ORIGINAL ARTICLE

Fractional Carbon Dioxide Laser Assisted Delivery of Tranexamic Acid Versus Ascorbic Acid in Treatment of Melasma, A Split Face Comparative Study with Digital Skin Analysis

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Abstract

Background: ***Melasma is characterized as a brownish-red facial pigmentation that is blotchy and appears on both cheeks and forehead.***

Aim and objectives: ***Comparing the safety and effectiveness of using a fractional CO2 laser in conjunction with topical tranexamic acid vs ascorbic acid in the treatment of melasma.***

Patients and methods: ***Forty individuals, spanning the ages of 20 to 50, diagnosed with melasma were included in this prospective split-face comparison investigation. From May 2023 through September 2024, patients were enrolled in the dermatology outpatient clinics at Al-Azhar University Hospitals.***

Results: ***Treatment resulted in noticeably higher mean melanin and masi scores on the L-side compared to the R-side (P=0.04 and P=0.002, respectively).***

Conclusion: ***For melasma, the best treatment is a combination of low-power fractional CO2 and post-laser TXA or vitamin C; however, TXA works better in resistant instances.***

Keywords: Fractional CO2 laser; Tranexamic acid; Ascorbic acid; Melasma; Digital skin analysis

1. Introduction

Melasma is a pigment condition that primarily affects women in their twenties and thirties. It is characterized by enhanced melanogenesis and vascularization. Symptoms include regions of sun-exposed skin that range in color from light brown to dark brown, as well as macules.[1]

Nobody knows what causes melasma. Solar radiation, specifically ultraviolet B (UVB) and visible light is believed to stimulate melanocytes, which in turn produce melasma lesions. The role of UV radiation as a melasma trigger has been recognized for many years. New evidence suggests that opsin-3, a particular sensor in melanocytes, is responsible for inducing hyperpigmentation in response to shorter wavelengths of visible light.[2]

The anti-inflammatory and anti-melanin-generating effects of tranexamic acid have led researchers to speculate that it could have a function in dermatology. When transdermalized, tranexamic blocks a signaling pathway that reduces the communication between keratinocytes (the skin cells) and melanocytes (the cells that produce melanin). As a potential new approach to treating melasma, this can alleviate the appearance of hyperpigmented skin lesions.[3]

Antera 3DTM, an Irish skin analysis camera system, employs light-emitting diodes and sophisticated software to provide a digital picture of the skin's pigmentation, redness, indentions, wrinkles, scar depth and severity, and overall roughness, as well as the depth and severity of scars.[4]

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Jalaly et al. performed a split-face, double-blinded, randomized trial comparing low-power fractional CO2 laser with LFQS 1,064 nm Nd: YAG laser. The fractional CO2 laser showed significant efficacy in decreasing the melanin index and the MASI score.[5]

The purpose of this research is to compare the safety and effectiveness of two fractional CO2 laser treatments for melasma: one using topical tranexamic acid and the other using topical ascorbic acid.

2. Patients and methods

Forty individuals, spanning the ages of 20 to 50, diagnosed with melasma were included in this prospective split-face comparison investigation. From May 2023 through September 2024, patients were enrolled from the dermatology outpatient clinics at Al-Azhar University Hospitals.

Ethical consideration:

Subjects gave their informed consent before they could be enrolled in the study, which was approved by the Al-Azhar Medical Research Ethics Committee.

Inclusion criteria:

Patients with melasma of different types, age: 20-50 years, and sex: both male and females were included.

Exclusion criteria:

Patients on other lines of treatment as topical Kligman's formula, topical hydroquinone or Q-Switched Nd: YAG Laser sessions, pregnant and lactating women, patients with endocrinal problems causing hyperpigmentation of the face as Addison's disease, active infection or inflammation of the face, patients with positive history of hypersensitivity reaction to ascorbic acid or tranexamic acid, female patients with menstrual disturbance or ovarian tumors, patients who fail to fulfill the inclusion criteria.

Methods:

Participants in the study were all asked to complete the following basic tasks:

Take a thorough medical history that includes the patient's age, sex, occupation, length of time on the job, and any drug use. At baseline and monthly throughout the trial, standardized digital photographs were captured using a Canon EOS750D digital camera. The clinical kind of melasma can be determined through clinical assessment and inspection. The purpose of the Wood's lamp test is to identify if melasma is on the dermal, epidermal, or mixed layer.

A dermoscopy can help find both major problems and more subtle signs of progress. Basically, the placement of the melanin in the skin's layers determines its hue in dermoscopy. On both the epidermal and dermal layers, this melanin deposit could appear a distinct color under the microscope. Dermoscopy was performed once at the start of the research and then monthly thereafter.

Hemi MASI score (Melasma Area and Severity Index (MASI)): Melasma severity is evaluated using this subjective professional scoring system. Two skilled dermatologists independently evaluated the melasma hemi-MASI score on both the right and left sides. At the start of treatment and continuing monthly for the next six months, evaluations were conducted.

Evaluation by the skin analysis camera system (Antera 3D™, Ireland):

The skin analysis camera system (Antera 3D™, Ireland) was used for objective evaluation. This system makes use of light-emitting diodes of various wavelengths, which are partially absorbed, scattered, and reflected by the skin. Once again, the camera gathers the reflected light, which is then sent to the designated complex program for analysis. The multispectral analysis allows it to measure the redness, amount of hemoglobin, pigmentation, indentations, wrinkles, and overall roughness of the skin. It can also estimate the uniformity of the melanin distribution.

Melanin relative variation describes pigmentation, while average hemoglobin concentration expresses erythema (vascularity) in the program.[4]

The images taken before and after treatment were opened through a specific software program. The targeted study sites before treatment were selected, and they were automatically matched with the exact same sites after treatment. Specific measurements were then applied. The results were represented in a percentage that was subsequently used in statistical analysis.

Patients were evaluated using Wood's light, dermoscopy, and the Antera 3DTM skin analysis camera system to determine if their melasma was epidermal, dermal, or a combination of the two.

Details of the sessions:

Fractional CO2 (BX300) was administered to all patients. Before applying tranexamic acid (100 mg/ml) on the right side and ascorbic acid (20% solution) on the left side under occlusion for one hour, the patient will undergo a laser session at a wavelength of 10,600 nm and a power output of 1–40W according to the parameters recommended by AMI Korea. The power input and frequency range are 220-240V~, 50/60 Hz. For a duration of six months or until complete recovery, sessions were repeated every four weeks.

Assessment and follow up:

For a duration of six months, patients

underwent clinical examinations and had post-procedure photos taken once a month. Patient happiness and the clinical look of facial pigmentation were the post-procedure outcomes assessed. The results of the treatment were evaluated using the hemi MASI scoring system, dermoscopy, and Wood's lamp test. Furthermore, an unbiased assessment was carried out using the Antera 3DTM skin analysis camera system from Ireland. At the conclusion of the trial, any adverse effects from the fractional CO2 laser or drug application will be noted.

Statistical analysis:

With the help of SPSS 26 for Windows (SPSS Inc., Chicago, IL, USA), we were able to compile, organize, and analyze all of the data. The Shapiro-Whitney U test was used to ensure that the data followed a normal distribution. Frequencies and relative percentages were used to represent the qualitative data. In order to determine the difference between the qualitative variables, the chi-square test (x2) and Fisher exact were employed. Parametric data was presented as mean ± SD (Standard deviation), whereas non-parametric data was presented as median and range.

3. Results

Table 1. Socio-demographic data of studied cases.

PARAMETER	
AGE(YEARS)	n=40
MEAN±SD	39.65±5.66
MEDIAN (RANGE)	41(27-48)
GENDER, N (%)	
MALES	2(5%)
FEMALES	38(95%)

Data were expressed as mean±SD and median(range), or frequency(percentage).

Table 1 showed that, the patients had mean disease duration 4.75 y, ranged between (1-9 y). Seventy percent of the patients had mixed melasma, while 30% had epidermal melasma. The dermoscopic ex of the R-side showed that 62.5% of the patients had fading of pseudo reticular network, 22.5% had fading telangiectasia, while the other 15% had no change. Considering the L-side, 55% had fading of pseudo reticular network, 40% had fading telangiectasia, while the other 5% had no change.

Table 2. Main clinical characteristics of the studied cases.

PARAMETER	
DURATION OF THE DISEASE (YEARS)	n=40
MEAN ± SD	4.75±2.21
MEDIAN(RANGE)	4.5(1-9)
WOOD EXAMINATION, N (%)	
MIXED MELASMA	28(70%)
EPIDERMAL MELASMA	12(30%)
DERMOSCOPIC EXAMINATION, N (%)	
RT-SIDE	
NO CHANGE	6 (15%)
(10-40%) FADING OF PSEUDO RETICULAR NETWORK	25 (62.5%)
(10-20%) FADING OF TELANGIECTASIA	9 (22.5%)
LT-SIDE	
NO CHANGE	16(40%)
(10-40%) FADING OF PSEUDO RETICULAR NETWORK	22(55%)
(10%) FADING OF TELANGIECTASIA	2(5%)

Data were expressed as mean ± SD and median(range), or frequency(percentage).

Fading of telangiectasia was significantly higher in the R-side compared to L-side (p=0.02). No change result was significantly higher in L-Side than the R-side (p=0.01), Table 2.

Table 3. Baseline characteristics of the studied cases before treatment.

PARAMETER		RT-SIDE (N=40)	LT-SIDE (N=40)	P-VALUE
MELANIN	mean±SD	0.75±0.06	0.76±0.06	p=0.45
	median(range)	0.76(0.63-0.87)	0.77(0.64-0.85)	t=0.74
VASCULARITY	mean±SD	1.92±0.28	1.76±0.24	p=0.007*
	median(range)	1.86(1.39-2.49)	1.72(1.28-2.22)	t=2.74
WRINKLES	mean±SD	11.39±1.23	11.36 ± 1.17	p=0.91 t=0.11
	median(range)	11.35(9.23-13.78)	11.1(9.37-13.42)	
TEXTURE	mean±SD	9.69±1.05	9.83±1.08	p=0.55
	median(range)	9.72(7.94-11.43)	9.81(7.98-11.57)	t=0.59
MASI SCORE	mean±SD	5.13±1.03	5.18±1.08	p=0.83
	median(range)	5.02(3.78-7.12)	5.26(3.76-7.23)	t=0.21

Data were expressed as mean±SD and median(range).

student t-test was applied. Masi: melasma area and severity index

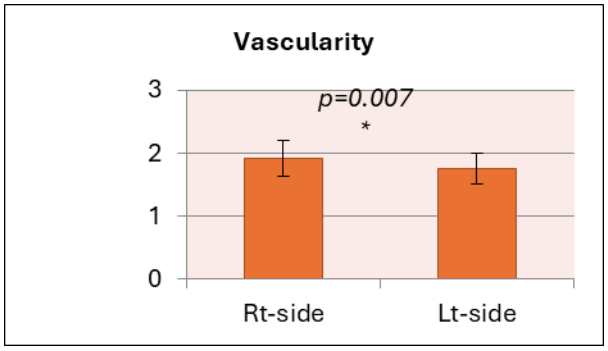

Figure 1. Comparison between Rt and Lt-sides regarding baseline vascularity.

Table 4. Characteristics of the studied cases after treatment.

PARAMETER		RT-SIDE	LT-SIDE	P-VALUE
MELANIN	mean±SD	0.70±0.07	0.73±0.06	p=0.04*
	median(range)	0.74(0.59-0.82)	0.73(0.61-0.83)	t=2.06
VASCULARITY	mean±SD	1.77±0.24	1.69±0.24	
	median(range)	1.74(1.31-2.17)	1.69(1.18-2.12)	p=0.14 t=1.49
WRINKLES	mean±SD	11.0±1.16	10.95±1.29	p=0.85
	median(range)	10.98(8.82-13.61)	10.68 (8.81-13.33)	t=0.18

TEXTURE	mean±SD	9.29±1.12	9.54±1.05	p=0.30
	median(range)	9.06(7.27-11.22)	9.58(7.78-11.23)	t=1.02
MASI SCORE	mean±SD	4.5±1.06	4.75±1.11	p=0.002*
	median(range)	4.18(2.75-6.98)	4.71(2.78-7.11)	t=3.13

Data were expressed as mean±SD and median(range).

student t-test was applied. Masi:melasma area and severity index

Table 4 showed that, the mean melanin and masi score were significantly higher in the L-side than the R-side after treatment (p=0.04 and p=0.002, respectively). Figure (2,3)

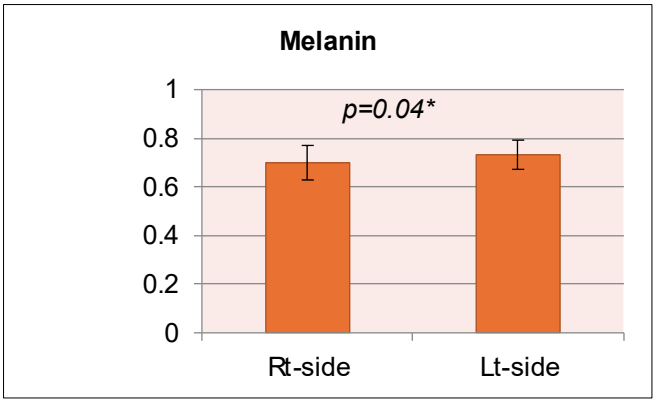

Figure 2. Comparison between Rt and Lt-sides after treatment regarding melanin.

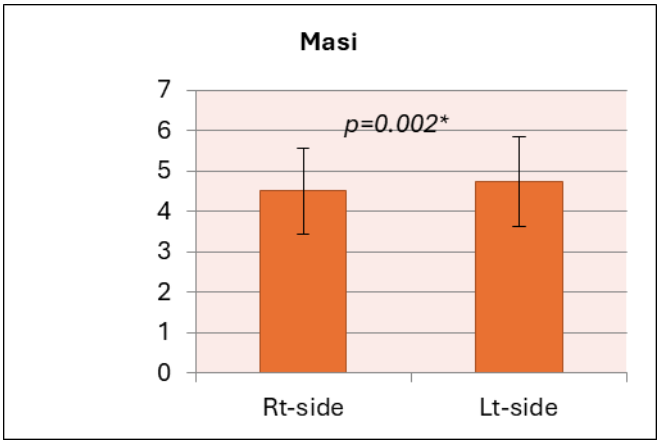

Figure 3. Comparison between Rt and Lt-sides after treatment regarding Masi score.

Table 5. Clinical outcome of the Rt-side before and after tranexamic acid treatment.

PARAMETER		BEFORE (N=40)	AFTER (N=40)	P-VALUE
MELANIN	mean±SD	0.75±0.06	0.70±0.07	p=0.001*
	median(range)	0.76(0.63-0.87)	0.74(0.59-0.82)	t=3.43
VASCULARITY	mean±SD	1.92±0.28	1.77±0.24	p=0.01*
	median(range)	1.86(1.39-2.49)	1.74(1.31-2.17)	t=2.57
WRINKLES	mean±SD	11.39±1.23	11±1.16	p=0.14
	median(range)	11.35(9.23-13.78)	10.98(8.82-13.61)	t=1.46
TEXTURE	mean±SD	9.69±1.05	9.29±1.12	p=0.1
	median(range)	9.72(7.94-11.43)	9.06(7.27-11.22)	t=1.65
MASI SCORE	mean±SD	5.13±1.03	4.51±1.06	p=0.009*
	median(range)	5.02(3.78-7.12)	4.18(2.75-6.98)	t=2.65

Data were expressed as mean±SD and median(range).

Paired student t-test was applied. Masi:melasma area and severity index

The clinical outcome of the Rt-side before and after tranexamic acid treatment showed that the means of melanin, vascularity and masi score were significantly decreased after tranexamic acid treatment than those before (p=0.001, p=0.01 and p=0.009, respectively) Table 5, figures (4-6)

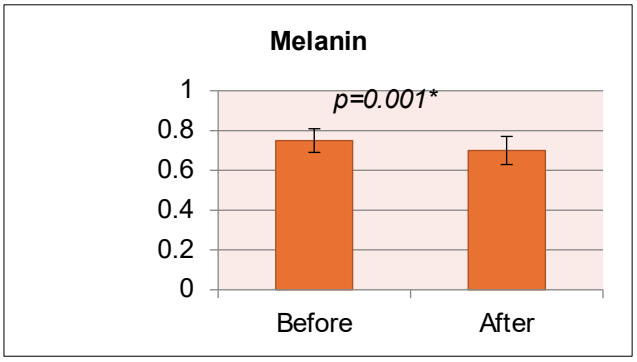

Figure 4. Comparison Rt-side melanin level before and after tranexamic acid treatment.

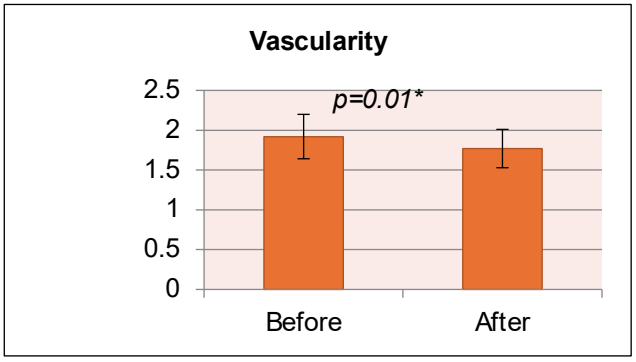

Figure 5. Comparison Rt-side vascularity level before and after tranexamic acid treatment.

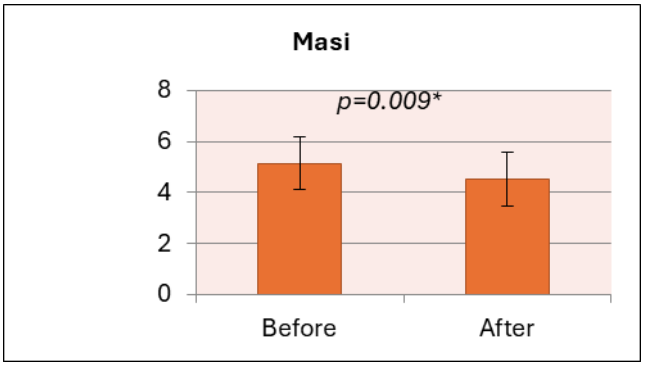

Figure 6. Comparison Rt-side masi score before and after tranexamic acid treatment.

Table 6. Clinical outcome of the Lt-side before and after ascorbic acid treatment

PARAMETER		BEFORE	AFTER	P-VALUE
MELANIN	mean±SD	0.76±0.06	0.73±0.06	p=0.02*
	median(range)	0.77(0.64-0.85)	0.73(0.61-0.83)	t=2.2
VASCULARITY	mean±SD	1.76±0.24	1.69±0.24	
	median(range)	1.72(1.28-2.22)	1.69(1.18-2.12)	p=0.19 t=1.3
WRINKLES	mean±SD	11.36±1.17	10.95±1.29	p=0.14
	median (range)	11.1(9.37-13.42)	10.68(8.81-13.33)	t=1.49
TEXTURE	mean±SD	9.83±1.08	9.54±1.05	p=0.22
	median(range)	9.81(7.98-11.57)	9.58(7.78-11.23)	t=1.21
MASI SCORE	mean±SD	5.18±1.08	4.75±1.11	p=0.08
	median(range)	5.26(3.76-7.23)	4.71(2.78-7.11)	t=1.7

Data were expressed as mean±SD and median(range).

Paired student t-test was applied. Masi: melasma area and severity index

The clinical outcome of the Lt-side before and after ascorbic acid treatment showed that the mean melanin level was significantly decreased after ascorbic acid treatment than before (p=0.02) Table 6. Figure 7.

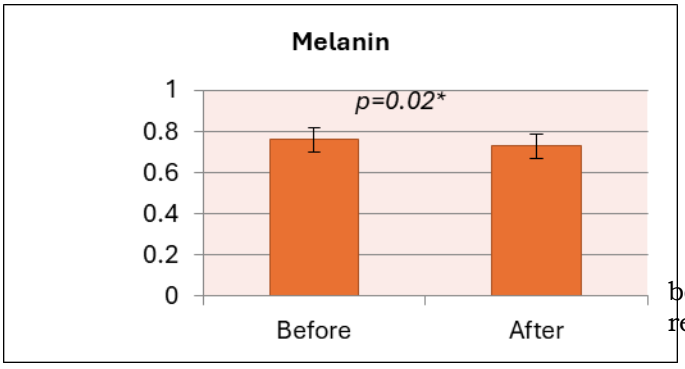

Figure 7. Comparison Lt-side melanin level before and after ascorbic acid treatment.

Case presentation:

Figures (8): I,ii,iii,iv and v showing clinical changes in a female patient 38-years old.

Before treatment(A) and after treatment(B) showing better improvement in the right side.

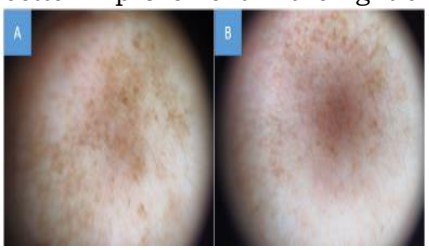

Figure (9): Dermoscopic changes of RT. Side before (A) and after(B). Showing fading of reticuloglobular network

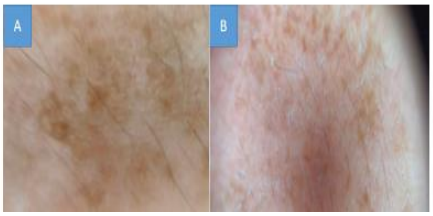

Figure (10): Dermoscopic changes of LT. Side before and after(B). Showing fading of reticuloglobular network.

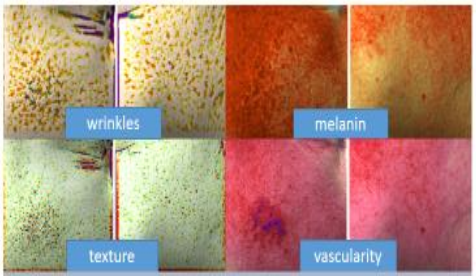

Figure (11): Antera changes at RT. Side before and after(B) tranexamic acid treatment.

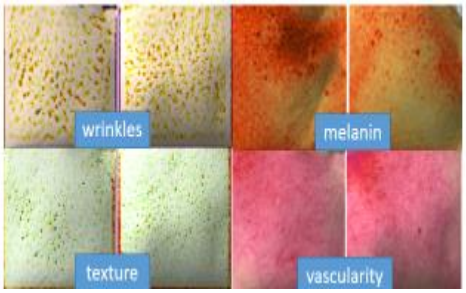

Figure (12): Antera changes at LT. Side before (A) and after(B) tranexamic acid treatment.

4. Discussion

Acquired hyperpigmented macules that are symmetrically distributed on sun-exposed skin are known as melasma. Microneedling the skin allows lightening chemicals to penetrate deeper layers of skin using a transdermal delivery mechanism.[6]

By inhibiting melanocytes' ability to produce melanin, tranexamic acid reduces pigmentation caused by ultraviolet light.[7]

Light and laser treatments can be used with caution as a second or third line of defense against stubborn melasma; however, low-energy settings are ideal because of the potential for post-inflammatory hyperpigmentation and melasma activation.[8]

The 40 patients with melasma who participated in this study were predominantly female (55%). Their ages ranged from 27 to 48 years, with an average age of 39.65±5.66 years. The patients' disease durations varied from 1 to 9 years, with an average of 4.75 years. Mixed melasma affected 70% of patients, while epidermal melasma affected 30%.

Conversely, 2,812 randomized participants were included in 59 studies that were part of a systematic review and meta-analysis. Liu et al.,[9] observed that, out of the few records regarding melasma type, 280 individuals belonged to the epidermal type, 105 to the mixed type, and 57 to the dermal type.

Our research was based on comparing the R- and L-side dermoscopy outcomes. There was a statistically significant difference in the rate of telangiectasia fading between the R and L sides (p=0.02). Sixty-2.5 percent of patients had fading pseudo reticular network, 22.5 percent had fading telangiectasia, and 15.0 percent showed no change, according to the dermoscopy examination of the right side. From the left side, we can see that 55% of patients experienced a fading pseudo reticular network, 40% a fading telangiectasia, and 5% no change at all.

In another study, Shanavaz et al.,[10] dermoscopy revealed a reticuloglobular pattern in 94(85.45%) of 110 cases, granules or dots in 30(27.3%) of patients, a perifollicular brown, black globule in 50(45.54%), and an uneven distribution of pigmentation in 21(19.1%) of patients. Additionally, telangiectasia was observed in 36(36%) of 110 patients. Twenty-seven individuals, or 24.5% of the total, exhibited hypopigmentation that was consistent with melasma topical treatments.

After treatment, the L-side had significantly higher mean melanin and masi scores than the R-side (p=0.04 and p=0.002, respectively), according to the current study. After tranexamic acid treatment, the means of melanin, vascularity, and masi score were considerably lower than those before (p-values were 0.001, 0.01 and 0.009, respectively) according to the clinical outcome of the Rt-side before and after tranexamic acid treatment. A statistically significant reduction in mean melanin level was observed following ascorbic acid treatment compared to pre-treatment results (p=0.02) in the Lt-side clinical outcome comparison. However, there were no discernible changes in masi score between the ascorbic acid groups.

In the same line, El Attar et al.,[6] designed to compare the safety and effectiveness of applying topical tranexamic acid to that of applying topical vitamin C following microneedling to treat melasma. The average age of the twenty patients studied in this split-face prospective randomized uncontrolled study was 39.45±6.95 years, and all twenty had facial melasma. After dermapen microneedling, the patient's faces were treated with topical tranexamic acid on the right side and topical vitamin C on the left.

In a recent Egyptian study, Tawfic et al.,[11] sought to compare the effectiveness of a low-power fractional CO2 laser applied topically or intradermally with that of the laser alone against tranexamic acid in treating melasma. The study included 56 melasma patients with an average age of 38.80±5.21 years. Results showed a considerable decrease in the melanin index and MASI score when fractional CO2 laser was used in conjunction with an intradermal TXA injection; this finding raises the possibility that this combination may be more effective than topical TXA alone.

The results of our study agreed with another study by Ismail et al.,[12] In a study that looked at the effects of vitamin C on melasma, thirty female patients underwent six sessions of microneedling and were also given topical ascorbic acid every two weeks. After the treatment, the patients' melasma improved, and their mean MASI score decreased from 8.61 to 5.75. By the end of the sessions, every single patient had made significant progress.

On the other hand, was a previous one by Raza et al.,[13] Thirty people with melasma, eleven men and nineteen women, took part in the study. Patients between the ages of 20 and 40 made up over 75% of the total patient population. Every single patient got micro-needled Tranexamic acid on their right cheeks and vitamin C on their left. Both sides showed improvement, although there was no statistically significant difference (p>0.05).

In another study conducted by Ebrahim et al.,[14] compared the effectiveness of micro-needling with that of intra-dermal injections of tranexamic acid (TXA). Using baseline mMASI values, we were able to determine that the treatment was effective;

melasma reduced significantly on both sides, although micro-needling resulted in higher patient satisfaction.

It is also possible to explain our results by considering that ascorbic acid effectively inhibits tyrosinase enzyme activity by interacting with copper ions at the tyrosinase-active site.15 Because One class of hemostatic drugs, tranexamic acid, inhibits plasminogen's conversion to plasmin by binding to its lysine residues. In addition, it has the potential to reduce the production of arachidonic acid and α-melanocyte-stimulating hormone (α-MSH), leading to a decrease in pigment formation in melanocytes.[16]

4. Conclusion

Melasma patients, particularly those with resistant instances, can find relief with a combination of low-power fractional CO2 and post-laser TXA or vitamin C. The results are best when achieved with TXA.

Disclosure

The authors have no financial interest to declare in relation to the content of this article.

Authorship

All authors have a substantial contribution to the article

Funding

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Conflicts of interest

There are no conflicts of interest.

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