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TO EVALUATE THE EFFICACY AND SAFETY OF MODIFIED KLIGMAN REGIMEN VERSUS TOPICAL TRANEXAMIC ACID (10 %) IN THE TREATMENT OF MELASMA

Dermatology

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ABSTRACT

INTRODUCTION: Melasma is a common acquired hypermelanosis. This study aims at assessing the efficacy and safety of topical tranexemic acid versus topical triple combination for treatment of melasma. **METHODOLOGY:** 40 subjects were divided into group A and B, each with 20. Group A received triple combination cream once daily at night for 8 weeks then biweekly for 4 weeks. Group B received topical Tranexemic acid cream (10%) twice daily for 8 weeks then biweekly for 4 weeks. Patients were followed-up and assessed by using MASI score at baseline and monthly for total of 12 weeks. Any side effects were noted. **OBSERVATION:** The mean MASI score of baseline in group A and group B was 4.02 and 3.98 respectively. After 12 weeks, it reached to 1.04 in group A ($P < 0.05$) and 1.35 ($P < 0.05$) in group B. Significant decrease of mean MASI score at each follow up visits in both the groups but no statistically significant difference between the groups. Faster reduction in pigmentation and side effects like erythema, irritation and telangiectasia were observed more in triple combination compared to tranexamic acid. **DISCUSSION**: Melasma poses a great challenge as its treatment modalities are unsatisfactory. Treatment using tranexamic acid is a novel concept. Topical tranexamic acid (10%) is a safer alternative of modified Kligman's formula to initiate the treatment in melasma. **COCLUSSION:** On the basis of this observation, both groups showed significant improvement in melasma. Topical tranexamic acid can be used as a new, effective, safe, and promising therapeutic agent in melasma.

KEYWORDS

Melasma, Modified Kligman Regimen, topical Tranexamic acid (10%) cream

INTRODUCTION

Melasma is a commonly acquired pigmentary disorder characterized by dark brown macules involving the face. The most common sites on face are the cheeks, bridge of the nose, forehead, chin and above upper lip. It is a common condition affecting individuals of all race and both genders. It typically affects women of reproductive age, though the condition can occur in men also[1]

A variety of treatment has been proposed and used in melasma. They include topical medications such as hydroquinone, azelaic acid, corticosteroids, procedural treatments like chemical peels, microdermabrasion and light based options like Q-switched Nd: YAG laser, intense pulse light, and so on. All of these target to decrease melanin production over the local area directly or indirectly. One of the most effective topical therapies is the triple combination, Kligman's formula. Kligman had originally used dexamethasone 0.1% along with tretinoin 0.1% and hydroquinone 5% in a cream base. It was modified where dexamethasone has been substituted with steroids such as hydrocortisone, mometasone, fluocinolone and the strength of tretinoin and hydroquinone have been altered to suit different skin types. A fluocinolone-based triple combination, a Modified kligman regimen (fluocinolone acetonide 0.01%, tretinoin 0.05%, and hydroquinone 2%) has very good results in the treatment of melasma but concerns about the side effects and long term safety.[2]

Tranexamic acid (TA) (trans-4-aminomethyl cyclohexanecarb oxylic acid) is a synthetic derivative of the amino acid lysine[3]. It is a plasmin inhibitor and used as a new treatment modality for the treatment of melasma. TA inhibits plasminogen activator which regulates the conversion of plasminogen to plasmin. It inhibits melanin synthesis in melanocytes by interfering with the interaction of melanocytes and keratinocytes.

AIMS & OBJECTIVES

The aim of our study was to evaluate the efficacy and safety of Modified kligman regimen and topical Tranexemic acid (10%) in patients of melasma.

MATERIALS AND METHODS

A cross sectional, observational study was conducted from July to December, 2019 at dermatology OPD in a tertiary care hospital in south Gujarat.

Number of patients enrolled: 40

Age-Group: 18 - 45 Years of Male and Female

Inclusion criteria:

Patients between 18 and 45 years of age with melasma who will give consent

Exclusion criteria:

- Patients who will not give consent
- Pregnant / lactating females
- Patients on hormone replacement therapy
- Bleeding disorders, concomitant use of anticoagulants, and any known drug allergy

Procedure

- A written informed consent was taken from each patient after clinical diagnosis before starting the study. They were thoroughly explained the procedure and possible effects and adverse effects of the procedure.
- 40 patients with melasma were divided into two groups.
- After obtaining detailed personal and medical history, a modified melasma area and severity index (MASI) scoring system was used to assess the severity of melasma. It was recorded at baseline and at 4 weeks followup visit.
- The MASI is an index devised to more accurately quantify the severity of melasma and changes during therapy. To calculate MASI, we followed the method introduced by Kimbrough-Green CK et al[4]. The face was divided into four regions [forehead (F) 30%; right malar (MR) 30%; left malar (ML) 30%, chin (C) 10%] and each area was given value (A, 0-6). The area of involvement in each was given a numerical value of 0–6, where 0 indicates no involvement, 1 indicates 0–9%, 2 indicates 10–29%, 3 indicates 30–49%, 4 indicates 50–69%, 5 indicates 70–89%, and 6 indicates 90–100%.
- The sum of severity for darkness (D, 0-4) and homogeneity (H, 0-4) of melasma was multiplied by the numerical value and percentage of each area. These values were then added to obtain MASI.

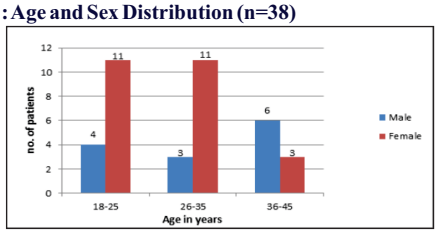
$$MASI = 0.3(DF + HF)\,AF + 0.3(DMR + HMR)\,AMR + 0.3(DML + HML)\,AML + 0.1(DC + HC)\,AC$$

- Group A: Each patient in group A had applied modified kligman cream (tretinoin, hydroquinone and fluocinolone) at night time for 8 weeks thereafter biweekly application for 4 weeks.
- Group B received topical Tranexemic acid cream (10%) twice daily for 8 weeks followed by biweekly application of the cream for 4 weeks. Both the groups were advised for application of sun protection factor-30. MASI score was calculated at baseline and at 4 weeks up to 12 weeks.
- Data obtained were statistically analyzed using SPSS 16 software.

P <0.05 was considered as statistically significant effect.

OBSERVATION

Graph 1: Age and Sex Distribution (n=38)



- Out of 40 patients with melasma, 38 had completed the study. Each group with 19 patients.
- The average age of the patient was 28.4 years (range 18–45). Most of the patients were females and belong to age group between 21 and 30 years.

Table 1: Mean MASI Score in Group A and B (n=38)

DURATION	GROUP A	GROUP B
0 WEEKS	4.02	3.98
4 WEEKS	2.78	3.16
8 WEEKS	1.90	2.05
12 WEEKS	1.04	1.35

- The mean MASI score of baseline in group A and group B was 4.02 and 3.98 respectively.
- After 12 weeks, it reached to 1.04 in group A (P <0.05) and 1.35 (P<0.05) in group B.
- The mean MASI score was 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 treatment with modified kligman regimen and tranexamic acid at all follow up visits.

Adverse Effects

- In group A, 58% showed side effects, 35% showed irritation, 29.6% showed erythema and 16.7% showed telangiectasia
- In group B, side effects are much less, only 13% showed erythema, 6.8 % showed irritation, and none of the patient showed telangiectasia.
- Side effects were more clinically evident in group A compared to group B, such as Erythema, irritation and telangiectasia.

DISCUSSION

Melasma is a common acquired condition characterized by irregular light to dark brown macules seen mainly in women and over sun-exposed skin over the face .[5] All the existing treatment modalities of melasma aim at reduction of the formation of melanin from melanocyte and elimination of pre-existing melanin pigment. Increased incidence of melasma in the age group of third decade may be due to increased occupational exposure to sunlight combined with physiological hormonal changes in reproductive life. More common incidence in females may be due to hormonal factors such as female sex hormones, higher prevalence of thyroid disorders, hormonal changes of pregnancy and reproductive life, oral contraceptives usage etc.[6]

Both groups showed statistically significant reduction in MASI score at subsequent follow-up visits. Intergroup comparison showed a faster reduction in pigmentation in Group A as compared to Group B and at 12 weeks, the results were statistically significant in each group (P <0.05). The efficacy was maintained throughout follow-up period. A study by sahu at al.[7] showed the reduction in MASI score in both the groups with modified kligman's regimen (30%) and topical tranexamic acid (5%). The effect of topical tranexamic acid was studied by Kim et al. [8], which showed significant decrease in MASI score.

A triple combination of fluocinolone acetonide 0.01%, 2% hydroquinone and 0.025% tretinoin is supposed to be used for a maximum of 4–8 weeks after which the treatment has to be stopped or withdrawn gradually and replaced with safer modalities of melasma management, this is because of the presence of fluocinolone acetonide in this combination which, being a mid-potent steroid has the propensity to cause side effects on the face when used for more prolonged periods.[9]

Topical tranexamic acid being a non-irritant drug with low side effects profile it can be safely prescribed for melasma and can be considered as an alternative mode of treatment for melasma. It can be considered as an add on therapy to many available anti melasma therapies.

More number of studies with larger sample size and longer duration of followup with topical tranexamic acid are needed to confirm its efficacy in melasma when compared to gold standard kligman's regimen.

CONCLUSION

- This study showed statistically significant (p< 0.05) decrease in melasma in both the groups.
- But there is no statistically significant differences (P >0.05) in between these two groups.
- Early and better response was observed with the modified kligman regimen as compared to topical tranexemic acid (10%) cream.
- Moreover, topical tranexemic acid (10%) had lesser side effects such as erythema, irritation, and telangiectasia as compared to triple combination therapy. Therefore, topical TA is a promising new therapeutic option for melasma.

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