The Efficacy of Intralesional Tranexamic Acid in the Treatment of Melasma in Iraqi Patients

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ABSTRACT:

BACKGROUND:

Melasma is an acquired hyperpigmentation of the skin. Exacerbating factors include pregnancy, use of oral contraceptives and sunexposure.

OBJECTIVE:

To study the effectiveness of intralesional tranexamic acid in the treatment of melasma.

PATIENTS AND METHODS:

This is an interventional single-blinded comparative outpatient study carried out at the Center of Dermatology, Baghdad Teaching Hospital during the period from March 2017 to May 2018.

Forty patients with melasma were included in the study. The patients were divided into three groups. Group A was treated with tranexamic acid 4mg/ml delivered by microneedling approach at monthly interval for 3 months with topical hydroquinone 4% daily at night for 3 months. Group B was treated with intradermal injection of 4mg/ml of tranexamic acid by using insulin syringe monthly for 3 months with topical hydroquinone 4% daily at night. Group C was treated with topical hydroquinone 4% daily at night for 3 months.

The severity of melasma was assessed before, during and after treatment with the melasma area and severity index (MASI) score. Every patient was instructed to apply a broad-spectrum sunscreen before sun exposure during the treatment period.

RESULTS:

Thirty-two patients with melasma completed the study. In group A: Eleven patients were included, the mean age and SD was 33.81 ± 4.55 years. The MASI score before treatment was 5.31 ±1.65, whereas after treatment it became 3.69± 1.79 (P value: 0.0001). The reduction of MASI score was 32.39%. In group B: Eleven patients were included, the mean age and SD was 39.72 ±6.27 years. The MASI score before treatment was 4.52±1.79, whereas after treatment it became 3.50 ±1.61 (P value: 0.002). The reduction of MASI score was 20.96%. In group C: Ten patients were included, the mean age and SD was 37.20 ± 7.55 years. The MAI score before treatment was 4.01±1.07 whereas after treatment became 3.13±0.17 (p value=0.002). The reduction in the MASI score was 14.11. The percent reduction in the MASI score at follow up visits was significantly higher in group A than in groups B and C (p value= 0.026) while there were no significant difference between group B and C.

CONCLUSION:

Tranexamic acid is an effective drug when it used with other conventional treatments of melasma, and the microneedling approach of delivering tranexamic acid showed better response than the other modes of drug delivery and this may be due to uniform delivery of the drug through the microchannels.

KEYWORDS: Melasma, Tranexamic acid, Micro needling

INTRODUCTION:

Melasma is a common acquired symmetrical hypermelanosis most commonly on the face. It is most prevalent among young to middle-age women. Exacerbating factors include sun exposure, pregnancy, and use of oral contraceptive pills[1].

Recent studies have suggested that a connection between vessels and cutaneous pigmentation could exist. Human melanocytes may respond to angiogenic factors[2].

Also, it has been reported that the topical plasmin inhibitor, tranexamic acid (TXA), is effective in the treatment of UV-induced hyperpigmentation, localized microinjection of TXA is thought to improve melasma in vivo[3].

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PATIENTS AND METHODS:

This study is an interventional single-blinded comparative outpatient study. It was carried out at the center of Dermatology, Baghdad Teaching Hospital during the period from March 2017 to May 2018.

Patients clinically presenting with melasma were included. Those using therapy told to stop any treatment for at least 2 months prior to using therapy. The use of a sunscreen with a sun protection factor (spf) more than 30 was recommended.

Pregnant and lactating women, patients with chronic illness, any patient with disease that interferes with skin pigmentation were excluded. At the first visit a history was taken from each patient including age, onset and duration of melasma, marital status, use of cosmetics, family history, sun exposure and drug history. Female Patients were also asked about the relation of melasma to pregnancy, premenstrual flare up and use of oral contraceptive pills. The diagnosis was made on clinical bases.

A careful examination of melasma was done as baseline and in follow-up visits and including Fitzpatrick skin type, distribution of melasma as either butterfly, centrofacial, mask-like, or localized, and Photographs for all patients were performed by using Galaxy camera note 3 and Galaxy S8+ in the same place of illumination.

Calculation of melasma area and severity index (MASI) score was carried out for each patient according to Rodrigues et, al[4].

Forty patients were included in the study, the patients were divided into 3 groups A,B and C according to the type of therapy:

Group A: Fourteen patients were included, eleventh completed three sessions and three defaulted. TXA at a concentration of 4mg/ml and with a total volume of two ml, was delivered to the whole area of melasma using a Derma pen micro needling approach with 1.5 mm depth, Derma pen is a motorised surgical instrument operates with a disposable needle tip cartridge that contains a variable number of needles(9,12,36,42). The derma pen used in the present work is called Dr.pen, it is supplied by ULTIMA-A6 , made of metal shell, wired and wireless with two rechargeable batteries and five-level of speed with a depth range from 0.25 to 2.5mm (0.25, 0.5, 0.75, 1.0, 1.25, 1.5, 1.75, 2.0, 2.25, 2.5 mm), the surface area of the cartridge is (0.78) cm2 and the number of needles of the used cartridge is 36 needles, the device was moved slowly and in multi directions to the whole area to be treated.

Group B: Eleven Patients were included in the study ,all of them completed 3 sessions. TXA in a concentration of 4mg/ml was delivered to the whole area of melasma by using an insulin syringe guage 29, the volume delivered was 2ml. In both groups sessions were repeated every 4 week to a total of three sessions and hydroquinone 4% supplied by jamjoom, was applied to the whole area of melasma daily at night for the whole period of treatment.

Group C: Fifteen Patients was included, ten completed 3 months of treatment by HQ 4% applied daily by the patients at night for 3 months.

All patients were advised to use sun screen with sun protection factor of more than 30 during and after treatment, and all have been followed up regularly with an assessment of the response to treatment by doing MASI score at each visit and taking photographs during the treatment period and the follow up visits (for two months after the treatment), local or systemic side effects were recorded.

RESULTS:

The age, duration of melasma and the demographic data for the patients are presented in table 1, 2 and 3 respectively.

Clinical results: Group A: MASI score before treatment was 5.31±1.65 while at the second visit (after one month) it became 4.14±1.67 (p value=0.002) and at the third visit (after two months), it became 3.69 ± 1.79 (p value=0.0001) and remained the same at the follow-up visits after one and two months of treatment, the percent reduction of MASI score at follow up compared to pretreatment was 32.39%.

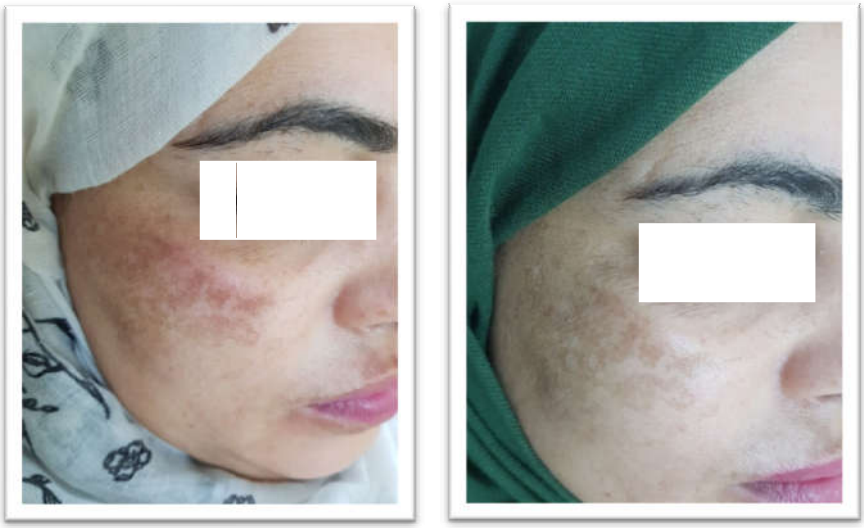
Group B: MASI score before treatment was 4.527 ± 1.79 while at the second visit after one month became 3.90±1.96 (p value=0.006) and at third visit (after two month of treatment), it became 3.50±1.61 (P value =0.002) and remained the same during the follow-up visits (one and two months after the treatment).

The percent reduction in MASI score at follow up compared to pretreatment was 20.96%.

Group C : MASI score before treatment was 4.01±1.07 while at the second visit after one month it became 3.24±0.79 (p value=0.002) and at the third visit it became 3.13±0.71(p value=0.002) and not changed during the follow up visits, the percent reduction in MASI score at follow up visits compared to pretreatment was 14.11%.

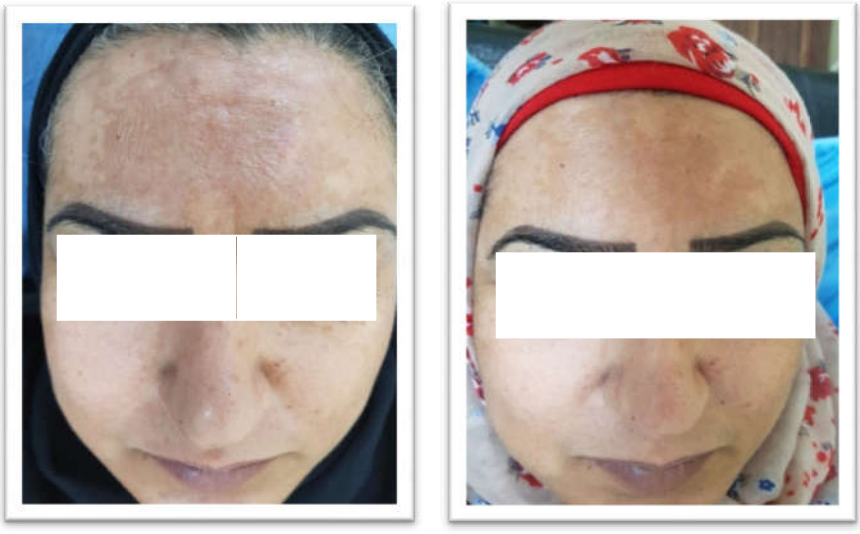
Comparing the three groups: the percent reduction at follow up between group A and B was significant with a p value =0.049 and between group A and C was also significant with a p value=0.026, but between group B and C was with p value=0.65 which was not significant, so the reduction in group A was higher than group B and group c.

Adverse effects: pain during the procedure was recorded in both group A and B and subside there after, erythema was recorded in both group A and B but mainly in group A and take few days then resolve. No side effects were reported in group C.



A **B**

Picture(1): A thirty eight years old female patient treated with Dermapen microneedling delivery of TXA +topical HQ4%: A) Before treatment, B) After 2 months off treatment



A **B**

Picture (2) : A forty years old women treated with intradermal injection of TXA with topical HQ 4%: A) Before treatment, B) after 2 months off treatment.

Table (1):Age (years) of patients in group A,B and C.

	N	Minimum	Maximum	Mean	SD
Group A	11	26.00	43.00	33.818	4.55671
Group B	11	31.00	48.00	39.727	6.27839
Group C	10	25.00	48.00	37.200	7.55425

Table(2): Duration of melasma (years) in group A,B and C.

	Group A		Group B		Group C		Total	
	No.	%	No.	%	No.	%	No	%
<1	1	9.09	0	0	0	0	1	3.12
1-5	4	36.4	5	45.5	7	70	16	50
5-10	6	54.5	4	36.4	1	10	11	31.25
>10	0	0	2	18.2	2	20	4	12.5
Total	11	100	11	100	10	100	32	100

Table (3): Patient's demographic data group A,B and C.

		Group A	Group B	Group C	Total
Gender	Male	2	0	0	2(6.25)
	Female	9	11	10	30(93.7)
Social status	Married	10	10	9	29(90.6)
	Unmarried	_	_	1	1 (3.12)
	Widow	1	1	_	2(6.66)
Skin type	II	1	1	0	2(6.25)
	III	3	4	6	13(40.6)
	IV	7	6	4	17(53.1)
Gyneocological History	History of melasma during pregnancy	4	5	6	15(51.7)
	History of OCP use	5	3	3	11(27.9)
Family History of melasma		2	6	4	12(37.5)
Sun exposure		8	6	6	20(62.5)
Pattern of melasma	Butterfly	5	2	4	11(34.3)
	Localized	4	5	5	14(43.7)
	Centrofacial	2	3	1	6(18.7)
	Mask like	_	1	_	1(3.12)

Table 4: MASI scores (mean ± SD) for patients in group A,B and C.

	First visit	Second visit	Third visit	Follow up visit
Group A	5.3182 ± 1.65156	4.1455 ± 1.67354	3.6945 ± 1.79731	3.6945 ± 1.79731
Group B	4.5273 ± 1.79838	3.9000 ± 1.96774	3.5000 ± 1.61741	3.5000 ± 1.61741
Group C	4.0100 ± 1.07956	3.2400 ± .79331	3.1300 ± .71655	3.1300 ± .71655

DISCUSSION:

Tranexamic acid is a widely used for the treatment of menorrhagia.. A number of studies were carried out to evaluate its effectiveness in the treatment of melasma. The method of administration of TXA varied from oral to topical to intralesional injection to delivery by micro needling approach [5].

In the present study, the MASI score reduction rate was 32.39%, 20.96% and 14.11% in the treatment group A, B, C respectively. The reduction rate was significantly higher in group A (TXA by micro needling + HQ 4%) than in group B (TXA by insulin syringe + HQ 4%) and group C (HQ 4% alone).

The mechanism of action of TXA in melasma may be related to inhibition of melanin synthesis by inhibition of plasminogen/plasmin pathway, thereby blocking the interaction between melanocytes and keratinocytes[6].

While HQ is thought to act by inhibition of tyrosinase, possibly by binding to the enzyme or by interaction with copper molecules at the enzyme's active site. This leads to altered melanosome formation and increased melanosome destruction, and even the inhibition of DNA and RNA synthesis[7].

The higher reduction rate may be attributed to the deeper and more uniform delivery of TXA by microneedles.

The present work is compatible with the large study done in 2006, in India by Lee et al, where 100 patients with melasma were treated with TXA 0.05ml(4mg/ml) weekly for 12 weeks via intradermal microinjection, a significant reduction in MASI score at 8 wk and 12wk of treatment with (p value<0.05)[3] , and it is also compatible with Budamakuntla , et al study, in 2013 where the micro needling delivery of TXA 4mg/ml monthly at 0,4,8 weeks showed better response than a microinjection approach, the reduction in the MASI score was 35.72% in the microinjection group and 44.41 % in the microneedling group[8].

Ibraheem et al treated melasma with a modified Kligman's formula with different concentrations of retinoid and resulted in that the better response was done by using a higher concentration of retinoids with a reduction rate of 35.3% [9], and so it was slightly better reduction rate than the best result of current study which was obtained by the micro needling approach.

A two recent studies were done in Iran in 2018 the first one by Tehranchinia ,et al a split face clinical trial, they found that TXA 100mg/ml + HQ4% were better than HQ4% in the treatment of melasma [10].

The second trial by Saki, et al, was also a split face study, they found that done between of TXA intradermal injection of TXA 4mg\ml monthly were better than HQ 4% daily for 3 months [11].

In the present work, the side effects were minimal and included pain mainly in group A and erythema. Pain was limited to the time of the procedure and didn't necessitate stopping of the procedure and erythema lasted for 1-2 days and then disappeared without treatment. Side effects were also reported in other studies such as erythema, burning sensation and discomfort that were minimal and didn't necessitate stopping treatment.

So in conclusion, tranexamic acid is an effective adjunctive drug when used with other conventional treatments of melasma. And the micro needling approach of delivering TXA resulted in better response.

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