Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/jptcp.v31i1.4063

COMPARISON OF THE EFFICACY OF COMBINATION OF TAM FORMULA VERSUS KLIGMAN FORMULA FOR MELASMA AT TERTIARY CARE HOSPITAL, KARACHI

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Abstract

Objective: Comparison of the efficacy of combination of TAM formula versus Kligman formula for melasma at Tertiary Care Hospital, Karachi.

Study design: Randomized controlled trail.

Place and duration of study: This study was conducted at Department of Dermatology, JPMC, Karachi from 1st January, 2022 till 31st January, 2023.

Material and methods: Data was prospectively collected from patients after taking consent. The sample size for the study was 122 patients, 61 in each group were included. Medical history, complete examination of skin and Melasma Area and Severity Index (MASI) Scores calculated before and after treatment to evaluate the change from baseline. Quantitative data was presented as simple descriptive statistics giving mean and standard deviation and qualitative variables was presented as frequency and percentages.

Results: The mean ages were 35.95 ± 7.17 years and 38.85 ± 7.80 years in Groups T and K, respectively. Both groups had a predominantly female distribution (98.4% in Group T, 88.5% in Group K). In terms of efficacy, TAM group demonstrated a higher response (98.4%) compared to Kligman group (90.2%). Over the eight weeks, group T and group K showed notable decrease in their mean MASI score, but group T has more better results.

Conclusion: In conclusion, the comparison between the TAM and Kligman formulas suggests that both have good efficacy and results in treating melasma patients, with TAM demonstrating more prominent decrease in mean MASI scores in a smaller time period and good patient satisfaction rates. However, further studies are needed to evaluate the long term results and side effects of this new formula.

Keywords: Melasma, kligman formula, TAM formula. Melasma Area and Severity Index.

INRODUCTION:

Melasma is a common skin condition characterized by irregular, light to gray-brown macules and patches that develop on sun-exposed areas of the skin.[1] It predominantly affects women, accounting for approximately 90% of cases, particularly those of child-bearing age with Fitzpatrick skin types IV to VI, especially in regions with intense UV radiation. The condition's causes are multifaceted and include factors such as pregnancy, sun exposure, hormone therapy, cosmetic use, and genetic influences. [2] The majority of cases are linked to sun exposure, pregnancy, or the use of oral contraceptives. Facial lesions in melasma can be categorized into three patterns: malar, centrofacial, and mandibular. Wood's lamp examination enables further classification into epidermal, dermal, mixed, and indeterminate variants. [3-4]

Conventional melasma treatment involves identifying and addressing potential causes, along with using sunscreen and depigmenting agents like hydroquinone, kojic acid, azelaic acid, deoxyarbutin, and ascorbic acid, either individually or in combination as found in formulations like the Kligman's formula. [5-7] These agents are often combined with additional therapies such as chemical peeling (using glycolic acid or trichloroacetic acid), dermabrasion, and laser therapy. Despite these efforts, managing this stubborn condition proves challenging and frequently falls short of achieving satisfactory outcomes. [8]

Addressing melasma proves challenging, and various treatments like bleaching agents, chemical peels, intense pulsed light (IPL), and fractional skin resurfacing have been employed, showing some success.[9] However, despite advancements, these therapies often yield unsatisfactory results and come with potential adverse effects. Hydroquinone, a commonly prescribed depigmenting agent, raises concerns due to its associated side effects. [10] Topical agents for hyperpigmentation are broadly classified into phenolic and non-phenolic groups. Hydroquinone, part of the phenolic group, has been considered the standard treatment for hyperpigmentation for the past five decades. [11] It acts by blocking the tyrosinase enzyme, thereby impeding the conversion of DOPA to melanin. The medication's potential mechanisms involve both the destruction of melanin and melanocytes, as well as the prevention of RNA and DNA synthesis.[12] For improved effectiveness, hydroquinone formulations often include antioxidants such as vitamin C and penetration-enhancing agents like tretinoin. [13]

The rationale for this study lies in the persistent challenge of treating melasma, a complex hyperpigmentation disorder. Current treatment methods have not proven to be consistently rapid and enduring. Despite an exhaustive review of the literature, no studies comparing the Tam formula to the Kligman formula were found. The recommended duration for the combination treatment is typically 4–8 weeks, after which a gradual withdrawal is advised, transitioning to safer melasma management options. This study seeks to contribute insights into the effectiveness of these formulas in our specific context, aiming to inform and enhance the implementation of updated management protocols in our clinical practice.

MATERIAL AND METHODS:

There were 122 patients between 25 to 65 years of age, both genders, who had melasma for over one month and presented to the Department of Dermatology, JPMC, Karachi, were included in our randomized control trial. Efficacy in either formula was assessed based upon the following grading, which was done based on subjective assessment. Efficacy was labeled in either group with patients achieving grade ≥ III.

- Grade I: Slight improvement, barely noticeable (up to 25%)
- Grade II: Moderate improvement, noticeable (25-50%)
- Grade III: Obvious improvement (51-75%)
- Grade IV: Marked improvement (>75%)

Participants who were pregnant, breastfeeding, currently taking birth control pills, or have plans to become pregnant during the study period. Additionally, those with a history of cutaneous

photosensitization, porphyria, or hypersensitivity to porphyrins or photodermatosis were excluded. Furthermore, participants with a history of an uncorrected coagulation defect or those currently using anti-coagulation medication, including heavy aspirin therapy, did not meet the eligibility criteria.
Participants with epidermal melasma on their face, as determined by a wood's lamp examination, were randomly selected. Patients were evaluated by a dermatologist with over 10 years of experience, in the presence of a researcher, and were graded. Random allocation to either the T= TAM formula (hydroquinone 2%, tretinoin 5% and 0.05% vitamin C) group or the K= Kligman formula (hydroquinone 4%, fluocinolone acetonide 0.01%, and tretinoin 0.05%) group was conducted using sealed opaque envelopes. Participants were instructed to apply the assigned regimen only on affected areas at night, starting with a 2-hour duration and gradually increasing if no side effects (erythema, burning, desquamation, dryness) are experienced. Strict sun protection, along with the use of broad-spectrum sunscreens, was advised.
Face, right cheek, forehead, and chin were different four specific areas for the evaluation of Melasma severity. Total affected area (percentage), Melasma darkness, and hyperpigmentation uniformity were three variables for the assessment of severity. Numeric values were assigned to each variable to denote the involvement. The melanin intensity of melasma (D) was contrasted with that of normal skin, while the uniformity of hyperpigmentation (H) was assessed using a scale ranging from 0 to 4. The MASI score is computed by calculating the severity grades for darkness (D) and homogeneity (H), then multiplying them by the numerical value of the affected areas (A) and the assigned percentages for the four facial regions.
For normally distributed variables, mean ± standard deviation will be reported, while non-normally distributed variables will be presented as median (interquartile range). Frequencies and percentages will be calculated for qualitative variables like gender and efficacy, with the chi-square test used to compare efficacy between groups, considering a significance level of $p \leq 0.05$.

RESULTS

The study population consisted of individuals with melasma, with a mean age of 35.95 ± 7.17 years in the TAM group and 38.85 ± 7.80 years in the Kligman group. The majority of participants fell within the 25-45 age range in the TAM group compared to majority belonging to the 46-75 in the Kligman group. Regarding gender distribution, the majority were female, constituting 98.4% and 88.5 in both groups respectively. Over the eight weeks, group T and group K showed notable differences in their mean MASI scores. The duration of melasma varied, with 41% of participants reporting duration of 15 days or less, and 36% reporting a duration exceeding 15 days in the TAM group. Whereas in the Kligman group, 70.5% reported a duration of more than 15 days. These demographic and clinical characteristics provide a comprehensive overview of the study population, essential for understanding the context of the investigation into melasma and its potential treatments. **(Table 1)**

Table-1 Baseline Characteristics Of The Tam Group Vs Kligman Group

Clinical Variables	Efficacy Group T n = 61	Efficacy Group K n= 61
Age (years)	35.95 ± 7.17	38.85 ± 7.80
Age		
25-45 Years	49 (80.3%)	18 (29.5%)
46-65 Years	12 (19.7%)	43 (70.5%)
Gender		
Male	01 (1.6%)	07 (11.5%)
Female	60 (98.4%)	54 (88.5%)
Duration of Melasma		
≤ 15 Days	25 (41%)	18 (29.5%)
> 15 Days	36 (59%)	43 (70.5%)

The comparison of efficacy between Group T (TAM formula: hydroquinone 2%, tretinoin 0.05%, and 5% vitamin C) and Group K (Kligman formula: hydroquinone 4%, fluocinolone acetonide 0.01%,

and tretinoin 0.05%) revealed notable findings. In Group T, 98.4% of participants reported efficacy, while 1.6% did not experience the intended therapeutic effect. Conversely, in Group K, 90.2% of participants indicated efficacy, with 9.8% reporting no improvement. The difference in efficacy between the two groups was assessed using a P-value of 0.08, suggesting a trend toward significance. **(Table 2). Table 3** displays the outcomes of a MASI comparison within both Group T and Group K across three time-points: baseline, four weeks, and eight weeks.

Table-2 Efficacy According To The Tam Group Vs Kligman Group

Groups	Efficacy Yes	Efficacy No	P-value
Group T	60 (98.4%)	01 (1.6%)	
Group K	55 (90.2%)	06 (9.8%)	0.08

Table-3 Comparison of Melasma severity (MASI score) in both groups

Groups	Severity of melasma	Mean ± SD	P-value
Group T	Baseline	14.69± 5.88	
	Four-weeks	11.72±5.49	0.001
	Eight weeks	7.92±4.49	
Group K	Baseline	16.89±6.29	
	Four-weeks	9.57±4.68	0.001
	Eight weeks	5.38±2.46	

DISCUSSION

Melasma is a common hyperpigmentation disorder prevalent in India. Clinicians typically diagnose melasma, and this study similarly identified and classified lesions using the MASI score. Clinical evaluation focuses on identifying the presence of the condition in the forehead, cheek, or jaw areas, with histological and Wood's lamp assessments differentiating between epidermal, dermal, or mixed types. Contributing factors include elevated UV ray exposure, pregnancy, contraceptive use, certain medications, hormone treatments, and genetic abnormalities. Individuals grappling with this condition endure both aesthetic and psychological distress due to its impact on facial skin and the challenge of treatment resistance. Beyond affecting social interactions, leisure activities, and emotional well-being, there is a preference for addressing facial skin in therapeutic interventions.[14-15]

The TAM formula, comprising hydroquinone 2%, tretinoin 0.05%, and 5% vitamin C, represents a therapeutic approach for managing melasma, a common hyperpigmentation condition. Hydroquinone is known for its skin-lightening properties, helping to reduce melanin production and alleviate hyperpigmentation. Tretinoin, a derivative of vitamin A, enhances skin cell turnover and promotes a more even complexion. The inclusion of vitamin C, a potent antioxidant, not only contributes to skin brightening but also provides protective benefits against oxidative stress. Together, these ingredients work synergistically to address different aspects of melasma, offering a comprehensive treatment approach. [16-17]

The Kligman formula, denoted as K, is a dermatological formulation designed to address melasma, a common hyperpigmentation disorder. This formula combines three active ingredients: hydroquinone at a concentration of 4%, fluocinolone acetonide at 0.01%, and tretinoin at 0.05%. Hydroquinone is recognized for its skin-lightening properties, inhibiting melanin production and diminishing hyperpigmentation. Fluocinolone acetonide, a corticosteroid, helps manage inflammation associated with melasma. Tretinoin, a derivative of vitamin A, promotes skin cell turnover, contributing to a more even skin tone. This formula exemplifies the ongoing efforts in dermatology to develop targeted and comprehensive approaches for the treatment of skin pigmentation disorders. [18-19]

According to the results, the TAM formula demonstrated a higher efficacy rate of 98.4%, while the Kligman formula showed a slightly lower efficacy at 90.2%. The superior efficacy of the TAM formula could be attributed to several factors. Firstly, the inclusion of vitamin C in the TAM formula may contribute additional antioxidant and skin-brightening properties, enhancing its overall effectiveness in managing hyperpigmentation. Secondly, the specific combination of hydroquinone, tretinoin, and vitamin C in TAM may be particularly well-suited for addressing the complex nature of melasma, targeting different pathways involved in pigmentation regulation.

On the other hand, the Kligman formula, while still demonstrating a substantial efficacy of 90.2%, may have a slightly lower performance due to factors such as the inclusion of fluocinolone acetonide. While fluocinolone acetonide possesses anti-inflammatory properties, its impact on pigmentation may not be as pronounced as the combination of hydroquinone, tretinoin, and vitamin C found in TAM.
It is important to consider the safety profile and potential side effects of each formula, as well as individual patient characteristics and skin types. Furthermore, variations in study design, sample size, and duration may influence the observed efficacy rates.

CONCLUSION:

In conclusion, the comparison between the TAM and Kligman formulas suggests that both are effective in treating melasma, with TAM demonstrating a notable decrease in mean MASI scores . The choice between these formulations should be made considering not only their efficacy but also the individual patient's skin condition, preferences, and potential tolerability. Further research, including long-term studies and larger sample sizes, may provide additional insights into the comparative effectiveness and safety of these formulations in the management of melasma.

LIMITATION:

This was a single center study with a smaller sample size. More studies are needed in future.

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