Comparing Efficacy and Safety of Oral Tranexamic Acid and 4% Topical Hydroquinone Cream in Melasma Treatment: A Randomized Controlled Clinical Trial and Review of Literature

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Abstract

Introduction. Melasma is a common skin pigmentation disorder affecting a patient's life psychologically and socially. Topical medications or lasers can have temporary and limited therapeutic effects on melasma. **Material and Methods.** This study is a prospective clinical trial comparing therapeutic effects of oral Tranexamic acid (TXA) and topical Hydroquinone (HQ) cream. A total number of 69 patients were examined. During the study, 10 patients failed to appear for the follow-up and 59 of them completed the trial. The patients were also divided randomly into two groups. Group A received TXA capsule 250 mg every 12 hours and group B received 4% topical HQ cream day and night. The patients from both groups were treated for 3 months. Melasma Area and Severity Index (MASI) scores were then calculated at the baseline, 4 weeks, and 12 weeks into the treatment and 3 months after the end of intervention. **Results.** MASI baseline, 4 weeks, 12 weeks, and 24 weeks in TXA group were 21.66, 13.69, 9.10, 9.24; respectively. Reduction of MASI between baseline and 4 weeks was statistically significant. Such a decreasing trend in MASI scores between baseline and 12 weeks was also reported as statistically significant ($p=0.001$). In the HQ group, MASI baseline, 4 weeks, 12 weeks, and 24 weeks were 21.46, 13.57, 10.93, 11.20; respectively. Reduction of MASI scores between baseline and 4 weeks was statistically significant. Moreover, a decline in MASI scores was observed between baseline and 12 weeks that was statistically significant ($p=0.001$). Considering both groups MASI scores were reduced but the difference between two study groups was not statistically significant ($p=0.98$). **Conclusion.** The efficacy of TXA and HQ was the same and both could significantly reduce MASI scores.

Key words: Melanosis; Tranexamic Acid; Dermatologic Agents; Hydroquinones; Administration, Topical; Treatment Outcome

Introduction

Melasma is a common pigmentation disorder of the face, which can be very debilitating psychologically and socially. Melasma often appears as symmetrical macules or patches on the face. It can also have three common patterns including *centrofacial* (involving the forehead, cheeks, nose, upper lip, and chin), *malar*, and *mandibular*. In addition, this disease is more common in the Asian and African race and can affect women with darker skin types (1, 3).

The precise pathogenesis of this disease is unknown; however, the hypothesis of the activation of melanocyte biology via ultraviolet has been discussed. Recent studies have further shown an increased incidence of angiogenic factors in the epidermis as well as increased vascularity in these areas (4, 5).

Moreover, a number of predisposing factors such as pregnancy, use of contraceptives, sun exposure, ovarian tumors, hormone replacement therapy (HRT) and anti-seizure medications have been designated (6).

The most commonly used treatments for melasma are the use of topical lightening drugs such as HQ, which are often inadequate or can even cause skin irritations. Furthermore, experiments have revealed that topical melasma treatments have therapeutic effects on most types of epidermal melasma, but not on dermal ones (7, 8).

TXA, chemically named Trans-4-aminomethyl cyclohexane carboxylic acid has been introduced as a new treatment for melasma and it is actually a synthetic derivative of the Lysine amino acid that can be effective in preventing bleeding. Efficacy of intradermal tranexamic acid injection has been reviewed in some studies (9). Studies and trials on the use of oral medications such as TXA in the treatment of melasma are limited. Therefore, the main purpose of this study is to design a prospective clinical trial which would compare the effects of oral TXA treatment on melasma and use of conventional treatments such as topical HQ cream.

Material and Methods

The present study is a prospective clinical trial, a case-control research, and a blinded analyst-and-assessor one evaluating the effect of oral TXA treatment on melasma. The study samples consisted of patients referred to a dermatology clinic from July 2017 to October 2018 for melasma treatment. To begin the study, the code of ethics was obtained (1396.714 IR.AJUMS.REC) and the study was registered on the Iranian Randomized Clinical Trial database with the code, IRCT20180111038311N1.

The inclusion criterion was being affected with melasma in the age range of 18 to 60 years. The melasma was also defined with clinical diagnosis of a dermatologist (if necessary, a skin biopsy was used to confirm the diagnosis).

Exclusion criteria were patients with a history of coagulopathy, history of thrombotic problems, evidence of any thrombotic events, use of coagulant drugs, use of anti-coagulant or antiplatelet medications such as aspirin or clopidogrel tablets, pregnancy, lactation, concomitant use of contraceptives or phenytoin, history of individual vitiligo or other pigmentation disorders, history of TXA susceptibility, kidney disease, history of melasma lightening treatment (3 months before the onset of the

study). The patients also underwent an examination by Wood's lamp and then the types of melasma (dermal, epithelial, mixed, and unspecified) were determined.

After entering the study, the patients received explanations about the research method, and they were prepared to give consent to be included in the study. Then, they were randomly categorized (in the premium block method) in one of the groups; group A, which included administration of 250 mg TXA capsules every 12 hours, and group B which involved administration of a 4% topical HQ cream applied locally in mornings and evenings. In group A patients, coagulation profile tests were also performed before treatment. Melasma severity was then measured by the formula of MASI scores and then recorded separately for patients. This scoring was described by Kimbrough-Green et al. (10), and the measurement method was as follows.

$MASI = 0.3(DF + HF) + 0.3(DMR + HMR) + 0.3(DML + HML) + 0.1(DC + HC) + AC$

The numbers of 0.3 and 0.1 are respectively related to the anatomical covered areas on the face, taking 0.1 of the face area in the chin, and 0.3 in the right and the left molar regions of the forehead.

D=Darkness, H=Homogeneity, A=Area, F=Forehead, MR=Right Malar, ML=Left Malar, C=Chin

To assess darkness "D" and color homogeneity "H", 0 to 4 degrees is given (Absent=0, Slight=1, Mild=2, Marked=3, Maximum=4).

In this formula, A is the amount of surface involvement of melasma in any anatomical area (Noninvolvement=0, 0-9%=1, 10-29%=2, 30-49%=3, 50-69%=4, 70-89%=5, 90-100%=6).

The MASI score is calculated from the multiplication of the A score by the sum of D and H and is computed for each of the 6 regions. The maximum score for each side of the face is 24 and the minimum one is 0.

Each group underwent treatment for 3 months. During this period, the patients were followed up and recommended to use sunscreens (without anti-pigmentation and SPF=30).

Within 1 and 3 months after the beginning of treatment and three months after its completion, each patient was reevaluated and MASI was calculated. Finally, 3 months after the end

of the treatment, the patient's satisfaction was determined as 1=excellent satisfaction, 2=relative and good satisfaction, and 3=dissatisfaction. Adverse effects were also documented.

Results

Among the 90 melasma patients referred to the dermatology clinic, 69 patients met the inclusion/exclusion criteria and were invited to participate in the study and they were then randomized into two groups: group A consisting of 34 patients treated with oral TXA and 35 patients in group B treated with topical 4%HQ cream.

Demographic information and background characteristics are summarized in Table 1. During the study, 5 patients from each group were excluded because they failed to appear at the check-up or the treatment was discontinued due to side effects; i.e. severe irritant contact dermatitis in the HQ group (1 patient) and gastrointestinal complications (1 patient) in the TXA group, and 4 patients in each group were also excluded because of poor

compliance. Finally, 29 patients in group A and 30 patients in group B were analyzed.

The mean age of the patients was 38.30 ± 6.97 (17-52) years. The mean age in group A was 37.31 ± 7.88 years and that was 39.26 ± 5.93 years in group B and no statistically significant difference was observed between the two groups ($p=0.28$).

In group A, 28 (96.6%) patients were females and 1 patient (3.4%) was male. In the cream group, 28 individuals (93.3%) were females and 2 patients (6.7%) were males. There was no statistically significant difference between the two groups in terms of gender status ($p=0.57$).

T-test was used to compare information and characteristics of both groups which showed no statistically significant difference (Table 1).

The mean MASI score was 21.66 ± 5.96 in group A (TXA) and 21.47 ± 7.00 in group B (HQ). There was no significant difference between MASI scores in the two groups during baseline ($p=0.916$).

Table 1. Demographics and background characteristics

Measure	TXA(29 patients)	HQ(30patients)	P _ value
Age (year)/Mean $\pm$ SD	37.3 $\pm$ 7.8	39.2 $\pm$ 5.9	0.28
Sex N (%)	28 females (96.6%) 1 male (3.4%)	28 females (93.3%) 2 males (6.7%)	0.57
Skin phototype N(%)	Type 2 - 1 (3.4%) Type 3 - 14 (48.3%) Type 4 - 12 (41.4%) Type 5 - 2 (6.9%)	Type 2 - 2 (6.7%) Type 3 - 14 (46.7%) Type 4 - 11 (36.7%) Type 5 - 3 (10%)	0.9
Disease duration (year)	4.8 $\pm$ 5.1	5 $\pm$ 5.7	0.927
Positive Familial history of melasma N (%)	31.0%	50%	0.13
Sun exposure N (%)	27 (93.1%)	25 (83.3%)	0.24
Pregnancy in recent years N (%)	10 (34.5%)	15 (50.0%)	0.22
OCP consumption (%)	4 (13.8%)	5 (16.7%)	0.75
Previous treatment for melasma N (%)	17 (58.6%)	14 (46.7%)	0.35
Melasma Type in wood lamp N (%)	Dermal 3 (10.3%) Epidermal 17 (58.6%) Mixed 9 (31.0%)	Dermal 1 (3.3%) Epidermal 17 (56.7%) Mixed 12 (40.0%)	0.49
Melasma region N (%)	Centrofacial 21 (72.4%) Malar 7 (24.1%) Mandibular 1 (3.4%)	Centrofacial 24 (80.0%) Malar 5 (16.7%) Mandibular 1 (3.3%)	0.77
Baseline MASI score Mean $\pm$ SD	21.66 $\pm$ 5.96	21.56 $\pm$ 7.00	0.46

Mean MASI score during the 4th week after the onset of treatment was 13.46 ± 5.70 in the TXA group and 13.57 ± 5.97 in the HQ group with no significant difference between MASI scores ($p=0.944$).

In the third month after the start of the treatment, the mean MASI score was 9.10 ± 4.93 in the TXA group and 10.93 ± 6.18 in the HQ group. There was no statistically significant difference between MASI scores in the two groups in the 12th week ($p=0.215$).

Three months after the end of the treatment period, the mean MASI score was 9.24 ± 5.11 in the TXA group and 11.20 ± 6.04 in the HQ group and no significant difference

between MASI scores in the two groups in the 24th week ($p=0.185$).

The mean MASI score of the patients in the TXA group during the 4th week compared with pretreatment ($p=0.001$) and within the 12th week compared with the 4th week ($p=0.001$) was significantly and statistically different. Moreover, the mean MASI score during the 12th week decreased significantly ($p=0.011$) compared with the baseline ($p=0.001$) (**Figure 1**).

The mean MASI score of the patients in the HQ group during the 4th week compared with pretreatment ($p=0.001$) and the 12th week compared with the 4th week ($p=0.001$)

Figure 1. Clinical photograph of melasma patients in the TXA group taken at the first visit (pretreatment) and after 3 months of treatment. (A) 31-year-old female, (B) 38-year-old female

Table 2. Efficacy of treatment by MASI score in treatment groups

Group	Pretreatment MASI	4 th week	12 th week	3 months after treatment cessation	p-value
TXA	21.66±5.96	13.46±5.70	9.10±4.94	9.24±5.12	p<0.001
HQ cream	21.47±7.00	13.58±5.97	10.93±6.18	11.20±6.05	p<0.001
p-value	0.916	0.944	0.215	0/185	

was reported as significantly statistically different. Moreover, the mean MASI score in the HQ group decreased significantly within the 12th week ($p=0.001$) compared with the baseline ($p=0.011$) (**Table 2, Figure 2**).

The mean MASI score in each group was determined separately based on different variables including skin photo types, familial history, and melasma type through examination with Wood's lamp and location of melasma on the face as well as duration of melasma before the start of the treatment, and the results are separately given in **Table 1**.

Treatment Complications

In the TXA group, 3 (10.3%) patients had gastrointestinal side effects, 13 (44.8%) of

them had no side effects. The most significant complication in the TXA group was hypomenorrhea, and that was irritant contact dermatitis in the HQ group. The number of complications in the TXA group was significantly higher than in the HQ group ($p=0.001$).

Patient's Satisfaction

In the TXA group, 6 (20.7%) patients expressed complete satisfaction, 19 (65.5%) of them reported good and relative satisfaction, and 4 (13.8%) of such patients expressed no satisfaction. In the HQ group, 2 (6.7%) patients expressed complete satisfaction, 18 (60%) of them reported relative and good satisfaction, and 10 (33.3%) of them had no satisfaction. There was also no significant difference between the two groups ($p=0.1$).

Discussion

Melasma is a common facial pigmentation disorder, which can be psychologically and socially disabling. It also has a great impact on quality of life.

TXA, chemically named Trans-4-aminomethyl cyclohexane carboxylic acid, has been also introduced as a new treatment for melasma, and is actually a synthetic derivative of the Lysine-amino acid that is effective in bleeding prevention (9). Nijor (1979) was the first scholar examining the effect of TXA on melasma. Maedaket et al. then investigated the role of TXA on human melanocytes and cultured keratinocytes. They found that TXA had inhibited the synthesis of melanin by inhibiting tyrosinase activity in epidermal melanocytes. In addition, it blocked interactions between melanocytes and keratinocytes through inhibiting plasmin/plasminogen system (9, 11).

In most studies on oral TXA at a dose of 250 mg per 12 hours, few complications were reported. Not even the women who had received high doses in treatment via menor-

Figure 2. MASI score reduction in 2 groups receiving 3-month treatment

them suffered from hypomenorrhea, 2 (6.9%) of these patients had gastrointestinal problems and hypomenorrhea, and 11 (37.9%) of them had no side effects. Additionally, in the HQ group, 7 (23.3%) patients had irritant contact dermatitis, 1 (3.3%) of them suffered from xerosis only, 1 (3.3%) patient had irritant contact dermatitis and xerosis, and 21 (70%) of

Table 3. Published articles about the role of oral TXA in the treatment of melasma

Clinical study	N	2 group	MASI changes
Cho HH 2012 (15)	51	A: Oral TXA 250 mg/q12h + laser NYD_YAG B: laser Nd:Yag	A: 43.8% in 2 week treatment B: 23.6%
Tanmay Padhi 2015 (24)	40	A: oral tranexamic acid + fluocinolone-based triple combination cream B: fluocinolone-based triple combination cream alone	A: 87.99% in 8 week treatment B: 54.66%
Lajevardi 2016 (14)		A: TXA + HQ 4% B: HQ 4%	A: 51% in 12 week treatment B: 33%
Karn 2012 (16)	260	A: Oral TXA 250 mg/BD B: Topical treatment	A: 30% in 12 week treatment B: 21%
Sufan Wu 2012 (19)	74	A: Oral TXA 500 mg daily	A: 59% in 6 month treatment
Chyen Lee 2016 (20)	553	A: Oral TXA 250 mg/BD	A: PGA assessment 89.7% improved. 10% no improvement. 0.4% worsened.
Aaron Wei 2016 (21)	25	A: Oral TXA 250 mg/BD	A: 69% in 12 week treatment
Sharma 2017 (18)	80	A: Oral TXA 250mg/BD B: Intradermal TXA 4 mg/Q4 w	A: 77.96% in 12 week treatment B: 79%
Del Rosario 2017 (23)	44	A: Oral TXA 250 mg/BD B: Placebo Capsules	A: 49% in 12 week treatment B: 18%

rhagia showed significant complications and there was no obvious increase in the risk of thromboembolism among them (12).

When TXA is used as a hemostatic drug, it is administered at a dose of 1000 mg every 8 hours. However, the prescribed dose for melasma treatment was at 250 mg every 12 hours in most of studies as well as in the present study (13).

In this study, the effect of TXA on melasma is characterized by decreasing MASI in the months after treatment. In the TXA group, MASI reduction between 0 and 12th weeks after treatment was also statistically significant ($p=0.001$).

In the HQ group, MASI reduction between 0 and 12th weeks after treatment was also statistically significant ($p=0.001$). In two groups before and after the start of the treatment, a decrease was also observed; nevertheless, no significant difference was reported between the rates of reduction in the HQ or TXA groups ($p=0.98$).

In other words, in both groups, MASI reduction was the same and no significant difference was observed. In this study; skin photo types, different types of melasma, familial history of melasma, and duration of

melasma before treatment had no effects on the response rate to treatment in the TXA group (**Table 1**).

In PubMed-based search for the effects of oral TXA on melasma treatment, there were also some studies on the role of oral TXA in the treatment of melasma with a control group (13, 18) or without it (19, 21). These studies are listed in **Table 3**.

Two studies by Cho et al. and Shin et al. in 2012 and 2013 (15, 22), were conducted on the combination of oral TXA treatment with low-fluency Q-switched Nd:YAG/IPL in the study by Cho et al. and low-fluency Q-switched Nd:YAG in the investigation by Shin et al.

Finally, in both studies, following the addition of laser to TXA treatment, MASI reduction was higher than in other groups treated with laser alone. This reduction was approximately 43.8% in the TXA-treated group combined with laser, and 23.6% in patients treated with laser alone. In the present study, the effect of TXA was MASI decline by about 58%.

Moreover, Sufan and Hangyan (2012) examined the therapeutic effect of oral TXA 500 mg daily. In this respect, 74 women were included in the study and treated for 6 months.

In general, melasma recovery was reported by 59.9%. The overall effect of oral treatment with TXA in this study was very similar to that of the present study, which had a 58% effect (19).

Lajevardi et al. (2016) also studied 100 patients with facial melasma in two groups. One group was administered oral TXA treatment combined with topical 4% HQ cream and the other one was administered 4% HQ cream alone. After three months of treatment in oral TXA combined with 4% HQ cream group, MASI reduction was 51% and that was only about 33% in the HQ cream alone. In the present study, the effect of TXA alone on MASI decrease was about 58% during 3 months and that was about 49% in the HQ cream alone group. In the present study, the effect of HQ cream alone on MASI reduction was reported to be higher (14).

Moreover, Karn et al. (2012) conducted a randomized prospective study on 260 patients with melasma. They divided their patients into two groups: group A received topical routine melasma treatment with TXA 250 mg twice daily for 3 months, and group B received only topical melasma treatment. Their response to treatment was evaluated by MASI and its re-

duction in group A and B after 3 months of treatment was by 30% and 21%; respectively, that being a significant difference (16).

Sharma et al. (2017) conducted a clinical trial on 80 patients with melasma. In one group, oral TXA was administered at a dose of 250 mg every 12 hours for 12 weeks and in the other group, 4 mg intradermal TXA was injected into the patient's melasma for 4 to 12 weeks. At the end of the three-month treatment, reduction in MASI in the oral TXA-treated group was 78% and that was 79% in the intradermal TXA-treated one (18).

Del Rosario et al. (2017) similarly divided women with melasma into two groups with 22 patients in each one. Accordingly, group A was treated with oral TXA 250 mg every 12 hours and group B received placebo. At the end of 3 months, MASI scores also decreased in the TXA group by 49%, compared with 18% decline in MASI scores in the placebo one. From the beginning of treatment with TXA the patients with severe melasma were found to respond to the treatment much better than those with moderate melasma. Three months after stopping treatment, 26% decrease in MASI score was observed in group A. Moreo-

Table 4. Complications reported with TXA administration for the treatment of melasma

Karn 2012 (16)	Oligomenorrhea(14.7%), Belching (9.2%), Abdominal cramps (6.9%) , Palpitation, urticarial rash and angioedema (each in one patient)
Sufanwu 2012	Gastrointestinal irritation such as nausea, diarrhea, abdominal pain (5.4%) Detectable hypomenorrhea (8.1%)
Cho HH 2012 (15)	Transient headache (4 patients)
Tanmay Padhi 2015 (24)	No side effects for TXA consumption
Chyen Lee 2016 (20)	Side effects in (7.1%): Abdominal bloating (12 patients) and headache (6 patients) ... Left lower limb DVT(1 patient)
Lajevardi 2016 (14)	Abdominal pain ,flank pain, edema of hands and feet, nausea, vomiting, headache
Aaron Wei 2016 (21)	No side effects
Del Rosario 2017 (23)	Gastrointestinal discomfort (22.7%),change in menstrual period (18.2%), headache (13.6%), myalgias (9.1%), somnolence (9.1%)
Sharma 2017 (18)	Hypomenorrhea (15.4%), Epigastric discomfort (2 patients)

ver, a 19% decline in MASI score was reported in group B. Finally, this study showed that oral TXA was an effective drug in treating moderate to severe melasma (13).

Padhi et al. (2015) also compared the effect of triple therapy with a cream containing fluocinoloneacetonide 0.01%, tretinoin 0.05%, and hydroquinone 2% in combination with oral TXA twice a day and other groups with a cream containing fluocinoloneacetonide 0.01%, tretinoin 0.05%, and hydroquinone 2%. Their treatment lasted 8 weeks and reduction in MASI in both groups was significant. MASI in the TXA-administered group in combination with topical treatment was also reported to have been reduced by 88%, and it was only about 55% in the topical treatment group. This amount was higher than that in the present study, which could be due to co-administration with topical medication (23).

Chyen Lee et al. (2016) also conducted a retrospective study on 553 patients treated with oral TXA 250 mg twice a day for an average of 4 months. The patients were then characterized as resistant to melasma treatment. Moreover, 89.7% of patients showed improvements after treatment, 10% of them showed no change and 0.4% of them got worse. The method for evaluating their treatment and recovery was Physician Global Assessment (PGA), which was different from that used in the present study (20).

In Singapore, Aaron Wei et al. (2016) also conducted a retrospective meta-analysis on 25 patients with resistant melasma who received 5-month treatment with topical medications and then were administered oral TXA 250mg twice a day. The patients were also examined by MASI. The results of MASI after treatment decreased by 69%, which revealed a little more decrease compared with that in the present study. Also, the average duration of taking TXA in this study was 3.7 months, which could be a reason for further decline in MASI in the present study (21).

According to the results of present study and the review of previous studies on the effect of TXA on melasma treatment, reduction in MASI was between 30% and 88% among patients treated with TXA (alone or in combination with other medications) in all studies.

According to the reports on TXA administration for melasma treatment in all investi-

gations and the present study, few complications were observed (**Table 4**). Therefore, this treatment can be considered as an appropriate and safe treatment for melasma.

The most unsafe side effect occurring in case of using TXA is deep vein thrombosis (DVT) which was not found in the present study. Among other investigations, only one patient had been affected with DVT following treatment with TXA. Next evaluations also found defects in the levels of S protein in the blood and positive familial history of thrombotic problems in patients (20).

In the present study, the efficacy of TXA did not show a significant difference with standard HQ treatment.

Conclusion

HQ can be considered as the first line treatment for melasma and TXA can be prescribed as a potential treatment in case of occurrence of complications during treatment with HQ or if melasma does not respond to HQ. As for the limitations of this study, there were few males patients in the study samples and the patients' follow-up was too short.

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Poređenje efikasnosti i bezbednosti oralne traneksaminske kiseline i topikalne hidrokinon kreme u lečenju melazme – nasumična kontrolisana klinička studija i pregled literature

Sažetak

Uvod. Melazma je poznata kao čest poremećaj pigmentacije kože koji utiče na život pacijenta i u psihološkom i u socijalnom smislu. S obzirom na to, topikalni lekovi ili laser mogu da imaju privremeni i ograničeni efekat na melazmu. **Materijal i metode.** Ova studija je prospektivno kliničko ispitivanje terapijskih efekata oralne upotrebe traneksaminske kiseline (TXA) i topikalne hidrokinon (HQ) kreme. Pregledano je ukupno 60 pacijenata. Tokom studije, 10 pacijenata se nisu pojavili na kontroli a 59 su završili ispitivanje. Pacijenti su nasumično podeljeni u dve grupe. Pacijenti iz grupe A primali su TXA kapsule 250 mg svakih 12 sati a pacijenti iz grupe B su nanosili na lice 4% topikalnu HQ kremu danju i noću. Tretmani za pacijente iz obe grupe trajali su tri meseca. Skor indeksa površine i težine melazme (*Melasma Area and Severity Index (MASI)*)

izračunat je na početku, četiri nedelje i 12 nedelja posle početka intervencije i tri meseca posle završetka intervencije a kasnije su ponovo evaluirani u bilo koje vreme. **Rezultati.** U grupi pacijenata tretiranih traneksaminskom kiselinom MASI na početku je bio 21,66; posle četiri nedelje 13,69; posle 12 nedelja 9,10 i posle 24 nedelje 9,24. Smanjenje MASI vrednosti na početku i posle četiri nedelje bilo je statistički značajno. Isti takav trend smanjivanja MASI vrednosti na početku i posle 12 nedelja primećen je i bio je statistički značajan ($p = 0,001$). U grupi pacijenata tretiranih topikalnom hidrokinon kremom, MASI je na početku bio 21,46, posle četiri nedelje 13,57, posle 12 nedelja 10,93 i posle 24 nedelje 11,20. Smanjenje MASI vrednosti na početku i posle četiri nedelje bilo je statistički značajno. Štaviše, primećeno je i smanjenje u MASI vrednostima na

početku i posle 12 nedelja, koje je takođe bilo statistički značajano ($p = 0,001$). Razmatrajući obe grupe, MASI vrednosti su bile smanjene ali razlika između dve grupe nije bila statistički značajna ($p = 0,98$). **Zaključak.** Efi-

kasnost traneksaminske kiseline i topikalne hidrokinon kreme bila je ista i oba leka mogu značajno smanjiti MASI skor.

Ključne reči: Melazma; Traneksaminska kiselina; Dermatološki preparati; Hidrokinoni; Topikalna primena; Ishod terapije

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