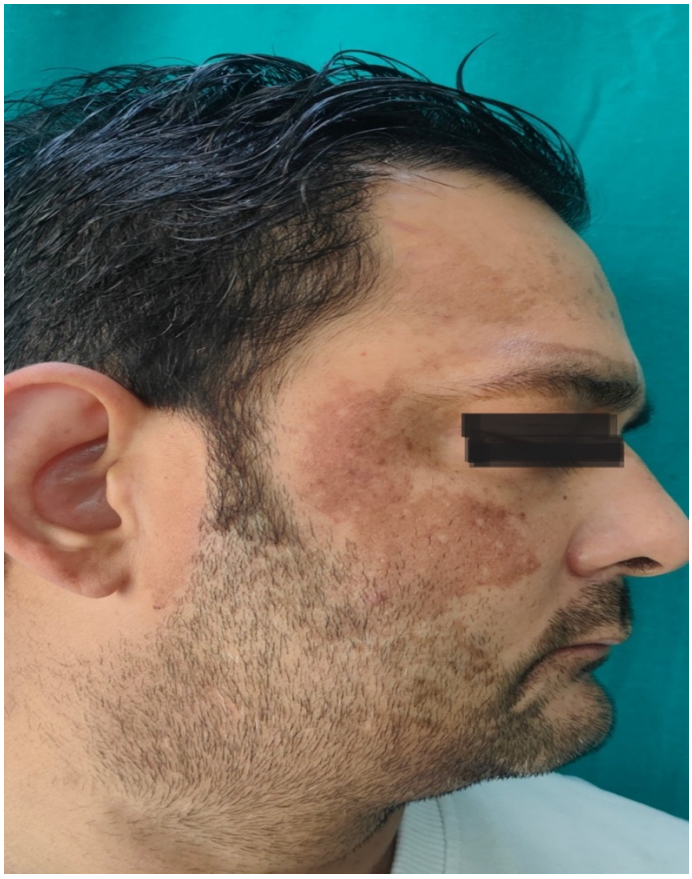

Figure 2(b): After four sessions of 35% glycolic acid chemical peel in same patient

Figure 3(a): Melasma in a 27 year-old-male before treatment

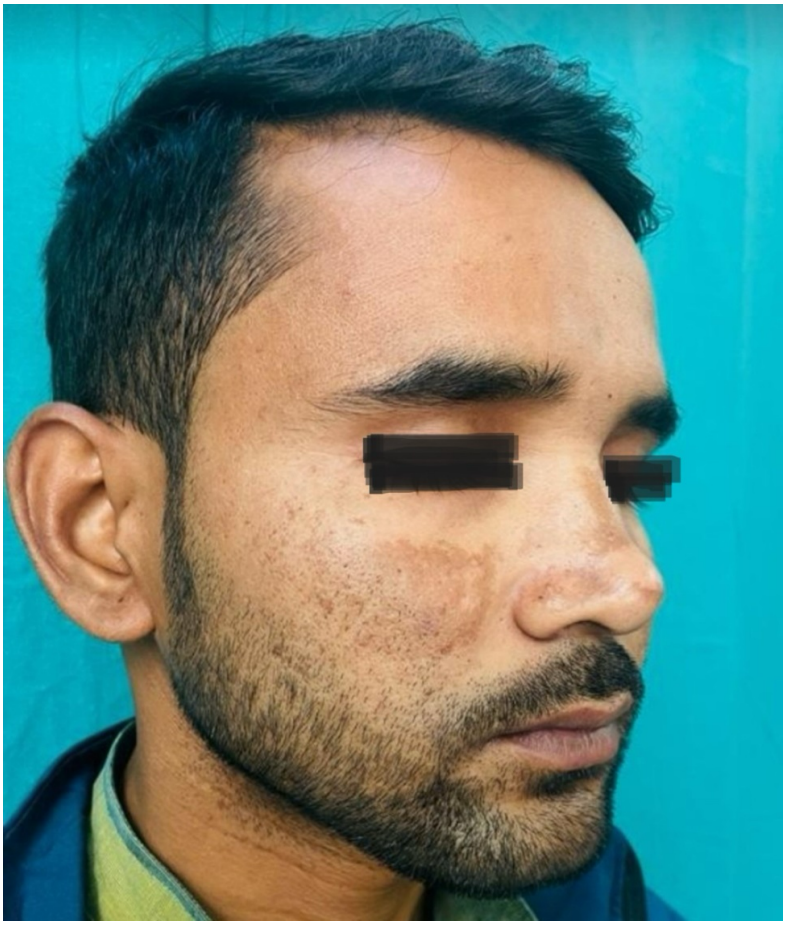

Figure 3(b): After 12 weeks of treatment with combination of liposomal 4nbutylresorcinol, kojic acid and arbutin cream

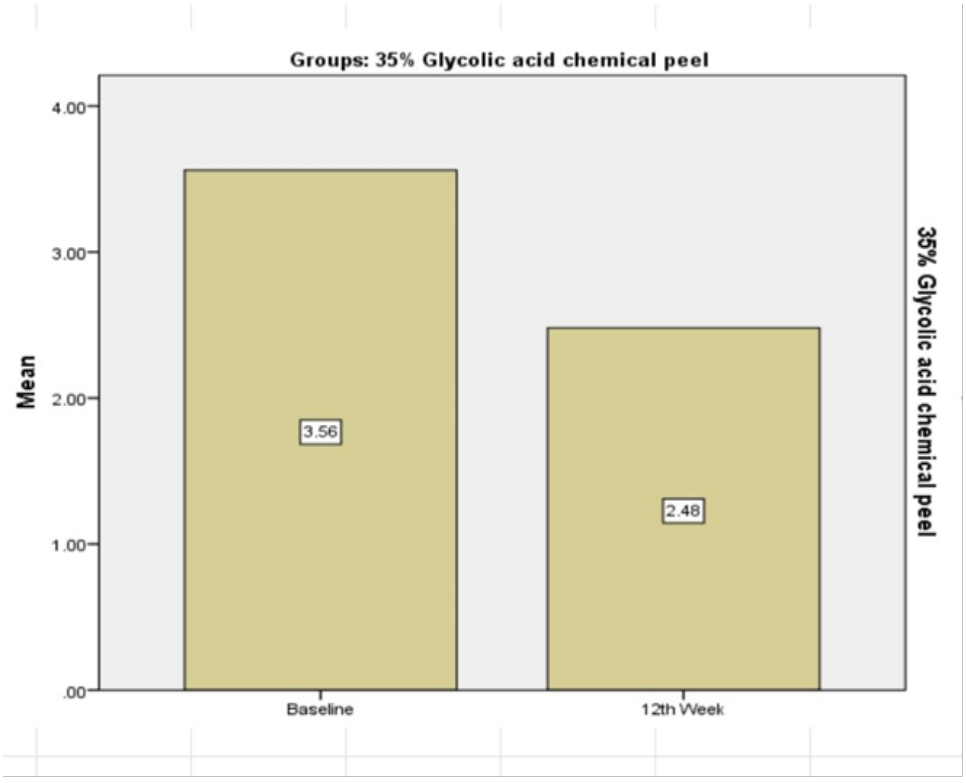

Figure 4: Bar graph showing mMASI reduction from baseline and after 12 weeks in group of patients treated with 35% glycolic acid chemical peel

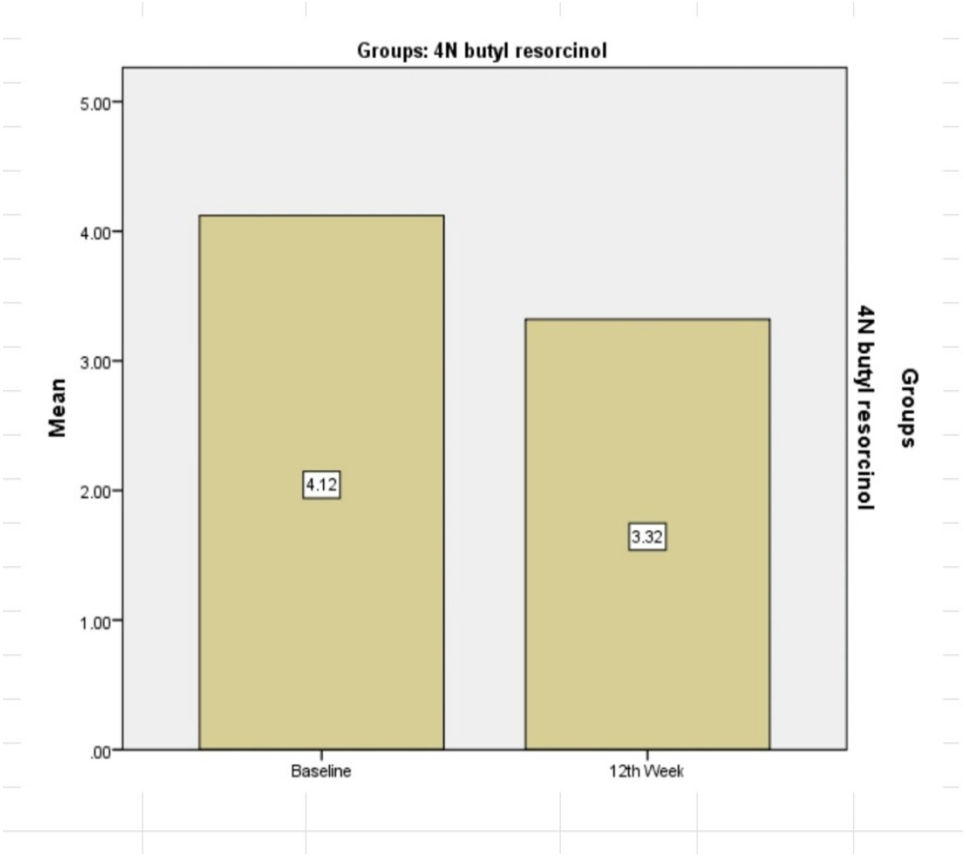

Figure 5: Bar graph showing mMASI reduction from baseline and after 12 weeks in group of patients treated with combination of liposomal 4nbutylresorcinol, kojic acid and arbutin cream

Table 1: Intragroup comparison between two groups from baseline and after 12 weeks using paired sample test.

Groups			Paired Differences					t	df	p-value
			Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Diff.				
						Lower	Upper			
4N butyl resorcinol	Pair 1	Baseline -12th Week	.80000	1.39181	.35936	.02924	1.57076	2.226	14	043
35% Glycolic acid chemical peel	Pair 1	Baseline -12th Week	1.08000	1.22544	.31641	.40137	1.75863	3.413	14	.004

Table 2: Intergroup comparison between two groups from baseline and after 12 weeks using independent sample test

Independent Samples Test										
		Levene's Test for Equality of		t-test for Equality of Means						
		F	Sig	t	df	p-value	Mean Difference	Std. Error Difference	95% Confidence - Interval of	
									Lower	Upper
Baseline	Equal variances assumed	485	.492	782	28	441	56000	71614	90695	2.02
12th Week	Equal variances assumed	1,742	.198	1,625	28	115	84000	51708	21919	1.89

Discussion

Melasma is a common and challenging disorder with a frequency to relapse. It has a significant bearing on individual's quality of life as well as social interactions.[1]

4-n-Butylresorcinol is a derivative of resorcinol that inhibits tyrosinase and tyrosinase related protein, an enzyme that catalyzes melanin biosynthetic pathway. [2]

A randomized controlled split face trial to evaluate safety and efficacy of liposomal-encapsulated 4-n-butylresorcinol 0.1% cream in management of melasma have shown a statistically significant reduction in melanin index on the treatment side. [12]

Demelanising agents such as arbutin are a hydroquinone derivative which acts by inhibiting melanogenesis and prevents melanosome maturation. [4] In a study 2.51% arbutin resulted in significant improvement in management of melasma. [13]

On the other hand, glycolic acid is an alpha hydroxy acid which acts by decreasing corneocytes adhesion leading to sloughing of dead cells and stimulation of new cell growth in the basal cell layer. [5]

Glycolic acid chemical peel results in resurfacing of epidermis and remodelling of collagen and elastic fibers with deposition of glycosaminoglycans in dermis. It also has a regulated effect on melanocytes and thus the process of melanogenesis. Hence, chemical peel targets multiple aspects involved in pathogenesis of melasma. [5]

In this study, we did a comparison between 35% glycolic acid chemical peel and combination of topical agents to assess the safety and efficacy in the treatment of melasma. Improvement was assessed on the basis of clinical photographs, modified MASI (melasma area and severity index) and any adverse event is noted.

Improvement with glycolic acid chemical peel was better than topical agents, though not significant.

This is probably because chemical peel targets multiple aspects involved in pathogenesis of melasma such as keratinocytes, dermal fibroblast, melanocytes etc.

No adverse effects were noted.

Limitations: The main limitations of the study were the small sample size and the lack of long term follows up to assess recurrence.

Conclusion

Both 35% glycolic acid chemical peel and combination of liposomal 4-n-butylresorcinol, kojic acid and arbutin are safe and effective method to treat melasma.

Comparison between two groups is statistically insignificant with a P value of 0.441.

Average mMASI reduction was more with 35% glycolic acid chemical peel.

No side effects and adverse events are noted with combination of liposomal 4-n-butylresorcinol, kojic acid and arbutin.

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