

Comparison of efficacy of hydroquinone versus hydroquinone plus tretinoin plus topical steroids in patients with melasma

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Abstract

Background Melasma is an acquired pigmentary disorder characterized by symmetrical hyperpigmentation of the face. Treatment of melasma is unsatisfactory most of the times and comes with various side effects such as contact dermatitis, irritation and scarring.

Objective To compare efficacy of hydroquinone versus hydroquinone plus tretinoin plus topical steroids in patients with melasma.

Methods This randomized Controlled Trial was conducted in Department of Dermatology, Nishtar Medical University, Multan from 15th February 2019 to 15th August 2019. A total of 114 patients were divided in two groups, Group A, having 57 patients, was treated with hydroquinone cream once daily at bed time while group B, having 57 patients, was treated with combination therapy. Baseline and post-treatment MASI scores were calculated and patients were assessed weekly till 12 weeks and the efficacy of the treatment was documented. Efficacy was measured in terms of at least 50% reduction of MASI score after 12 weeks of therapy, compared with baseline MASI score.

Results This study comprised of a total of 114 patients meeting our inclusion criteria. Of these 114, 37 (32.5%) were male patients while 77 (67.5%) were female patients. Mean age in this study was 27.22±5.08 years. Mean age of the male patients was noted to be 27.89±4.53 years while that female patients was 26.90±5.32 years (p=0.330). Majority of the study cases i.e. 81 (71.1%) were aged up to 30 years. Of these 114 study cases, 43 (37.7%) belonged to rural areas and 71 (62.3%) belonged to urban areas. Fitzpatrick skin type III was noted in 78 (68.4%) and type IV in 36 (31.6%). Mean body mass index of our study cases was 25.68±2.59 kg/m² and obesity was present in 11 (9.6 %) of our study cases. Mean disease duration was 10.29±8.23 months and 82 (71.9%) had duration of illness up to 1 year. Of these 114 study cases, 46 (40.6%) were illiterate and 68 (59.6%) were literate. Efficacy was noted in 75 (65.8%) of our study cases, Efficacy in group A was 49.1% while in group B, efficacy was noted in 82.5%.

Conclusion Combination therapy with hydroquinone plus tretinoin plus topical steroids is more effective, reliable and safe in treatment of melasma as compared with hydroquinone alone and it provides rapid and sustained clinical improvement in the treatment of melasma.

Key words

Melasma, hydroquinone, tretinoin, triple therapy, steroids.

Introduction

Melasma is an acquired pigment disorder

showing symmetrical hyperpigmentation of the face characterized by light to dark brown patches with indistinct borders on both cheeks.

Melasma in middle-aged women may be due to harmless hormonal imbalances. It is also known as the mask of pregnancy and is prevalent in most child-bearing women.¹⁻³ Three clinical presentations of melasma are identified based on histopathologic findings: epidermal melasma, when the pigment is deposited in the basal and suprabasal layer; dermal melasma, when melanophages filled with melanin are found in the superficial and middle dermis; mixed melasma, when findings of the two previous types of melasma are present. The examination with Wood's light helps to differentiate epidermal from dermal melasma in types I-IV of Fitzpatrick scale. Considering its recalcitrant characteristics, treatment can rarely keep the individual free of melasma for a long time, despite the various therapeutic options.^{4,5} Melasma is reported to account for 4-10% of new dermatology hospital referrals. It is shown to be more common in people of Hispanic origin and among Asians. Treatment of melasma is unsatisfactory most of the times, even by tolerating various side effects such as contact dermatitis, irritation, and scarring.^{6,7} According to the most recent Cochrane review, there is insufficient evidence to provide robust guidance for practice, and more randomized clinical trials are needed in the field of melasma treatment.⁸ The range of treatments investigated for melasma cover all systemic, procedural, and topical modalities. Topical treatments have their own advantage over systemic therapies.⁹ The first gold standard treatment approved by Food and drug administration (FDA) for melasma was Kligman and Willis regime; A triple combination therapy consisting of hydroquinone at a concentration of 5% in combination with steroid (0.1% dexamethasone) and tretinoin

(0.05%) regimen. Improvement with this treatment is usually observed at 4 to 6 weeks, with a plateau at 4 months. An Indian study reported 58 % efficacy of hydroquinone¹⁰ while the efficacy of hydroquinone plus tretinoin plus steroid was 83.33%.¹¹

Material and Methods

This randomized Controlled Trial was conducted in Department of Dermatology, Nishtar Medical University, Multan from 15th February 2019 to 15th August 2019. Patients were selected via Non-probability consecutive sampling. A total of 114 patients were enrolled meeting the inclusion criteria. Both male and female patients with melasma, between ages 20 to 40 years, having Fitzpatrick skin type III, IV and V with Baseline MASI score > 12 were included in the study. Fitzpatrick skin type I, II and VI, those already taking treatment for melasma within 3 months, patients with history of hypertrophic scars, hirsutism and menstrual dysfunction, diabetics and hypertensive patients, pregnant females, those taking oral contraceptives and patients who showed lack of compliance with the therapy were excluded from the study. 114 patients were divided in two groups by lottery method. Group A, having 57 patients, was treated with hydroquinone cream once daily at bed time while group B, having 57 patients, was treated with combination therapy. Night-time moisturizer was applied in all patients. Patients were asked for follow up visits weekly till 12 weeks. Baseline and post-treatment MASI scores were calculated and the efficacy of the treatment was documented.

Results

This study comprised of a total of 114 patients meeting our inclusion criteria. Of these 114, 37 (32.5%) were male patients while 77 (67.5%) were female patients. Mean age was 27.22±5.08

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years (with minimum age of our study cases was 20 years while maximum age was 40 years). Mean age of the male patients was noted to be 27.89±4.53 years while that of female patients was 26.90±5.32 years (p=0.330). Majority of our study cases i.e. 81 (71.1%) were aged up to 30 years. Of these 114 study cases, 43 (37.7%) belonged to rural areas and 71 (62.3%) belonged to urban areas. Fitzpatrick skin type III was noted in 78 (68.4%) and type IV in 36 (31.6%). Mean body mass index was 25.68±2.59 kg/m² and obesity was present in 11 (9.6%) of our study cases. Mean disease duration was 10.29±8.23 months and 82 (71.9%) had duration of illness up to 1 year. Of these 114 study cases, 46 (40.6%) were illiterate and 68 (59.6%) were literate. Efficacy was noted in 75 (65.8%) of our study cases, efficacy in group A was 49.1% while in group B, efficacy was noted in 82.5%. (Table 1). Efficacy was stratified with regards to gender, age, residential status, Fitzpatrick Skin type, obesity, disease duration and literacy (Table 2).

Discussion

Melasma is a human melanogenesis dysfunction that results in localized, chronic acquired hypermelanosis of the skin. It occurs symmetrically on sun exposed areas of the body, particularly cheek, forehead, nose and chin.¹¹⁻¹⁴

Melasma has a significant impact on appearance, causing psychosocial and emotional distress, and reducing the quality of life of the affected patients. Patients commonly report feelings of shame, low self-esteem, anhedonia, dissatisfaction, and the lack of motivation to go out. Suicidal ideas have also been reported in the literature. There is also a clear genetic predisposition, since over 40% of patients reported having relatives affected with the disease¹⁵.

Our study comprised of a total of 114 patients meeting inclusion criteria of our study. Of these 114 study cases, 37 (32.5%) were male patients

Table 1 Distribution of efficacy among study cases.

Efficacy (n= 114)	Group A		Group B		P value
	Frequency	%	Frequency	%	
Yes (n =75) (65.8%)	28	49.1	47	82.5	0.000
No (n=39) (34.2 %)	29	50.9	10	17.5	
Total	57	100	57	100	

Table 2 Stratification of efficacy.

		Group A		Group B		P value
		Yes	No	Yes	No	
With respect to gender	For male	26	08	17	03	0.069
	For female	19	21	30	07	0.004
With respect to age	≤ 30 years	21	20	33	07	0.004
	> 30 years	07	09	14	03	0.032
With respect to residential status	Rural	07	14	18	04	0.002
	Urban	21	15	29	06	0.037
With respect to Fitzpatrick skin type	Skin type III	21	19	33	05	0.001
	Skin type IV	07	10	14	05	0.090
With respect to obesity	Obese	02	03	05	01	0.242
	Non-obese	26	26	42	09	0.001
With respect to duration of disease	≤1 year	21	21	32	08	0.006
	> 1 year	07	08	15	02	0.021
With respect to literacy	Illiterate	11	13	18	04	0.016
	Literate	17	16	29	06	0.009

while 77 (67.5%) were female patients. Similar results have been reported in many different studies indicating high female gender preponderance over male patients. A study conducted by Ejaz *et al.*¹⁶ from Kharian has also reported high female gender predominance with 85 % female patients which is following our study results. An Indian study conducted by Puri *et al.*¹⁴ has reported 6.5:1 female gender predominance which is in compliance with our study results.

Mean age of our study cases was 27.22±5.08 years (with minimum age of our study cases was 20 years while maximum age was 40 years). Mean age of the male patients was noted to be 27.89±4.53 years while that of female patients was 26.90 ±5.32 years (p=0.330). Our study results have indicated that majority of our study cases i.e. 81 (71.1%) were aged up to 30 years. A study conducted by Ejaz *et al.*¹⁶ from Kharian has reported 30.4±5.8 years mean age of the patients with epidermal melasma which also follows our study results. Ali *et al.*¹⁷ from Lahore reported similar mean of patients in which majority of them were young with melasma i.e. 29.90±7.18 years. Their findings are close to our study findings. Similar results have been reported by Halder *et al.*¹⁸

Of these 114 study cases, 43 (37.7%) belonged to rural areas and 71 (62.3%) belonged to urban areas. Fitzpatrick skin type III was noted in 78 (68.4%) and type IV in 36 (31.6%). Mean body mass index of our study cases was 25.68±2.59 kg/m² and obesity was present in 11 (9.6%) of our study cases. Mean disease duration was 10.29±8.23 months and 82 (71.9%) had duration of illness up to 1 year. The study conducted by Ejaz *et al.*¹⁶ reported similar results.

Efficacy was noted in 75 (65.8%) of our study cases, Efficacy in group A was 49.1% while in group B, efficacy was noted in 82.5%. An Indian

study reported 58% efficacy of hydroquinone¹⁹ while the efficacy of hydroquinone plus tretinoin plus steroid was 83.33%.²⁰ These results are close to our study results.

Conclusion

Our study results have indicated that combination therapy with hydroquinone plus tretinoin plus topical steroids is more effective in treatment of melasma as compared with hydroquinone. The results of this study support use of combination therapy among targeted population.

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