Original Research Article

A comparative study of modified kligmans regimen with a combination of 4-n-butylresorcinol, α- arbutin and licorice extract in the treatment of melasma

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Abstract

Background: Melasma is one of the most common causes of acquired, symmetrical hyper melanosis of the face. It affects all racial groups. Women are more affected than men. Numerous therapeutic modalities are available like hydroquinone, tretinoin, and topical steroids have been used singly or in combination with variable results. Newer formulations that are being tried include Tranexamic acid, 4-n-butyl resorcinol, Arbutin, aloesin, green tea extracts, coffeeberry, soy, and liquorice extract. However, very few agents have produced a completely satisfactory response. **Objective**: To compare the efficacy of modified Kligman's regimen with a combination of 4-n –butyl resorcinol, α-Arbutin and liquorice extract in the treatment of melasma. **Materials and Methods**: The study group includes 50 patients of all age groups presenting with melasma to the department of DVL, Santhiram medical college and General Hospital, Nandyal. All the Patients will be divided into two groups and allocated alternately to Group A, and Group B. GROUP A (n=25) receives modified Kligman's regimen. GROUP B (n=25) gets a combination of 4-butyl resorcinol, alpha arbutin and liquorice extract. Assessment of the severity was done by modified Melasma Area Severity Index(MASI). Photographs were taken at each visit. **Results**: Most of the patients were females constituting 96% of patients. Most common age group is 25 to 35 years with an average of 29.2. The mean modified MASI score is decreased in both groups, indicating that both the groups showed significant improvement during the study period ($P < 0.05$). According to subjective assessment, At the end of 8th week, in group A, 34.7% and in group B, 30.2 % of the patients were very satisfied. **Conclusion:** The study revealed that pigmentation was decreased in both groups, but the Combination of 4-n –butyl resorcinol, α-Arbutin and liquorice extract had lesser side effects compared to modified Kligman's regimen

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INTRODUCTION

Melasma is the most common cause of acquired hypermelanosis of the face. It is characterised by hyperpigmented macules on the face which become more pronounced after exposure to the sun, in particular, the cheeks, forehead, upper lip, nose, and chin. It affects all racial groups. Women are more affected than men, and it is more common among the women of child-bearing age.[1] It is a psychologically stressful condition for affected individuals and has adverse effects on social interactions, recreation, and emotional well-being.[3] There is no effective specific therapy for treating melasma. 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. As there is no perfectly satisfactory agent available for melasma,

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research is ongoing to develop a newer and safer treatment for treating this condition.[5]

AIM AND OBJECTIVE

To compare the efficacy of modified Kligman's regimen with a combination of 4-n –butyl resorcinol, α-Arbutin and liquorice extract in the treatment of melasma.

PATIENTS AND METHODS

This study is a comparative prospective Interventional study which was conducted at Department of DVL, Santhiram medical college and General Hospital, Nandyal from June 2019 to August 2019. The study group includes 50 patients of all age groups presenting with melasma to the OPD. Females and males of all the age groups and Patients willing to give consent for enrollment in the study and follow up were included in the study. Un-cooperative patients, patients with Post-inflammatory hyperpigmentation and Other pigmentary disorders and Patients who are already on treatment were excluded from the study. Informed written consent is obtained from patients in the study.The study was undertaken after Ethical clearance from the institutional ethics committee. The patients data was recorded in a Prestructured proforma that includes detailed clinical history, general and cutaneous examination. All the Patients will be divided into two groups and allocated alternately to Group A, and Group B. GROUP A (n=25) receives modified Kligman's regimen and are advised to apply topically once daily at night. GROUP B (n=25) receives a combination of 4-butyl resorcinol, alpha arbutin and liquorice extract and are advised to apply topically once daily at night. All patients are advised to apply broad-spectrumm sunscreen. Assessment of the severity was done by modified Melasma Area Severity Index(MASI). Pre-treatment photographs at baseline visit and at each follow up visit were taken. Patients were advised for follow up visits once monthly for two months. Results were assessed both objectively and subjectively. Objective assessment was done by modified MASI SCORE. Subjective assessment was graded as Not satisfied/satisfied/very satisfied.

Table 1: modified Melasma Area Severity Index

Modified MASI total score =	0:3 × A (forehead) × D (forehead) + 0:3 × A (left malar) × D (left malar) + 0:3 × A (right malar) × D (right malar) + 0:1 × A (chin) × D (chin)

A = Area of involvement, rated from 0 to 6: 0 indicates absent; 1 <10%;2 , 10%-29%; 3, 30% - 49%; 4, 50% - 69%; 5, 70% - 89%; 6, 90% - 100%;D = Darkness; rated from 0 to 4: 0 indicates absent; 1- slight; 2- mild; 3- marked; 4-severe. Total mMASI score range is 0 - 24 and is calculated by adding scores over 4 areas of the face.

RESULTS

In the present study,out of 50 patients ,most of them were females constituting 96% . Most common age group is 25 to 35 years with an average of 29.2 . The duration of melasma is for less than a year in 24% of the patients and greater than a year in 76%. 28 % of the patients reported the start of melasma before pregnancy and 72% after it. The most common site of distribution of melasma was malar(cheeks) seen in 68% of patients,followed by centrofacial (cheeks,nose,forehead)seen in 32% of patients.None of the patient had taken treatment before. Fitzpatrick skin type IV was seen in 68% of the patients and Skin type V in 22%. The mean MASI score at the baseline was 4.3 in group A and after 8 weeks,it reached to 2.02 (P=0.01) and in group B, it was 4.7 at baseline, and after 8 weeks, it reached to 2.2 (P=0.01) .The mean modified MASI score is decreased in both groups, indicating that both the groups showed significant improvement during the study period ($P < 0.05$). However, there was no statistical significant difference between both therapies at baseline and all reassessment visits ($P > 0.05$). Group B shows similar decrease in pigmentation compared to triple combination group A. According to subjective assessment, At the end of 8th week, in group A, 34.7% of the patients were very satisfied, 65.3% were satisfied and in group B, 30.2 % of the patients were very satisfied, 69.8% were satisfied. Side effects were more clinically evident in group A, such as skin irritation compared to group B.

Table 2: sex distribution

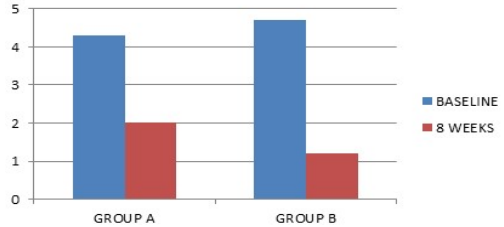
Gender	Number	Percentage
Female	48	96%
male	2	4%

Table 3: Age distribution

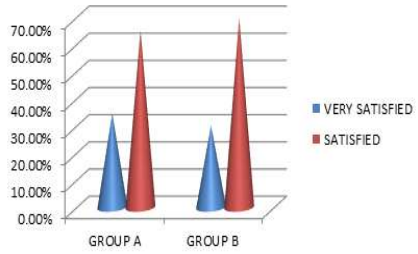
Age	Number	Percentage
21-30 yrs	12	24%
31-40 yrs	21	42%
41-50 yrs	9	18%
51-60 yrs	8	16%

Table 4: Distribution of melasma

Site	Number	Percentage
Malar	34	68%
Centrofacial	16	32%



Graph 1: modified MASI score



Graph 2: subjective assessment

Group A 1(a): before Group A 1(b): after

Group A 2(a): before Group A 2 (b): after

Group B 1(a): before Group B 1(b): after

Group B 2 (a): before Group B 2 (b): after

DISCUSSION

Melasma is a common, therapeutically challenging, and universally relapsing disorder of hyperpigmentation . The exact etiology of melasma is unknown, multiple factors have been implicated in the etiopathogenesis of this condition. These include genetic factors, exposure to UV radiation, pregnancy, oral contraceptives, estrogen-progesterone therapies, thyroid dysfunctions, usage of cosmetics and antiepileptic drugs. Existing treatment agents have varying degrees of effectiveness, and the condition more often than not, relapses.[5] over the last three decades, Kligman's triple combination formula has been one of the most popular treatment options in melasma The original Kligman's formula underwent many modifications i over the years and the most recent modification is a triple combination of 2% hydroquinone, 0.025% tretinoin, and 0.01% flucinolone acetonide. In present study, the efficacy and safety of combination of 4-n –butylresorcinol, α-Arbutin and liquorice extract were compared with modified triple combination therapy in the treatment of melasma. Triple therapy over 8 weeks in Group -A reduced MASI scores significantly. This reduction was observed as early as 4 weeks after treatment. This rapid decrease in melanin after 4 weeks is due to hydroquinone, as a tyrosinase inhibitor and also due to penetration enhancement effect of tretinoin. Tretinoin can also reduce melanin synthesis by inhibition of tyrosinase transcription after 8 weeks of use and this mechanism adds to hydroquinone action.The MASI score decreased from 4.3 to 2.02 in 8 weeks. This was similar to the study done by Ahmad Nasrollahi et al, where the mean MASI score at baseline was 3.61±0.81, after 4 weeks was 2.81±1.41, after 8 weeks was 2.45±0.80. Few patients complained of skin irritation but it was transient.[12,13]

In Group-B, Combination therapy was used for treatment.4-n-butylresorcinol, inhibits both tyrosinase and tyrosinase related protein, the enzymes in the melanin biosynthetic pathway. Thus ,helpful in treatment of melasma. Arbutin, which is extracted from Beaberry plant of genus Arctostaphylos, acts by the inhibition of tyrosinase and melanosome maturation thereby decreasing melanin formation. Alpha arbutin is the synthetic form of arbutin and shows greater inhibition of tyrosinase.[5,7] Liquorice is the root of the perennial herb Glycyrrhiza glabra. liquorice extract has been shown to have tyrosinase inhibitory as well as anti-inflammatory properties and has shown benefit in treating melasma [5].In group-B, the mean MASI score decreased from 4.7 to 2.2 in 8 weeks.No side effects were noted. In a study done by Sun Young Huh, M.D on 4-n-butylresorcinol; all the patients were women, and the mean age was 40.40±6.03 years (age range: 28~49 years). Mean Melanin index (MI) was decreased by 3.43% which was statistically significant observed after 4 weeks of application.After 8 weeks, the mean MI showed a significant decrease of 4.87%.[11] In study done by NT Madhan mohan et al, Out of total 52 subjects, 90.38% were females. The mean age was 38.5±7.8 years. There was significant decrease in Mean MASI score from baseline score which was 14.73 to 11.09 after 4 weeks (P=0.001) and 6.48 after 8 weeks (P=0.001).[8]

CONCLUSION

Our data suggest that pigmentation decreased in both groups but Combination of 4-n –butylresorcinol, α-Arbutin and liquorice extract had lesser side effects such as erythema, irritation as compared to modified kligman's regimen.Therefore, combination of 4-n –butylresorcinol,

α-Arbutin and liquorice extract is an effective addition to the therapeutic management of melasma with good safety, efficacy, and tolerability.

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