Advanced Medical Journal, Vol.9, No.3, P.142-150,2024 https://doi.org/10.56056/amj.2024.287

Topical Ascorbic Acid Mesotherapy with Microneedling versus Topical Tranexamic Acid Mesotherapy with Microneedling for Melasma: A Therapeutic Comparative Study

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Abstract

Background & objectives: Melasma is a common skin hyperpigmentation syndrome that frequently includes reproductive-aged females, and numerous therapies with various consequences have been suggested. Thus, the objective was to compare the microneedling and mesotherapeutic effects of ascorbic acid versus tranexamic acid for melasma treatments.

Methods: This interventional therapeutic prospective study was conducted on 40 patients with melasma at Khabat Consultation Center for Skin Diseases, Sulaimaniyah, Iraq, from March 2022 to August 2022. Sociodemographic data of patients were collected together with a family history of melasma using a well-designed questionnaire. Half of the patients were treated with ascorbic acid, while the rest were treated with tranexamic acid using a derma pen.

Results: Highly significant reduction of MASI score were seen before and after treatment ($p<0.001$) were seen in mean scores before and after treatments for both types of treatments (ascorbic acid and tranexamic acid). Moreover, ascorbic acid results in the highest mean score reduction in skin type III ($p=0.746$), while tranexamic acid results in the highest mean score in skin type IV ($p<0.05$). Furthermore, the dermal melasma recorded the highest mean score, and the lowest level was observed in the epidermal melasma for both ascorbic acid and tranexamic acid groups. No significant difference was found between both studied groups in sociodemographic data and other studied variables (family history, skin type, previous treatment, and duration of melasma).
Conclusions: Both types of therapy mesotherapy was effective in treating melasma; however, their potencies varied on different skin types and according to melasma types.

Keywords: Advanced technique, Acid mesotherapy, Microneedling, Melasma.

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Introduction

Melasma is a common skin problem described by slight brown to dark hyperpigmented patches with unclear borders that results from melanogenesis impairment. The patches are most commonly observed in areas exposed directly to sunlight, such as the cheeks, forehead, upper lip, nose, chin, and neck.[1] Melasma more prominently affects individuals with darker skin tones (skin types IV to VI), such as those in East Asia, India, Pakistan, Middle East and Mediterranean-Africa. However, individuals of all races and skin colors might be affected.[2]Regarding the etiology of melasma, it is of unknown etiology However, sun exposure, pregnancy, oral contraceptives/steroids, ovarian tumors, hormone replacement therapy, use of cosmetics and photosensitizing drugs, stress, and genetic factors might enhance melasma development.[2] The pathogenesis of melasma is multifactorial and not well-known. Activated melanocytes in affected skin are the initial steps to develop melasma, and when melanocytes exposed to ultraviolet (UV) radiation, high amounts of melanin are produced by melanosomes. Melanin production comprises the enzymatic change of tyrosine to melanin pigment, then melanin transferred to nearby keratinocytes that leads to skin pigmentation. Thus, melanin increased in epidermal keratinocytes and dermal macrophages.[3]This disease commonly affects middle-aged women, especially pregnant females (70%) and 10% of men. The melasma incidence ranges from 8.8 to 40%, reliant on ethnicity, skin type, and exposure to sun. The specific cause of the disease is still unknown.[4] Histologically, melasma has been categorized into epidermal, dermal, and mixed type, in which the first type has more pigment throughout the epidermal layers.[5] Currently, different therapeutic aspects are utilized to avoid melasma lesions and inhibit their recurrences, such as topical and systematic agents together with light-based treatments and lasers.[6] Whereas retinoic acid, azelaic acid, ascorbic acid (AA), tranexamic acid (TA), salicylic acid, glycolic acid and broad-spectrum sunscreens are other treatment choices for melasma treatment.[7] Ascorbic acid is a water-soluble molecule with various biological activities, including anticancer, antioxidant, and antimicrobial effects.[8] Dermatologists also use it topically to prevent hyperpigmentation and reduce the alterations caused by photoaging.[9] In addition, studies assessed the potential efficacy of AA for melasma treatment due to its long-time freshness and sensuality to the skin and its preventive effect on melanin production.[10]On the other hand, TA is a novel drug with decent ability in treating melasma.[11] The physiological mechanism of TA is through inhibiting the plasmin activity persuaded by UV exposure in keratinocytes. This acid blocks plasminogen binding to keratinocytes and thus decreases prostaglandin formation, stimulating tyrosinase activity.[12] Additionally, the depigmenting efficacy of TA has yet to be fully elucidated. Therefore, this study designed to address the effect of microneedling and mesotherapy with AA versus TA for melasma treatment.

Patients and methods

This interventional therapeutic prospective study was done on 40 patients with melasma at Khabat Consultation Center for Skin Diseases, Sulaimaniyah, Iraq, from March 2022 to August 2022. The contributors were equally divided into groups A (n=20) and B (n=20) regarding MASI score. Then, group A patients were treated with AA solution (MC CM, Spain), while group B patients were treated with TA solution (mccosmetics, NY, Spain) mesotherapies with microneedling.

Patients aged >18 years with clinically confirmed melasma lesions with skin type III and IV, and those who had melasma for at least 6 months without treatment for at least three months were enrolled in this study. On the other hand, pregnant and breastfeeding patients were excluded from this study as those with other skin diseases or endocrine disorders. Additionally, those on chronic medications, chemotherapy, or oral contraceptives were excluded.Kurdistan Higher Council for Medical Specialists (KHCMS), Sulaimaniyah, Iraq, approved the study protocol of this research and gave a number of 61/11/01/2022. Written informed consent was taken from each patient, and they felt free to leave the study anytime they desired without giving a reasonable cause. A questionnaire was used to collect the patient's gender, age, marital status, occupation, number of pregnancies, family history/duration of melasma, history of medication, history of sun light exposure, and Fitzpatrick skin type. After gentle cleansing of the face with medical soap, topical EMLA cream (5%; Aspen, Ireland) was applied over the area to be treated for 30 minutes. Then, patients in groups A were treated with AA mesotherapies intradermal injection for three months with 2-weeks interval. Whereas patients in groups B were treated with TA mesotherapies intradermal injection for three months with 2-weeks interval. For this purpose, a derma pen (Thappink, Spain) with 36 needles and labelling the depth from 1.0 mm to introduce the drugs intradermally into the skin was used. This pen also has a disposable head with vibrator effects to decrease pain. The procedures were done every two weeks in six sessions and followed up for a further three months after the last session to evaluate the drug's effectiveness. Patients were experienced mild pain during treatment process. Additionally, sunscreen was prescribed to patients after treatments. Furthermore, wood's lamp was used to determine the melasma type (dermal, epidermal, or mixed). Finally, based on Melasma Area Severity Index (MASI) (Figure 1),[13] the melasma severity score was assessed (Table 1).The data were analyzed using Statistical Package for the Social Sciences (SPSS, version 26). The shapiro-Wilk test was used to determine the normal distribution status of the data. T-test and ANOVA tests were used to find the relationship between the normally distributed quantitative variables. At the same time, the Independent Mann-Whitney and Kruskal-Wallis tests were used to test the non-normally distributed quantitative variables. A $P \leq 0.05$ considers significant, and a $p<0.001$ is highly significant.

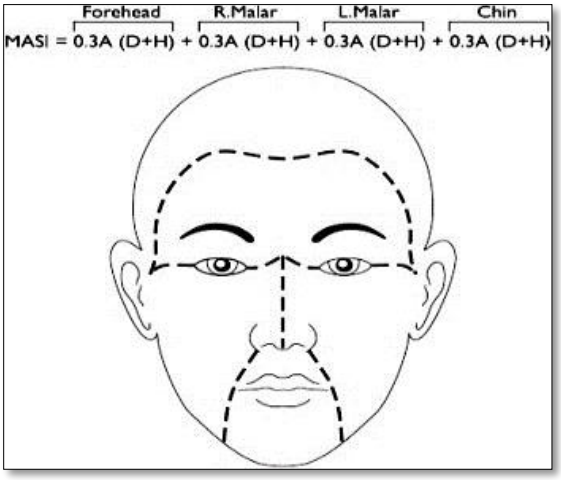

Figure (1): Shows Melasma Area Severity Index (MASI) calculation.[13]

Table (1): Melasma severity scores using Melasma Area Severity Index (MASI).

Variable	Score	Involvement
Area (A)	0	No
	1	<10%
	2	11-29%
	3	30-49%
	4	50-69%
	5	70-89%
	6	90-100%
Darkness (D)	0	Normal skin color
	1	Barely visible hyperpigmentation
	2	Mild hyperpigmentation
	3	Moderate hyperpigmentation
	4	Severe hyperpigmentation
Homogenity (H)	0	Normal without evidence of hyperpigmentation
	1	Specks of involvement
	2	Small patchy areas of involvement (<1.5 diameter)
	3	Patchy of involvement (>2.0 cm diameter)
	4	Uniform skin involvement without any clear areas

Results

In the present study, most of the patients (62.5%) were aged 31-39 years, females (80%), housewives (62.5%), married (87.5%) and with positive pregnancy (65%). Also, most patients had no melasma history (67.5%), had type III skin (85%) without medication history (65%), had at least 1-5 years melasma (77.5%) and duration of sunlight exposure for 90 minutes (57.5%). However, no significant differences ($p \geq 0.05$) were found between patients of two groups in regards to sociodemographic data (age, gender, occupation, marital status, and pregnancy history), family history, skin type, previous treatment, and duration of melasma, as seen in Table (2).

Table (2): Correlation between sociodemographic data and some variables of melasma patients.

Variable		Used drug			p value
		Ascorbic Acid (No.; %)	Tranexamic Acid (No.; %)	Total (No.; %)	
Age (Year)	≤30	2 (10)	5 (25)	7 (17.5)	0.44
	31-39	14 (70)	11 (55)	25 (62.5)	
	>40	4 (20)	4 (20)	8 (20)	
Gender	Male	4 (20)	4 (20)	8 (20)	0.65
	Female	16 (80)	16 (80)	32 (80)	
Occupation	Driver	1 (5)	2 (10)	3 (7.5)	0.69
	Engineer	1 (5)	0 (0)	1 (2.5)	
	Earners	0 (0)	1 (5)	1 (2.5)	
	Finance	1 (5)	0 (0)	1 (2.5)	

	Housewife	12 (60)	13 (65)	25 (62.5)	
	Nurse	1 (5)	0 (0)	1 (2.5)	
	Teacher	3 (15)	4 (20)	7 (17.5)	
Marital status	Married	18 (90)	17 (85)	35 (87.5)	0.5
	Single	2 (10)	3 (15)	5 912.5)	
Pregnancy history	Negative	8 (40)	6 (30)	14 (35)	0.37
	Positive	12 (60)	14 (70)	26 (65)	
Family history of melasma	Negative	12 (60)	15 (75)	27 (67.5)	0.25
	Positive	8 (40)	5 (25)	13 (32.5)	
Skin type	Type III	17 (85)	17 (85)	34 (85)	0.69
	Type IV	3 (15)	3 (15)	6 (15)	
Previous treatment	Laser/Peel	1 (5)	1 (5)	2 (5)	0.16
	No	11 (55)	15 (75)	26 (65)	
	Peel	0 (0)	1 (5)	1 (2.5)	
	Tropical	6 (30)	0 (0)	6 (15)	
	Tropical/Laser	1 (5)	1 (5)	2 (5)	
	Tropical/Peel	1 (5)	2 (10)	3 (7.5)	
Duration of melasma (Year)	<1	3 (15)	2 (10)	5 (12.5)1	0.4
	1-5	3 (65)	18 (90)	31 (77.5)	
	>5	4 (20)	0 (0)	4 (10)	
Duration of sunlight exposure (Minute)	≤90	11 (55)	12 (60)	23 (57.5)	0.74
	≥90	9 (42.5)	8 (40)	17 (42.5)	

Concerning the melasma severity using MASI score, highly significant differences ($p<0.001$) between mean scores before treatment (Mean±SD of 63.5±34.22) and after treatment (Mean±SD of 31.3±21.5) for AA mesotherapy were seen. The same results were obtained for TA mesotherapy before treatment (Mean±SD of 57.5±30.58) and after treatment (Mean±SD of 29.5±21.4) ($p<0.001$), as seen in Figures (2, 3A and 3B).

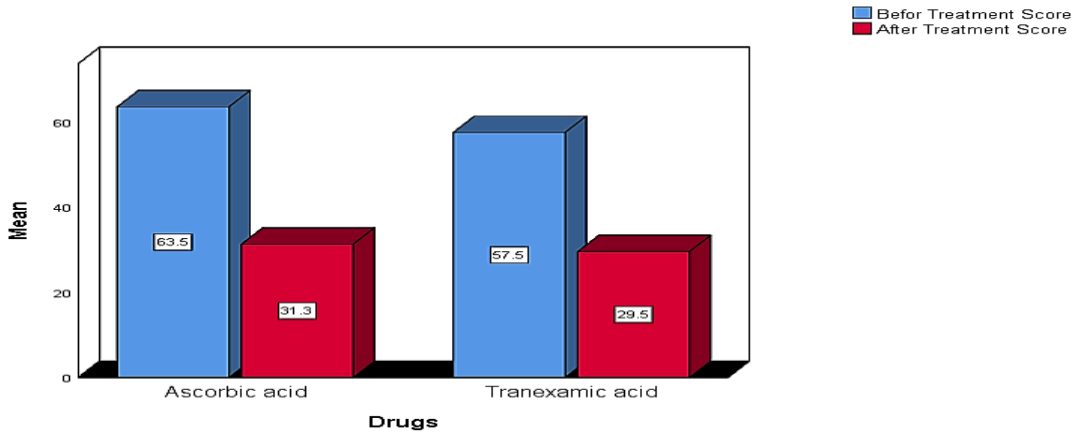

Figure (2): Distribution of mean score before treatment and *a*fter treatment of the two study groups.

A mesotherapy results in the highest mean score improvement in skin type III (Mean±SD of 32.65±22.78) (p=0.746). Whereas TA mesotherapy results in the highest mean score improvement in skin type IV (Mean±SD of 53.33±23.09) (p<0.05), as seen in Table 3.

Figure (3A): Photographs of the patient before treatment (left) and after treatment (right) with ascorbic acid.

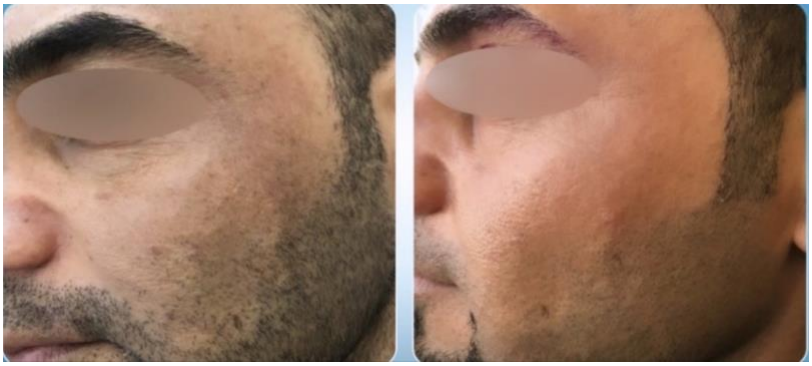

Figure (3B): Photographs of the patient before treatment (left) and after treatment (right) with ascorbic acid.

Table (3): Comparison of the mean score levels among skin types of the two studied groups.

Drug	Statistic	Skin Type			p value
		Type III	Type IV	Total	
Ascorbic Acid	Mean±SD	32.65±22.78	23.33±11.55	31.25±21.51	0.746
	No.	17	3	20	
Tranexamic acid	Mean±SD	25.29±18.75	53.33±23.09	29.50±21.39	0.023 *
	No.	17	3	20	

*Significant difference using independent samples Mann Whitney U test

Regarding the correlation between used drugs (AA & TA) and melasma type, the highest mean score was recorded in the dermal type of melasma for the AA group (Mean±SD of 46.67±25.17). At the same time, the lowest level was observed in the epidermal type of melasma (Mean±SD of 25.77±17.3) (p>0.05). Also, in the other group, the highest mean level was observed in the dermal type of melasma (Mean±SD of 50±25.82), and the lowest level was in the epidermal type of melasma (Mean±SD of 19.23±9.54) (p=0.006), as shown in Table (4).

Table (4): Comparison of the mean score levels among different types of melasma in the studied groups.

Drug	Statistic	Melasma Type				p value
		Dermal	Epidermal	Mixed	Total	
Ascorbic Acid	Mean±SD	46.67±25.17	25.77±17.3	37.5±29.86	31.25±21.51	0.269
	No.	3	13	4	20	
Tranexamic acid	Mean±SD	50.0±25.82	19.23±9.54	46.67±28.87	29.50±21.39	0.006*
	No.	4	13	3	20	

*Significant difference using Independent samples Kruskal-Wallis test

Discussion

Melasma is an acquired condition that can have significant negative impacts on the quality of life of affected patients, especially childbearing women. Presently, various treatment modalities for melasma are available, with different results and satisfactory outcomes.[8] Using either AA or TA for treating skin ailments is not new, as previously, they were used for treating skin cancer, skin ulcers, hyperpigmentation, lentigo, and melasma.[14, 15] Regarding their mechanism in melasma treatment, TA interacts with keratinocyte-melanocytes and Vitamin C (VC) works by dropping melanin formation that leads to skin change and whitening.[16]Thus, in this study, we used AA and TA separately for two groups of patients, to whom the drug's effects on MASI melasma lesion scores, skin type, and melasma type were assessed. We found that both AA and TA mesotherapies remarkably improved the melasma lesions with highly significant differences ($p<0.001$) before and after treatments. In this respect, Tahoun et al. tried TA vs AA with microneedling (MN) in treating melasma in a comparative, split-face, single-blinded study. They treated the right side with MN + TA and the left side of the face with MN + AA twice weekly for 5-weeks. They found that MASI diminished significantly ($p<0.001$), and both sides displayed significant reduction in fine dark granules ($p<0.001$), homogeneous pigmentation ($p=0.005$) and pseudoreticular brown network ($p=0.028$).[17] Consequently, Zhao et al. in a split-face controlled trial of 8 weeks receiving transdermal TA or VC injections via Myjet on the right or the left side of the face, a reduction in MASI score was observed for TA and VC separately without significant difference ($p<0.05$).[16] Moreover, in a split-face comparative trial by Pazyar et al., it was found that intradermal injection of AA combined with TA leads to a significant reduction in MASI scores at the 8th and 12th weeks.[8] Similarly, Iraji et al. in a split-face comparative trial, used a combination of TA (4.0 mg/mL) and AA (3%) on the left side of the melasma patient's face, with a mesotherapy technique for six times with 2-week intervals and showed a significant reduction (1.28±0.64) of MASI score ($p<0.001$).[4] Whereas Balvei et al. assessed the effect of AA and salicylic acid (SA) mesotherapies in a clinical trial for two months with 2-week intervals between sessions and found a greater decrease in MASI scores in treated patients.[18] Also, a clinical trial by Dayal et al. on patients with epidermal using a combination therapy of 5% AA cream and trichloroacetic acid suggested a significant reduction in MASI score was observed after treatment.[19] Moreover, Kumawat et al. discovered that TA and glutathione (GSH) intradermal microinjections were effective in treating melasma, but TA was more effective.[20]In the

current study, AA and TA showed various effects on different skin types, as AA was more effective on type III skin, while TA was more effective on type IV skin, with a significant difference. For AA, our results are consistent with that conducted by Pazyar et al. who found that MN with topical AA (20%) significantly decreased the MASI score from 3 sessions onward in Fitzpatrick skin phototypes III patients.[8] Also, it is similar to that found by Ismail et al. who concluded that MN with topical AA was an effective and safe treatment for melasma patients with Fitzpatrick skin phototypes III.[21] For the TA, our results are consistent with that found by Karrabi et al. who declared that TA mesotherapy was significantly (p=0.049) correlated to type IV skin improvement during melasma therapy.[5] However, our results disagreed with Aamir and Naseem, who found that oral TA had the same effect on both skin types.[22] On the other hand, the effects of these AA and TA mesotherapies were different according to melasma types, and both of them were more effective on dermal melasma than epidermal or mixed type. These outcomes are contrary to that found by Aamir and Naseem, who reported a significant reduction after 16 weeks of oral TA treatment in all types of melasma (dermal, epidermal, and mixed type); however, they mentioned that epidermal melasma improvement was more significant at the end of treatment than other types.[22] Moreover, MN+ AA was found effective for epidermal melasma,[21] while AA was believed to be more effective for mixed-type melasma.[18]

Conclusions

Both mesotherapies (AA and TA) were potentially effective in treating melasma. However, their potencies varied on different skin types, as AA was more effective in patients with type III skin, while TA was more effective in patients with type IV skin. Moreover, the effects of these 2 mesotherapies were different according to melasma type, as both of them were more effective on dermal melasma than epidermal or mixed type.

Conflict of interest

The author reports no conflicts of interest.

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