Galore International Journal of Health Sciences and Research
Vol.4; Issue: 1; Jan.-March 2019
Website: www.gijhsr.com
Original Research Article *P-ISSN: 2456-9321*

Study on Effectiveness and Safety of Combination of Daily 10% Tranexamic Acid Gel Application and Weekly Iontophoresis Versus Daily 10% Tranexamic Acid Gel Alone in Treatment of Melasma

Dr. Riddhi Arora[1], Dr. Ramesh Sharma[2]

[1]Senior Resident, Dept. of Dermatology, Chandulal Chandrakar Medical College & Hospital, Kachandur, Durg, Chhattisgarh
[2]Professor (Skin and DVD), Dept. of Dermatology, Lata Mangeshkar Hospital, NKPSIMS, Nagpur

Corresponding Author: Dr. Ramesh Sharma

ABSTRACT

Objectives of the study: To compare the effectiveness of the combination of daily 10% tranexamic acid gel application and weekly iontophoresis versus daily 10% tranexamic acid gel alone (randomized split-face study) in the treatment of melasma and to compare the safety of the combination of daily 10% tranexamic acid gel application and weekly iontophoresis versus daily 10% tranexamic acid gel alone (randomized split-face study) in the treatment of melasma.

Materials and Methods: A prospective, randomized and evaluator blind split face study was conducted at tertiary care center. The study population was included patients presenting with melasma to Dermatology out-patient (OPD) of tertiary care center. Inclusion criteria: Patients willing to participate in the study, age more than 18 years and newly diagnosed untreated cases of Melasma were included in the study. After getting approval from the ethical committee, written informed consent was obtained from all participants before enrolment, procedures were explained and patients were acknowledged about all potential risks, benefits and side effects.

Masi Score: A subjective measurement based on the area and severity of the hyperpigmentation determined by Kimbrough-Green et al. was used for clinical assessment.

Results: All the participants were followed at weekly intervals till 12 weeks. The primary parameters considered to assess the efficacy of the treatment were area of the melasma and the darkness of melasma; both were graded on a scale of 1 to 4. As per the study findings, the iontophoresis combination treatment has resulted in reduction in the area of the melasma early at about 5 weeks, as compared to topical tranexamic acid alone, which has resulted in area of the melasma only after 7thweek of treatment. However, there was only marginal reduction in the area.

Conclusion: The most common type of melasma was type 1 melasma as seen in 80.00% of patients. The combined therapy resulted in faster reduction in the size of the melasma, but the reduction in size is comparable between both treatment groups as the time progresses. Both therapies achieved statistically significant reduction in area and darkness. However, this response was slight. Results obtained with modalities were comparable and no therapy was superior than other in this split face randomized trial. Both topical TXA and topical TXA plus iontophoresis therapy was well tolerated and were found to be safe.

Key words: tranexamic acid, melasma, iontophoresis, hyperpigmentation, combination treatment

INTRODUCTION

Melasma (also known as chloasma or mask of pregnancy) is an acquired, chronic, symmetrical Hyper-Melanesia, characterized by brown patches of variable darkness on sun exposed area of the body. This typical disease mostly affects women of reproductive age from all racial group but has a predilection for darker skin types. [1] Melasma is more common in women than in men. Men have been reported to represent 10% of cases and demonstrate the same clinical and histological characteristics as women. [2]

Factors involved in the pathogenesis of the condition include geriatric influence, exposure to UV radiation, pregnancy and hormonal therapy, other factors implicated are phototoxic drugs, anticonvulsant medications and use of certain cosmetics, it presents as single lesion to multiple patches located usually symmetrically on the face and occasionally the V-neck area. It has been classified into different types clinically, histologically, on basis of woods lamp and according to natural history of lesion. Melasma is clinically recognizable in three arears of the face. Centro facial (63%, forehead, nose, chin and upper lips), malar (21% nose and cheeks) and mandibular (16% ramus mandibular) forms. [2] Light microscopic findings of melasma include increased deposits of melanin in the epidermis and dermis, or both when compared with adjacent normal skin, and dermis, or both when compared with adjacent normal skin, and a mild perivascular lymphohistiocytic infiltrate. [3] The precise etiology of melasma is not known. Multiple factors are implicated including exposure to UV radiation and visible light, genetic influences, pregnancy, oral contraceptive, estrogen and progesterone therapy, diethylstilbestrol, certain cosmetics and endocrine factors associate with mild ovarian dysfunction in women and reticular resistance in men. [2] The thyroid dysfunction and medications including anticonvulsants and photosensitizing agents have also been implicated. [4]

The pathogenesis of melasma is still unknown. The common denominator of melasma irrespective of the pathophysiology is an increase in the number and activity of melanocytes. This results in the transfer of large number of melanosomes to the epidermis and dermis. The objectives of melasma therapy are protection from sunlight and depigmentation. First-line treatment usually consists of topical compounds that interfere with the melanin synthesis, broad-spectrum photo protection, and camouflage. Chemical peels are often added to second-line therapy. Laser and light therapies represent potentially promising options for patients who are refractory to other modalities but also carry a significant risk of worsening the disease. [5]

In recent times, some researchers found that tranexamic acid (TA), a traditional haemostatic drug, has hypo pigmentary effect on melasma lesions and prevents UV-induced pigmentation. [6-9] The intracellular release of arachidonic acid (AA), a precursor of prostanoid, and the level of alpha- melanocyte-stimulating hormone increase as the result of plasmin activity. These two substances can activate melanin synthesis. Therefore, the anti-plasmin activity of TA is thought as the main mechanism of hypo pigmented effect of this agent. [10-12] The result of a clinical trial of localized microinjection of TA proved to be promising. A significant decrease in the Melasma Area and Severity Index (MASI) score with no significant side effects was seen after 8 weeks of microinjection of TA. [6] In another study, Kondou et al. found that the TA emulsion had improved the pigmentation in 80% of subjects with melasma and 75% of subjects with freckles. [13] Moreover, in a very recent study, a significant decrease in epidermal pigmentation and reversion of melasma-related dermal changes were seen after using both oral and topical TA of 8 weeks. [9] However, skin penetration of TXA is of concern. Iontophoresis has been used in the past to facilitate transdermal delivery of active therapeutic agent. The current study is aimed to study the effectiveness and safety of the combination of daily 10% tranexamic acid gel application and weekly iontophoresis versus daily 10% tranexamic acid gel alone (randomized split-face study) in the treatment of melasma.

Objectives of the Study

The objectives of the study include,

- To compare the effectiveness of the combination of daily 10% tranexamic acid gel application and weekly

iontophoresis versus daily 10% tranexamic acid gel alone (randomized split-face study) in the treatment of melasma.

- To compare the safety of the combination of daily 10% tranexamic acid gel application and weekly iontophoresis versus daily 10% tranexamic acid gel alone (randomized split-face study) in the treatment of melasma.

MATERIALS AND METHODS

Source of Data: A prospective, randomized and evaluator blind split face study was conducted at tertiary care center.

Study Population: The study population was included patients presenting with melasma to Dermatology out-patient (OPD) of tertiary care center. Inclusion criteria: Patients willing to participate in the study, age more than 18 years and newly diagnosed untreated cases of Melasma were included in the study. Exclusion criteria: Pregnant and nursing females or patients taking oral contraceptive pills, Patients using other topical therapies or other topical steroids over face since longer duration and Patients with active infection over local site Study period: The data collection for the study was done between December 2015 to May 2017. Study Procedure: After getting approval from the ethical committee, written informed consent was obtained from all participants before enrolment, procedures were explained and patients were acknowledged about all potential risks, benefits and side effects. **MASI SCORE:** A subjective measurement based on the area and severity of the hyperpigmentation determined by Kimbrough-Green et al. was used for clinical assessment. According to the MASI, the whole face is divided into four areas: 30% forehead, 30% RM,30% LM,10% chin(C). The grade of melasma index severity was determined by three variables: A= the percentage of total area involved on a scale of 0(no involvement) to 6 (90-100% involvement), D=darkness on a scale of 0(absent) to 4(maximum), and H=homogeneity of hyperpigmentation on a scale of 0(minimum) to 4(maximum). The MASI is then calculated by the following equation:

0.3(DF+HF)AF+0.3(DMR+HMR)AMR+0.3(DML+HML)AML+ 0.1(DC+HC)AC . The evaluation was done on the basis of Area of involvement (A) and darkness of the face (D) criteria of MASI Score only. A total of 33 patients were enrolled. Patients were advised to apply 10% tranexamic acid at bed time every day over both sides of the face and wash the face prior and after timed application of the drug. Weekly iontophoresis to one side of the face was done for 12 weeks, after applying tranexamic acid gel to one side and iontophoretic session was done for 30 minute at every visit. Randomization was done by tossing the coin if head side appears, the right side of the face was chosen. The patients were advised to avoid excessive sun exposure, apply abroad-spectrum sunscreen with 30 SPF or higher in the morning and reapply every 2 hourly. Evaluation: Clinical evaluation of area and darkness was done every week till 12 weeks while photographic evaluation of MASI score was done during baseline, 6^{th} and 12^{th} week respectively. Subjective measurement was done only on two parameters of MASI: A(area) and D(darkness) i.e. A= the percentage of total area involved 0=no involvement 1= less than 10% involvement 2=10-29% 3=30-49% 4=50-69% 5=70-89% 6=90-100% D= darkness of melasma as compared to normal skin on a scale of 0-4 0=normal skin color without evidence of hyperpigmentation, 1=barely visible hyperpigmentation, 2=mild hyperpigmentation, 3=moderate hyperpigmentation 4=severe hyperpigmentation Methods of Collection of Data: The data was collected using a structured proforma designed for the study. Ethical considerations: Clearance was obtained from the ethical committee of MUHS, written and informed consent was sought from the patients and their

attendants. They were given the option of quitting from the study if so desired by them. No element of compulsion was exerted. All data was kept confidential. Statistical Methods: Area of the lesion and darkness were considered as primary outcome variables. The treatment group was considered as primary explanatory variables. Area of the lesion and darkness were compared between the two intervention groups at different follow up visits using median interquartile range. Mann Whitney U test was used to assess statistical significance. Procedure of preparation of tranexamic acid gel 10%:As there is no commercial preparation of 10% tranexamic acid, this was prepared in-house specifically for the current study. Weighed quantity of carbopol 93 was taken and soaked in water overnight. The required amount of tranexamic 10% in water was taken and incorporated with prepared carbopol gel and with continuous overhead stirrer the gel gets neutralized by adding triethanolamine and transferred to the container.

RESULTS

A total of 30 subjects were included in final analysis as there was drop out of 3 patients in the initial period of the study.

Table 1: Descriptive Analysis for Age in Study Subjects (n = 30)

Parameter	Mean ± SD	Median	Min	Max
Age	30.3 ± 6.303	30	20	41

The mean age was 30.3 ± 6.3SD years, the youngest person was aged 20 years and eldest was aged 41 years in the study population.

Table 2: Descriptive Analysis for Duration (in months) in Study Subjects (n = 30)

Parameter	Mean ± SD	Median	Min	Max
Duration	28.3 ± 33.29	12	1	120

The mean duration of melasma was 28.3 ± 33.29 months, which was ranging from 1 to 120 months.

Table 3: Descriptive Analysis of Duration in months in Study Subjects (n = 30)

Duration in Months	Frequency	Percentages
1-12	17	56.67%
13-60	8	26.67%
61-120	5	16.67%

Among the study population, the duration was 1 to 12 months in 17 (56.67%) subjects, 13 to 60 months in 8 (26.67%) subjects, 61 to 120 months was in 5 (16.67%).

Table 4: Descriptive Analysis of Type of Melasma Study Subjects (n = 30)

Type of Melasma	Frequency	Percentages
Type 1	24	80%
Type 2	3	10%
Type 3	3	10%

Among the study population, type 1 melasma (epidermal) was 24 (80.00%), type 2 melasma (dermal) was 3 (10.00%) and type 3 melasma (mixed)was 3 (10.00%).

Table 5: Descriptive Analysis of Type of Melasma Study Subjects (n = 30)

Type of Melasma	Frequency	Percentages
Type 1	24	80%
Type 2	3	10%
Type 3	3	10%

Among the study population, type 1 melasma (epidermal) was 24 (80.00%), type 2 melasma (dermal) was 3 (10.00%) and type 3 melasma (mixed) was 3 (10.00%).

Table 6: Descriptive Analysis in Relation to Pregnancy Study Subjects (n = 30)

In Relation to Pregnancy	Frequency	Percentages
Before	4	13.33%
During	5	16.67%
After	21	70%

Among the study population, 4 (13.33%) were before relation to pregnancy, 5 (16.67%) were in relation to pregnancy, and 21 (70.00%) were in relation to pregnancy.

Table 7: Descriptive Analysis of Cosmetic Use in Study Subjects (n = 30)

Cosmetic Use	Frequency	Percentages
Present	7	23.33%
Absent	23	76.67%

Among the study population, 7 (23.33%) were used cosmetic and 23(76.67%) were not using cosmetic.

Table 8: Comparison area at Different Visits in Iontophoresis Plus Topical & Topical Alone			
Area	Iontophoresis + Topical Median (IQR)	Topical Alone Median (IQR)	Mann-Whitney U Test Comparing the Distribution of Area between Two Groups
Visit 1	4 (4,4)	4 (4,4)	0.317
Visit 2	4 (4,4)	4 (4,4)	1.0
Visit 3	4 (4,4)	4 (4,4)	0.317
Visit 4	4 (4,4)	4 (4,4)	0.078
Visit 5	3 (4,4)	4 (4,4)	0.155
Visit 6	3 (3,4)	4 (3,4)	0.033
Visit 7	3 (3,3)	3.5 (3,4)	0.020
Visit 8	3 (3,3)	3 (3,4)	<0.001
Visit 9	3 (3,3)	3 (3,4)	0.001
Visit 10	3 (3,3)	3 (3,3)	0.054
Visit 11	3 (3,3)	3 (3,3)	0.265
Visit 12	3 (3,3)	3 (3,3)	0.055

The median area of melasma was similar in both the study groups in the initial 4 visits, with no statistically significant difference (P Value >0.05). The median area of the melasma stated declining from the fifth visit in iontophoresis plus topical group, but remained same in topical alone group. The decline in the median area of the melasma started late at 7th visit in topical alone group. But the median area was comparable between both the groups from 8th to 12th visit. The differences in the distribution of the area of the melasma were statistically significant between the two groups from 6th to 9th visit. Hence from the above table it can be concluded that the combined therapy results faster reduction in the size of the melasma, but the reduction in size is comparable between both treatment groups as the time progresses.

Table 9: Comparison of Darkness at Different Visits in Iontophoresis Plus Topical & Topical Alone			
Area	Iontophoresis + Topical Median (IQR)	Topical Alone Median (IQR)	Mann-Whitney U Test Comparing the Darkness between Two Groups
Visit 1	4 (4,4)	4 (4,4)	1.0
Visit 2	4 (3.50,4)	4 (4,4)	0.169
Visit 3	3 (3.3, 5)	4 (3,4)	0.317
Visit 4	3 (3,3)	3 (3,4)	0.078
Visit 5	3 (3,3)	3 (3,3)	0.155
Visit 6	3 (3,3)	3 (3,3)	0.033
Visit 7	3 (3,3)	3 (3,3)	0.020
Visit 8	3 (3,3)	3 (3,3)	<0.001
Visit 9	3 (2,3)	3 (2.75,3)	0.001
Visit 10	2 (2,3)	3 (2,3)	0.010
Visit 11	2 (2,2)	2.5 (2,3)	0.002
Visit 12	2 (2,2)	2.5 (2,3)	0.002

Table 10: No. of patients (Percentage) having reduction in the area per visit between two groups			
Visits	Group 1 (Only topical TXA) n = 30	Group 2 (Weekly Iontophoresis + topical TXA) n = 30	p value
Week 1	0 (0%)	0 (0%)	*
Week 2	0 (0%)	0 (0%)	*
Week 3	0 (0%)	1 (3.33%)	*
Week 4	0 (0%)	3 (10%)	*
Week 5	7 (23.33%)	10 (33.33%)	0.39
Week 6	11 (36.67%)	18 (60%)	0.07
Week 7	16 (53.33%)	26 (86.67%)	0.005
Week 8	30 (100%)	28 (93.33%)	0.15
Week 9	30 (100%)	30 (100%)	*
Week 10	30 (100%)	30 (100%)	*
Week 11	30 (100%)	30 (100%)	*
Week 12	30 (100%)	30 (100%)	*

*No statistical test was applied considering "0" subjects in one of the cells

The median and IQR (inter quartile range) of darkness of melasma were comparable between both the groups in the first two visits 4(4,4). But the darkness had shown reduction at the third visit in iontophoresis plus topical group, whereas the decline started in the 4th week in topical alone group. But the darkness was comparable

between the two groups from 5th to 9th visits. From visit 10 to 12 median area of melasma was 2 (2, 3) in combined therapy group, and was slightly higher in topical alone group (3(2,3) at visit 10 and 2.50(2,3) at visit 11 and 12) the difference in the darkness between the two groups was statistically significant from visit 10 to 12 (P Value <0.05).

Table 10: there is no reduction in the area in first two weekly visits in both the groups. During visit 3(3rd week), there is 3.33% reduction in the area in group2 but no improvement or reduction in group1. Visit 4 shows 10% reduction in area in group2 participants. From 5thvisit onwards there is no significant reduction in the area in both the groups until week 6. From week 7 there is significant reduction in the area in both the groups (p<0.05). From visits 8th until the last visit (week12) almost all the participants show significant reduction in the area of melasma.

Table 11: No. (Percentage) patients having reduction in the Darkness per visit between two groups

Visits	Group 1 (Only topical TXA) n = 30	Group 2 (Weekly Iontophoresis) n = 30	p value
Week 1	0 (0%)	0 (0%)	*
Week 2	3 (10%)	5 (16.67%)	0.45
Week 3	9 (30%)	22 (73.33%)	<0.001
Week 4	16 (53.33%)	29 (96.67%)	<0.001
Week 5	24 (80%)	29 (96.67%)	0.04
Week 6	30 (100%)	30 (100%)	*
Week 7	30 (100%)	30 (100%)	*
Week 8	30 (100%)	30 (100%)	*
Week 9	30 (100%)	30 (100%)	*
Week 10	30 (100%)	30 (100%)	*
Week 11	30 (100%)	30 (100%)	*
Week 12	30 (100%)	30 (100%)	*

*No statistical test was applied considering "0" subjects in one of the cells

DISCUSSION

The present study has compared the efficacy and safety of the combination of daily 10% tranexamic acid gel application and weekly iontophoresis versus daily 10% tranexamic acid gel alone (randomized split-face study) in the treatment of melasma. Randomized split face design was used by the study. All the participants were followed at weekly intervals till 12 weeks. The primary parameters considered to assess the efficacy of the treatment were area of the melasma and the darkness of melasma; both were graded on a scale of 1 to 4. As per the study findings, the iontophoresis combination treatment has resulted in reduction in the area of the melasma early at about 5 weeks, as compared to topical tranexamic acid alone, which has resulted in area of the melasma only after 7thweek of treatment. However, there was only marginal reduction in the area. The other important outcome parameter assessed in the study was darkness of melasma. Even though the median grade of darkness was comparable between two groups in the initial follow-up visits, the iontophoresis combination therapy had resulted in better reduction darkness of melasma as compared to topical tranexamic acid alone. Again, reduction was marginal. There were no side effects noted in both the groups and therapy was found to be safe. Although there are randomized split face or non-split face studies in the literature comparing various treatment modalities in melasma, till date there is no single study comparing daily 10% TXA alone versus daily 10% TXA and weekly iontophoresis for treatment of melasma. However, other few interventional studies comparing TXA creams or other demelanizing creams are available. But these interventions were studied individually or were compared with other interventions. In our study, we found that most patients were having epidermal or superficial melasma. This could have been the reason for good response to topical TXA in both the groups. [14]

Study by Kanechorn Na et al [15] has studied the effect of daily two times application of topical 5% tranexamic acid along with its vehicle on the other side along with prescribed sunscreen daily morning. Melanin index fall was reported in 18 (78.2%) of patients on one or both sides of face at the end of 12 weeks than baseline. On both tested sides, significantly, reduced MASI scores were reported and the difference was not statistically significant. Study findings however concluded that although there were no significant results between two regimens, lightening of pigmentation was induced by topical TA. ($p > 0.05$). However, in our study, there was reduction in area and darkness when topical TXA 10% was applied and there was reduction in area and darkness in TXA + iontophoresis group and the difference was statistically significant. This was probably because 10% TXA was used in our study as against 5% TXA used by Kanechorn NA et al. In the similar study, erythema was significant on the TA-applied site ($p < 0.05$). However, our patients showed no erythema in both the groups. This was surprising as we used higher concentration of TXA. This is possibly because study by Kanechron NA et al was done in Thai population who have type 3 or type 4 Fitzpatrick skin type which is more susceptible for erythema as against Indian people who has Type 4 or 5 skin.

Our study showed early improvement when TXA + iontophoresis group (5 weeks) as compared to topical TXA group that showed delayed improvement i.e. 7 weeks. This confirms utility of iontophoresis for inducing early response as compared to topical TXA alone. However, response was slight reduction in area and darkness in both the groups and no significant reduction could be achieved. We conclude that, there wide variations in the nature of interventions tested for their efficacy in treatment of melasma. Even though iontophoresis has been proved effective by individual studies, not enough number of well controlled trials is available in literature documenting the superiority with various existing interventions.

REFERENCES

1. Pawaskar MD, Parikh P, Markowski T, McMichael AJ, Feldman SR, Balkrishnan R. Melasma and its impact on health-related quality of life in Hispanic women. J Dermatolog Treat. 2007;18(1):5-2.
2. Cestari TF, Hexsel D, Viegas ML, Azulay L, Hassun K, Almeida AR, et al. Validation of a melasma quality of life questionnaire for Brazilian Portuguese language: the MelasQoL-BP study and improvement of QoL of melasma patients after triple combination therapy. Br J Dermatol. 2006; 156 Suppl 1:13-20.
3. Rendon MI. Utilizing combination therapy to optimize melasma outcomes. J Drugs Dermatol. 2004;3(5 Suppl):S27-34.
4. Lutfi RJ, Fridmanis M, Misiunas AL, Pafume O, Gonzalez EA, Villemur JA, et al. Association of melasma with thyroid autoimmunity and other hyroidal abnormalities and their relationship to the origin of the melasma. J Clin Endocrinol Metab. 1985;61(1):28-31.
5. Shankar K, Godse K, Aurangabadkar S, Lahiri K, Mysore V, Ganjoo A, et al. Evidence-based treatment for melasma: expert opinion and a review. DermatolTher (Heidelb). 2014;4(2):165-86.
6. Lee JH, Park JG, Lim SH, Kim JY, Ahn KY, Kim MY, et al. Localized intradermal microinjection of tranexamic acid for treatment of melasma in Asian patients: a preliminary clinical trial. Dermatol Surg. 2006;32(5):626-31.
7. Maeda K, Naganuma M. Topical trans-4-aminomethylcyclohexanecarboxylic acid prevents ultraviolet radiation- induced pigmentation. J PhotochemPhotobiol B. 1998;47(2-3):136- 41.
8. Cho HH, Choi M, Cho S, Lee JH. Role of oral tranexamic acid in melasma patients treated with IPL and low fluence QS Nd:YAG laser. J Dermatolog Treat. 2013;24(4):292-6.
9. Na JI, Choi SY, Yang SH, Choi HR, Kang HY, Park KC. Effect of tranexamic acid on melasma: a clinical trial with histological evaluation. J EurAcadDermatolVenereol. 2013;27(8):1035-9.

10. Wang N, Zhang L, Miles L, Hoover-Plow J. Plasminogen regulates pro-opiomelanocortin processing. J Thromb Haemost. 2004;2(5):785- 96.
11. Chang WC, Shi GY, Chow YH, Chang LC, Hau JS, Lin MT, et al. Human plasmin induces a receptor-mediated arachidonate release coupled with G proteins in endothelial cells. Am J Physiol. 1993;264(2 Pt 1):C271-81.
12. Ando H, Matsui MS, Ichihashi M. Quasi-drugs developed in Japan for the prevention or treatment of hyperpigmentary disorders. Int J Mol Sci. 2010;11(6):2566-75.
13. Kondou S. Clinical study of effect of tranexamic acid emulsion on melasma and freckles. Skin Research. 2007;6:309-15.
14. Bolanca I, Bolanca Z, Kuna K, Vukovic A, Tuckar N, Herman R, et al. Chloasma- the mask of pregnancy. CollAntropol. 2008;32 Suppl 2:139-41.
15. Kanechorn Na Ayuthaya P, Niumphradit N, Manosroi A, Nakakes A. Topical 5% tranexamic acid for the treatment of melasma in Asians: a double-blind randomized controlled clinical trial. J Cosmet Laser Ther. 2012;14(3):150-4.

How to cite this article: Arora R, Sharma R. Study on effectiveness and safety of combination of daily 10% tranexamic acid gel application and weekly iontophoresis versus daily 10% tranexamic acid gel alone in treatment of melasma. Galore International Journal of Health Sciences & Research. 2019; 4(1): 99-106.

******