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Original Research Article.

Efficacy of Oral Tranexamic Acid Over Melasma

Md. Rashidul Hasan[1], Mohd. Nurul Alam[2], Richmond Ronald Gomes[3], Anzirun Nahar Asma[4], Mohammad Farhad[5]

[1]Associate Professor and Head, Department of Dermatology and Venereology, Us-Bangla Medical College and Hospital, Narayanganj, Bangladesh.
[2]Associate Professor, Dermatology & Venereology Dept., Ibn Sina Medical College & Hospital, Dhaka, Bangladesh.
[3]Associate Professor of Medicine, Ad din Women's Medical College and Hospital, Maghbazar, Dhaka, Bangladesh.
[4]Associated Professor, Department of Dermatology and Venereology, Popular Medical College, Dhaka, Bangladesh.
[5]Lecuturer, Cox's Bazar Medical College, Cox's Bazar, Bangladesh.

ABSTRACT

Background: Now a day's melasma is a common pigmentary syndrome among Asians and treatment is challenging. Oral tranexamic acid (TA) has materialized as a potential treatment for refractory melasma.

Objective: In this study our main objective is to evaluate efficacy of oral tranexamic acid over melasma.

Method: This opened clinical trial study was carried out at Tertiary medical hospital Dhaka from June 2016 to July 2018 where informed consent was sought from the total 120 patients to take part in the study. At the baseline visit, history of melasma regarding length of time present, relationship to pregnancy, oral contraceptive, drug history were noted.

Result: During the experiment, maximum patients belong to 21-25 years age group and percentage of female were 82% higher than male. Also, after 6 months follow up of 250mg dose of tranexamic acid (TA) treatment result, where patients rating for excellent, good, fair, and poor outcome accounted 21% patients, 66%, 13%, and 11 % patient, respectively.

Conclusion: From our result and analysis we can say that, oral TA can be a very much effective treatment for refractory melasma. Careful screening for personal and familial risk factors for thromboembolism should be done before introduction.

Keywords: Melasma, Tranexamic Acid (TA), Pigmentary Syndrome.

***Correspondence to:**

Dr. Md. Rashidul Hasan,
Associate Professor and Head,
Department of Dermatology and Venereology,
Us-Bangla Medical College and Hospital,
Narayanganj, Bangladesh.

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INTRODUCTION

Melasma is a collective acquired symmetric hypermelanosis considered by irregular light to grey brown macules involving sun exposed areas.

Melasma more normally occurs in women associated to men and in the dark-skinned people. This disease can be initiate in the average age of 27.5±7.8 years old and rarely establish in puberty. This illness affects more than five million people in America.

Melasma has been related with hormonal imbalance, sun damage and genetic predisposition. It has been deliberated to arise from pregnancy, oral contraceptives, endocrine dysfunction, genetic factors, medications, nutritional deficiency, hepatic dysfunction, and other factors. It is a macular hyperpigmentation and usually involves sun exposed area of the cheeks, upper-lips, chin and forehead.[1-3]

Tranexamic acid (TA) is a synthetic derivative of the amino acid lysine that has been extensively used as a hemostatic. The hemostasis of TA is based on the antifibrinolytic effect, and it does not affect with the blood-clotting parameters. Its usage in the treatment of melasma was first reported in 1979. In recent times, tranexamic acid (TA) is demanded to have whitening effects especially for ultraviolet-induced hyperpigmentation including melasma.[4]

The intracellular release of arachidonic acid (AA), a precursor of prostanoid, and the level of alpha-melanocyte-stimulating hormone rise 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 hypopigmentory effect of this agent. The outcome of a clinical trial of localized microinjection of TA showed to be promising. Momentous decrease in the Melasma Area and Severity Index (MASI) score with no significant side effects was seen after 8 weeks of microinjection of TA.[4]

In this study our main objective is to evaluate the efficacy and safety of TA for melisma treatment.

OBJECTIVE

General Objective

- To assess effectiveness of oral tranexamic acid over melasma.

Specific Objective

- To identify possible causes of melasma.
- To detect the side effect using tranexamic acid treatment.

Fig 1a,1b: Shows a 40-year-old woman with facial melasma, after 6 months of treatment with tranexamic acid (TA).

METHODOLOGY

Type of study: Opened clinical trial study.

Place of study: US Bangla Medical College Hospital, Narayanganj, Different Private Chamber at Dhaka.

Study period: July 2018 to May 2019.

Study population: Patients suffering from melasma

Sampling technique: Purposive

Inclusion Criteria

- Patient of 15 to 50 years of age group
- Both male and female of above age group
- Female not taking oral contraceptive pill
- Patient taking no other medication for melasma treatment.

Exclusion Criteria

- Patient unwilling to give informed consent to take part in the study
- Pregnant woman
- Patient suffering from any endocrine disorder Patient suffering from any liver disease
- Patient taking oral contraceptive pill, phenytoin, mephenytoin
- Known hyper sensitivity to TA.

Method

Informed consent was sought from the total 120 patients to take part in the study. At the baseline visit, history of melasma regarding length of time present, relationship to pregnancy, oral contraceptive, drug history were taken. Patients were asked about previous use of any other medications and any hypersensitivity to those agents. Patient were advised to apply the above mentioned combination therapy over the melasma once daily in the night and the patient were asked to report on 4th, 6th, 12th months for evaluation. The efficacy was evaluated using Melasma Area and Severity Index (MASI) Score. At each visit, side effects were determined in the treatment area.

Statistical analysis

Statistical analyses of the results were obtained by using window based computer software devised with Statistical Packages for Social Sciences (SPSS-13) (SPSS Inc, Chicago, IL, USA). All the relevant collected data were compiled on a master chart first. The results were presented in tables, figures and diagrams. Percentages were calculated to find out proportion of the findings. Statistical analyses were done by using appropriate procedure like chi square test, student t test where applicable. Statistical significance is set at 0.05 level and confidence interval at 95% level.

Table 1: Age distribution of the patients

Age group	%
15-20 year	1.5%
21-25y ears	55%
26-30 years	23%
31-35 years	9.5%
36-40 years	7.5%
>40 years	3.5%

Table 2: Epidemiological characteristics of the patients

Variable	%
Duration(years):	
>1	8%
1-5	51%
>5	41%
Pattern:	
Malar	30%
Centrofacial	13%
Mandibular	5%
Mixed	55%
Type:	
Epidermal	65%
Mixed	20.5%
Dermal	11.5%
Family History:	
Yes	42%
No	58%

Table 3: Side effect using tranexamic acid treatment

Variable	%
Gastrointestinal irritations	8%
Hypomenorrhea	5%
No side effect	84%

RESULTS

In table-1 shows age distribution of the patients where maximum patients belong to 21-25 years age group.

In figure-2 shows gender distribution of the patients where 91% were female, which was 82% higher than male.

In table-2 shows epidemiology characteristics of the patients where the duration of melasma ranged from 3 months to 17 years and 42% patients had a positive family history of melasma.

In figure-3 shows possible causes of melasma formation where 71% patients of pregnancy.

In figure-4 shows 250mg dose of tranexamic acid treatment result with 6 months follow up where patients rating for excellent, good, fair, and poor outcome accounted 21% patients, 66%, 13%, and 11 % patient, respectively.

In figure-5 shows the amount of changes in the mean MASI score of in different medicine group where the patients' self-assessment

of melasma improvement was evaluated at week 12; 3%, 27.3%, 30.3%, and 39.4% of patients graded melasma improvement of the side which was treated with TA as excellent good, fair, and poor, respectively, while it was 6.1%, 33.3%, 39.4%, and 21.2% respectively for hydroquinone.

In figure-6 shows physician assessment of improvement at week 12 based on the patients where it was 27.3%, 42.4%, and 30.3% as excellent, good, fair respectively for TA and 24.2%, 48.5%, 24.2%, and 3.0% as excellent, good, fair respectively for hydroquinone.

In table-3 shows side effect using tranexamic acid treatment where most of the patients did not face any kind of side effect, only 8% patients had gastrointestinal irritations such as nausea, diarrhea, and abdominal pain.

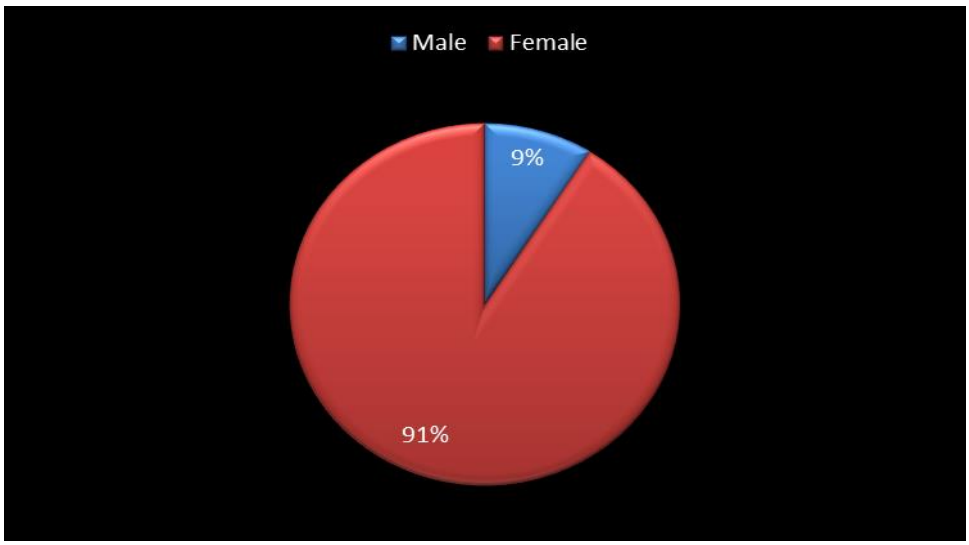

Figure-2: Gender distribution of the patients.

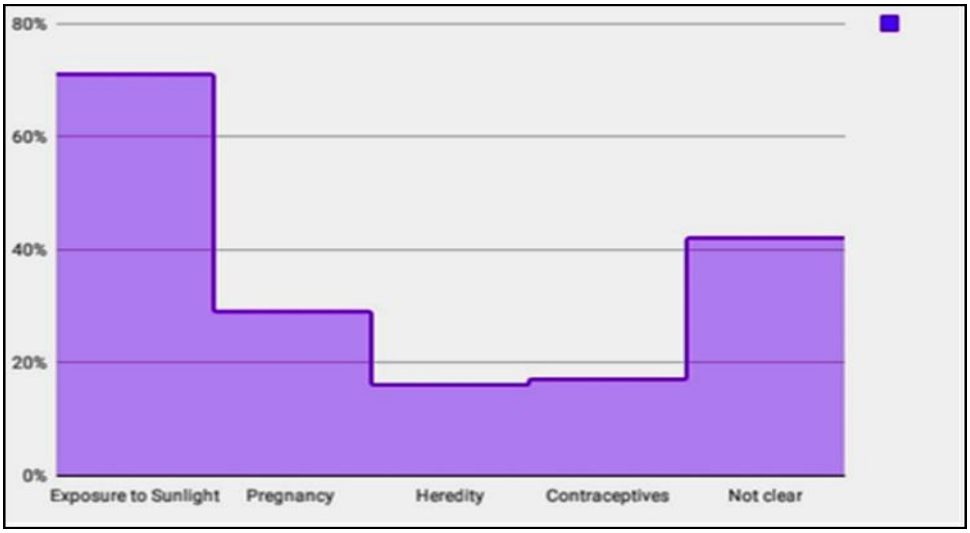

Figure-3: Possible causes of melasma.

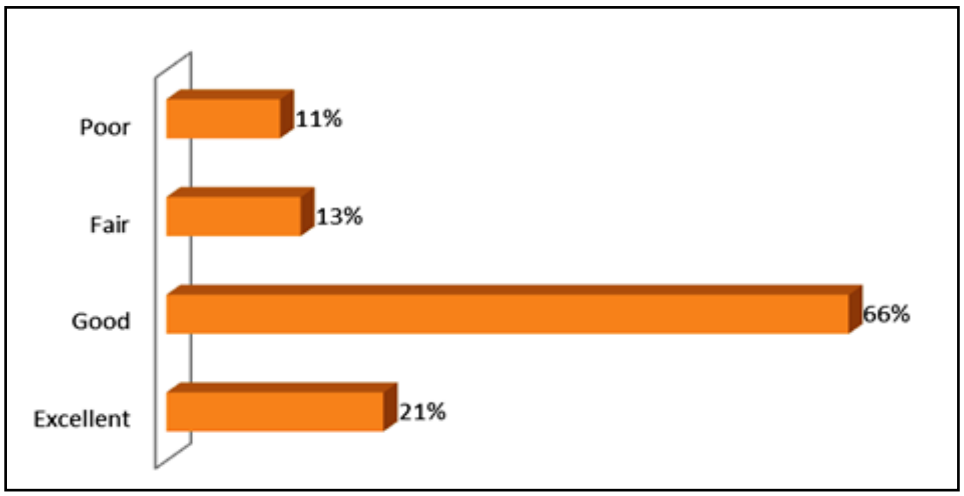

Figure 4: 250mg dose of tranexamic acid treatment result with 6 months follow up.

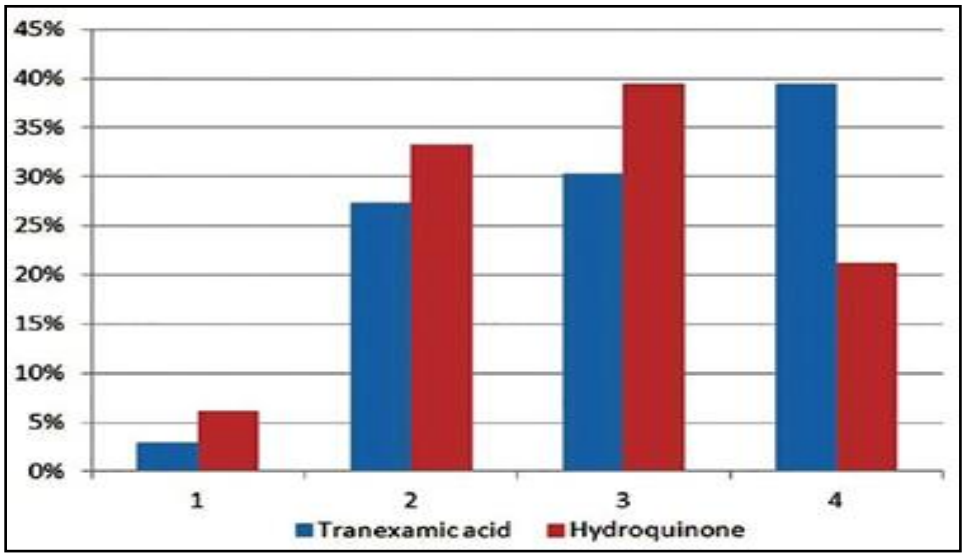

Figure-5: The amount of changes in the mean MASI score of in different medicine group.
***where >75% lightening (excellent), 2 = 51-75% (good), 3 = 26-50% (fair), and 4 = 0-25% lightening (poor).**
Source by: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4235096/. [5]

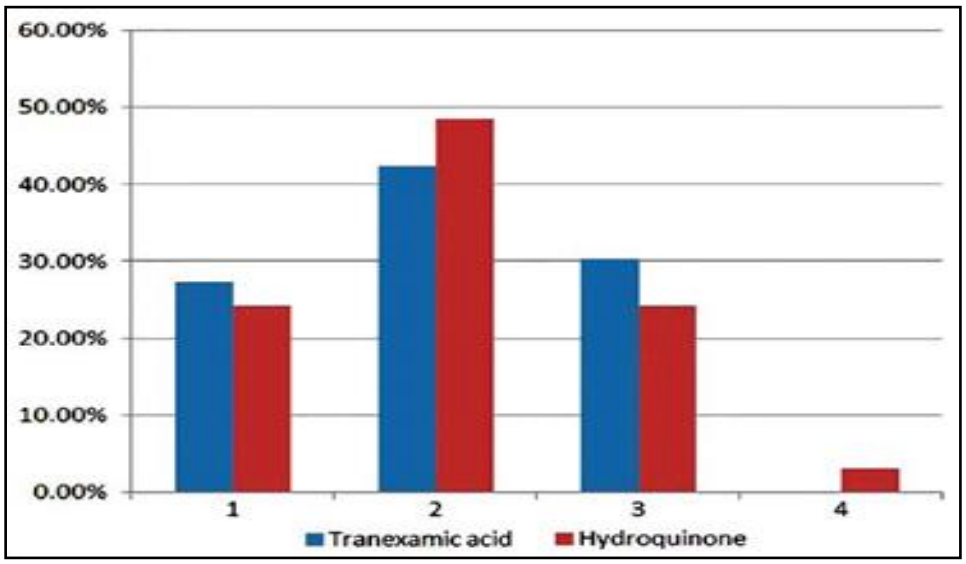

Figure-6: Physician assessment of improvement at week 12 based on the patients.
***where >75% lightening (excellent), 2 = 51-75% (good), 3 = 26-50% (fair), and 4 = 0-25% lightening (poor).**
Source by: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4235096/.[5]

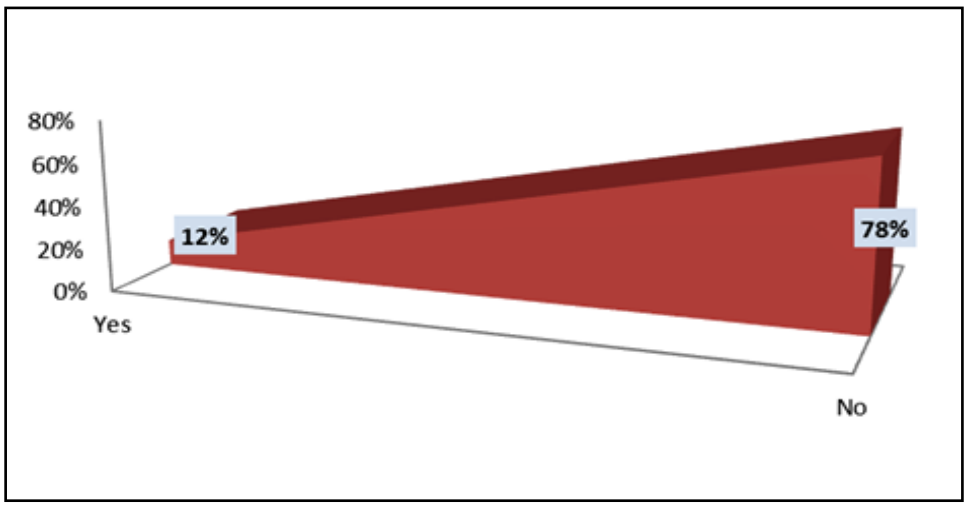

Figure 8: Recurrence of melasma.

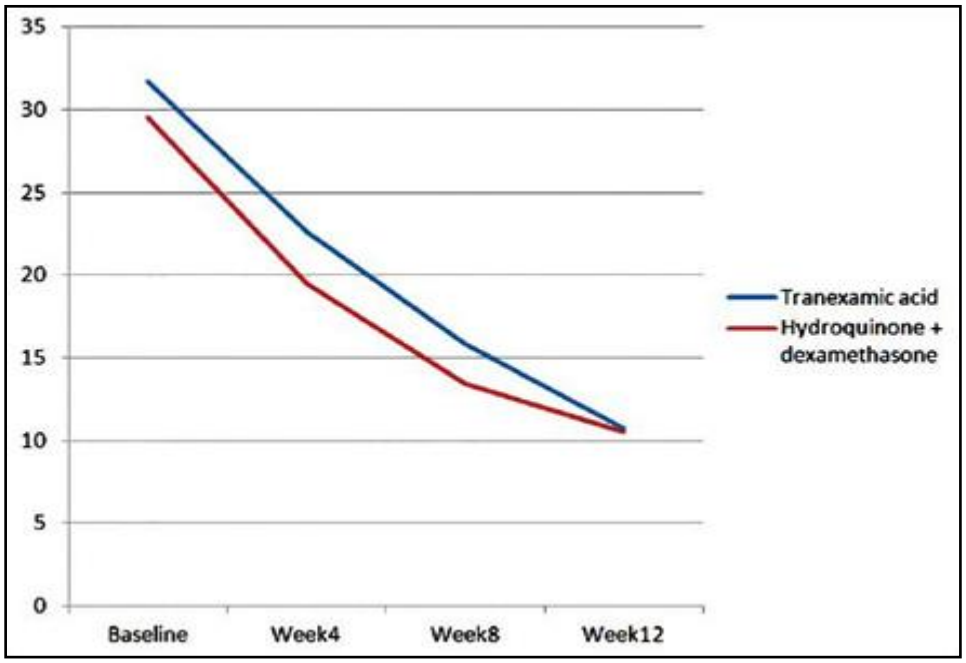

Figure-9: Changes of melasma area and severity index score of two groups.
***Source by: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4235096/. [5]**

In figure-8 shows distribution of the patients according to recurrence of melisma where only 12% patients faced recurrence of melisma.

In figure-9 shows changes of melasma area and severity index score of two groups where the mean MASI score of the baseline in TA group was 31.68 ± 10.32 while after 12 weeks it reached to 10.76 ± 9.43 (*P* = 0.00). Furthermore, in Hydroquinone group it was 29.52 ± 11.72 at baseline and after 12 weeks it reached to 10.48 ± 7.84 (*P* = 0.00).

DISCUSSION

Melasma can be seen frequently worldwide now a days specially in women. Its rate of incidence was not clear till now.

During the study, maximum patients belong to 21-25 years age group and most of them were female, which was 82% higher than male. This is supported by different study. In one study reported that,the largest number (n = 61; 78%) was in the 22-26 years age range and 78.21% were female.

In this study, the average age of patients and duration of the disease is comparable to studies from India.[6] The types of melasma in our patients are also similar to the study from India probably due to same skin type.[7] In this study and most other studies the collective pattern of melisma was malar followed by Centro facial.[6,7]

In the treatment of melasma, TA has been regularly used through oral administration, and it also could be used with intradermal microinjection. Furthermore, intravenous administration was originally tried. Although TA therapy is becoming a distinctive method for the treatment of melasma in Asia, few studies have examined its clinical and basic researches. The report showed that TA, a plasmin inhibitor, stops ultraviolet induced pigmentation in guinea pigs by preventing the binding of plasminogen to the keratinocytes and results in the decrease of melanocyte tyrosinase motion. A report following recommended that TA inhibits melanin synthesis in melanocytes by interfering with the interface of melanocytes and keratinocytes through inhibition of the plasminogen system.[5]

In the study we found that, where most of the patients did not face any kind of side effect, only 8% patients had gastrointestinal irritations such as nausea, diarrhea, and abdominal pain. Which is very much similar to other study.

A clinical trial study was conducted with 25 women for 8 weeks in Seoul, South Korea where volunteers were instructed to take 250 mg tranexamic acid tablets three times a day and apply a tranexamic acid topical agent twice a day for 8 weeks. This study found out that tranexamic acid will decrease epidermal pigmentation that related with melasma and also reversed melasma-related dermal changes, such as vessel number and increased numbers of mast cells.

Another clinical trial study carried out where enrolled 74 volunteers in China. Tranexamic acid tablets were approved at a dosage of 250 mg twice daily for a therapeutic period of 6 months. All the volunteers were observed for more than 6 months after the treatment.

The effects of treatment were assessed by two physicians independently and by the patient based on the improvement of pigmentation and reduction in melasma size.[8,9]

Tranexamic acid with its anti-hemorrhagic property, if being used for long duration can result in side effects such as cerebrovascular accidents, myocardial infarction, pulmonary embolism, and venous thromboembolism.

CONCLUSION

Finally, from our result it was concluded that oral TA seems to be a potentially new medication which can lead to quite rapid results without significant and serious side effects for melasma, particularly for the epidermal type. Further studies are essential to find out the rate of usage, long-term benefits, and combination therapy with other medications and methods of melasma treatment to find the additive effect of it.

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