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To compare the effect of combination of oral Tranexamic acid with modified Kligman regimen and modified Kligman regimen alone in the treatment of melasma

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Abstract:

Background & Methods: The aim of the study is to compare the effect of combination of oral Tranexamic acid with modified Kligman regimen and modified Kligman regimen alone in the treatment of melisma. All the patients with melasma, satisfying the inclusion criteria were enrolled and written consent was obtained from them. Detailed history regarding sociodemographic data such as name, age, sex, address etc. was obtained and entered and proforma. Date of admission was noted along with detailed history regarding presenting complaints, past history, drug history, family history, personal history.
Results: Erythema was the only adverse effect observed in 4.7% cases in group 1 whereas in group 2, erythema, hypomenorrhea and burning were the adverse effects noted in 7.1%, 4.7% and 1.2% cases respectively. Although adverse effects were observed in higher proportions of cases in group 2 (12.9%) as compared to group 1 (4.7%), the observed difference was statistically insignificant (p>0.05).
Conclusion: Based upon the findings of present study, it could be concluded that modified Kligman regimen with or without oral tranexamic acid is effective in reducing the severity of melasma after 4 weeks of treatment. However, addition of oral Tranexamic acid to modified Kligman regimen resulted in faster therapeutic effect as compared to modified Kligman regimen alone after 8 weeks of treatment.

Keywords:

Oral, tranexamic, kligman & melisma

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Introduction

Melasma is an acquired condition of skin, which is characterized by symmetric hyperpigmented patches, especially in the sun exposed areas e.g. nose, forehead, cheeks, lips, chin etc.[1] Certain risk factors and aggravating factors associated with melasma include female gender, sun exposure, pregnancy, sex hormones (estrogens and progesterone), contraceptive pills, thyroid disease, cosmetics, genetic susceptibility and phototoxic drugs.[2-5]

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Sun exposure is the most important etiopathological factor linked to melasma. Alpha-melanocyte-stimulating hormone, corticotropin, endothelin 1, and interleukin 1 are produced when exposed to UV light. These elements promote the formation of melanin by stimulating intraepidermal melanocytes. Long-term sun exposure causes melanogenesis to increase and fibroblast activation and dermal inflammation, which in turn upregulates the stem cell factors in the dermis.[6,7]

Melasma is mostly diagnosed clinically and can be categorized into three types: mandibular, malar, and centrofacial, depending on the pattern of facial involvement. The most prevalent pattern among these is centrofacial melasma, involves the forehead, upper lips, and nose and is seen in more than half of the cases.[9] While the jawline and chin are afflicted in the mandibular variant, the malar cheeks are impacted in the malar pattern. In addition to this, extra-facial melasma may also be seen which involve non-facial body regions including the sternum, neck, upper limbs, etc..[9] Melasma may be classified into three morphological forms based on Wood Lamp examination and histological analysis: epidermal, dermal, and mixed. Dermal melasma is typified by bluish and light brown, ill-defined patches, while epidermal melasma is characterized by well-defined, dark brown patches. The light and dark brown spots with blue discoloration that define the mixed variety.

Method

The present study entitled "To compare the effect of combination of oral Tranexamic acid with modified Kligman regimen and modified Kligman regimen alone in the treatment of melasma" was conducted as an observational prospective comparative study on a total of 170 cases with melasma, seeking care at Department of Dermatology, People's College of Medical Sciences, & Research Centre, and associated People's Hospital Bhopal, Madhya Pradesh.

Sample size: 170 (As per Yamane's formula)

- Group 1 (n=85): OPD numbers ending with odd numbers (Modified Kligman regimen).
- Group 2 (n=85): OPD numbers ending with even numbers (Modified Kligman regimen with) oral tranexamic acid.

Inclusion criteria:

- Patients belonging to age range of 20 to 60 years
- Patients diagnosed with Melasma and not taking oral/ topical medication during the last 3 months
- Patients who give consent for the study.

Exclusion criteria:

- H/O Thrombotic events, stroke, myocardial infarction.
- Pregnant women, Women with menstrual irregularities.
- Patients taking oral contraceptives.
- Patients with sensitive skin (burning sensation or allergic to any topical creams).
- Photosensitivity disorders (SLE, porphyria, drugs).
- Patients who underwent recent surgeries within a period of 3 months and undergoing any cosmetic procedure.

Result

Table 1: Comparison of age between two groups

Age (in years)	Group 1 (n=85)		Group 2 (n=85)	
	n	%	n	%
≤30	33	38.8	30	35.3
31-40	34	40	28	32.9
41-50	15	17.6	22	25.9
51-60	3	3.5	5	5.9
Mean	33.88±7.67		35.62±9.2	
P value	0.467			

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The mean age of patients of group 1 was 33.88±7.67 years whereas the mean age of patients of group 2 was 35.62±9.2 years. The majority of patients in group 1 belonged to age range of 31 to 40 years (40%) whereas the majority of patients in group 2 belonged to less than 30 years of age, however, the observed difference in age composition between two groups was statistically insignificant, thus two groups were comparable with respect to age (p>0.05).

Table 2: History of OCP intake in patients with melasma

History of OCP Intake	Group 1 (n=85)		Group 2 (n=85)		Total (n=170)	
	n	%	n	%	n	%
No	77	90.6	77	90.6	154	90.6
Yes	8	9.4	8	9.4	16	9.4

History of OCP intake was present in 9.4% cases with melasma overall. 9.4% cases in each group had history of OCP intake

Table 3: Clinical pattern of patients with Melasma

Clinical Pattern of Melasma	Group 1 (n=85)		Group 2 (n=85)		Total (n=170)	
	n	%	n	%	n	%
Centrofacial	37	43.5	53	62.4	90	52.9
Malar	44	51.8	30	35.3	74	43.5
Mandibular	4	4.7	2	2.4	6	3.5
P value	0.051					

Most common clinical pattern of melasma observed in our study cohort was centrofacial (52.9%), followed by malar (43.5%) and mandibular melasma (3.5%). About 43.5% cases in group 1 had malar melasma whereas 62.4% patients in group 2 had centrofacial melasma, the observed difference in clinical pattern of melasma between two groups was statistically insignificant, indicating two treatment groups to be comparable with respect to clinical pattern(p>0.05).

Table 4: Comparison of MSI score between two groups

MSI score	Group 1(n=85)		Group 2(n=85)		P value
	Mean	SD	Mean	SD	
Baseline	9.96	4.6	10.6	5.6	0.18
Week 4	7.37	4.11	6.99	4.06	0.554
Week 8	5.82	3.88	4.4	2.9	0.007
Week 12	4.24	3.5	2.05	1.84	0.001
3 months	4.58	3.5	2.3	1.8	0.001
P value	0.001		0.001		

Mean MSI score in group 1 was 9.96±4.6 whereas that in group 2 was 10.6±5.6 at baseline. The mean MSI score between two groups was comparable at baseline (p>0.05). In group 1, mean MSI reduced from 9.96 at baseline to 7.37 at 4 weeks, 5.82 at 8 weeks, 4.24 at 12 weeks and thereafter it slightly increased to 4.58 at 3 months. Overall, we found that Modified Kligman regimen was effective in improving mean MSI score in patients with melasma (p<0.05).

Similarly, in group 2, mean MSI score reduced significantly from 10.6 at baseline to 6.99 at 4 weeks, 4.4 at 8 weeks and 2.05 at 12 weeks, with slight increase to 2.3 at 3 months. Thus, Modified Kligman regimen with oral TA was also effective in

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improving melasma score during 3 months observation period as compared to baseline ($p<0.05$).

Intragroup analysis revealed no significant difference in mean MSI score between 2 groups at 4 weeks, whereas from 8 weeks to 3 months, the reduction in mean MSI score was significantly higher in group 2 as compared to group 1 ($p<0.05$).

Table 5: Comparison of adverse effects between two groups

Adverse effects	Group 1 (n=85)		Group 2 (n=85)	
	n	%	n	%
Burning	0	0	1	1.2
Erythema	4	4.7	6	7.1
Hypomenorrhea	0	0	4	4.7
Nil	81	95.3	74	87.1
P value	0.126			

In the present study, erythema was the only adverse effect observed in 4.7% cases in group 1 whereas in group 2, erythema, hypomenorrhea and burning were the adverse effects noted in 7.1%, 4.7% and 1.2% cases respectively. Although adverse effects were observed in higher proportions of cases in group 2 (12.9%) as compared to group 1 (4.7%), the observed difference was statistically insignificant ($p>0.05$).

Discussion

Melasma is a skin condition characterized by symmetrical hyperpigmented patches, particularly in areas exposed to sunlight, such as nose, forehead, cheeks, lips, and chin. Clinically, melasma has been categorized into 3 clinical types, centrofacial (most common), malar and mandibular.[10] Various treatment modalities are available for melasma with varying clinical efficacy, advantages and disadvantages. To date, the triple combination therapy remains the gold standard. This triple therapy, which includes hydroquinone, a retinoid, and a corticosteroid, is an exceptionally effective and safe treatment for melasma.

Prathyoosha S et al (2024) also observed melasma in higher proportions of females (>80%) and 46.66% of the patients with melasma belonged to age range of 31 to 40 years. The mean age of patients was 33.39 years[11]. Rao NN et al (2023) also documented female predominance for melasma in their study with female to male ratio of 10:1. Out of 90 cases, 82 cases were females[12].

The duration of melasma was less than 1 year in majority of patients of group 1 (47.1%) as well as group 2 (34.1%) whereas the duration of melasma was more than 5 years in 5.9% cases in group 1 and 8.2% cases in group 2. In the present study, history of OCP intake was present in 9.4% cases and history of melasma in first degree relative was present in 21.2% cases. We observed no significant difference in clinical history between two groups ($p>0.05$)[13].

Sun exposure, pregnancy, sex hormones (estrogens and progesterone), contraceptive pills, and genetic susceptibility are among risk factors associated with melasma. According to research by Ebrahim AA et al. (2020), the mean duration of melasma was 4.4±1.3 years. However, in a study of Mushtaq S et al. (2022), the duration of melasma was 9.77 ± 2.13 years.[14] The mean duration of melasma in a study of Kothari P et al (2018) was 3.1 years ranging from 1 months to 25 years and family history of melasma was positive in 27.7% cases whereas 16.2% cases had history of taking OCP. However, mean duration of disease ranged from 18.1 to 19.5 months in a study of Prathyoosha S et al (2024).[15] History of familial predisposition and intake of OC pills was present in 24.4% and 8.8% cases in a study of Susmitha M et al (2023). However, positive family history of melasma was present in 33.3% cases in a study of Achar A et al (2011).[16]

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Conclusion

Most common clinical pattern of melasma observed in our study cohort was centrofacial (52.9%), followed by malar (43.5%) and mandibular melasma (3.5%). Erythema was the only adverse effect observed in 4.7% cases in group 1 whereas in group 2, erythema, hypomenorrhea and burning were the adverse effects noted in 7.1%, 4.7% and 1.2% cases respectively. Although adverse effects were observed in higher proportions of cases in group 2 (12.9%) as compared to group 1 (4.7%), the observed difference was statistically insignificant ($p>0.05$).

Based upon the findings of present study, it could be concluded that modified Kligman regimen with or without oral tranexamic acid is effective in reducing the severity of melasma after 4 weeks of treatment. However, addition of oral Tranexamic acid to modified Kligman regimen resulted in faster therapeutic effect as compared to modified Kligman regimen alone after 8 weeks of treatment.

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