SUNTEXT REVIEWS

SunText Review of Medical & Clinical Research
ISSN: 2766-4813

Open Access
Research Article
Volume 4:2

Effectiveness of Oral Tranexamic Acid and Oral Pycnogenol in the Treatment of Melasma: A Comparative Study

Khanam R[1,*], Sultana N[2], Siddique MR[3] and Sharmin S[4]

[1]*Assistant Professor, Department of Skin and Venereal Diseases, Medical College for Women & Hospital, Uttara, Dhaka, Bangladesh*
[2]*Assistant Register, Department of Skin and Venereal Diseases, Shaheed Suhrawardy Medical College & Hospital, Dhaka, Bangladesh*
[3]*Junior Consultant, Department of Skin and Venereal Diseases, Saheed Ziaur Rahman Medical College & Hospital, Bogura, Bangladesh.*
[4]*Assistant Professor, Department of Skin and Venereal Diseases, US-Bangla Medical College Hospital, Narayangonj, Dhaka, Bangladesh*

[*]**Corresponding author:** Khanam R, Assistant Professor, Department of Skin and Venereal Diseases, Medical College for Women & Hospital, Uttara, Dhaka, Bangladesh; E-mail: nituhuq@gmail.com

Received date: 28 April 2023; **Accepted date:** 04 May 2023; **Published date:** 07 May 2023

Citation: Khanam R, Sultana N, Siddique MR, Sharmin S (2023). Effectiveness of Oral Tranexamic Acid and Oral Pycnogenol in the Treatment of Melasma: A Comparative Study. SunText Rev Med Clin Res 4(2): 175.

DOI: https://doi.org/10.51737/2766-4813.2023.075

Copyright: © 2023 Khanam R, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Abstract

Background: Melasma is an acquired, chronic recurrent hypermelanosis occuring exclusively in sun exposed area of the body especially in women. Melasma is recalcitrant to treatment and relapses are common. Tranexamic acid, a plasmin inhibitor is effective in the treatment of Melasma. Now-a-days pycnogenol containing monomeric phenolic compounds has been reported to be more effective.

Objective: The aim of the study was to compare the efficacy of oral tranexamic acid and oral pycnogenol in the treatment of Melasma.

Methods: A comparative study was conducted on 100 women and men with facial Melasma were randomly selected and divided into the following two groups. Group A (Tranexamic acid 250mg orally twice daily) or group-B (Pycnogenol 50 mg twice daily). Evaluations were performed before and 3 months after treatment by clinical assessment and also MASI and MELASQoL scoring system. All patients were instructed to use sunscreen.

Result: Among 100 patients 89% are female and 46% belong to 30-40 years age. 81% patients had central facial Melasma and epidermal type is 60%, Dermal 10% and mixed 30%. After treatment with oral tranexamic acid MASI score and MELASQoL score improved (P value <0.04 and <0.365), whereas with oral pycnogenol MASI score and MELASQoL score improved significantly (both p value <0.001).

Conclusion: Pycnogenol is well tolerated and more effective orally (50mg 12 hourly for 3 months) than oral tramexamic acid (250mg 12 hourly for 3 months).

Keywords: *Oral tranexamic acid; Oral pycnogenol; Melasma*

Introduction

Melasma is the most common pigmentary disorder affecting sun exposed areas such as: forehead, checks, nose, upper lip and chin and occasionally the neck and forearms [1]. It is commoner in asian women (90%) but also occurs in male (10%). It is common in 3rd and 4th decade of life [2]. Melasma causes cosmetic morbidity and psychological embarrassment affecting quality of life [3,4]. There is a higher incidence of genetic predisposition (70%) in developing Melasma. Other etiological factors are pregnancy, Oral contraceptives, endocrine dysfunction, hormone replacement therapy, thyroid disorders, drugs, cosmetic contact

sensitivity, light exposure including both sun and artificial light and stress [5,6]. Pigmentation is usually confined to the epidermis but dermis is also affected. Ultra violet ray causes dermal vascular proliferation and dermal proangiogenic factors such as, vascular endothelial growth factor (VEGF), basic fibroblast growth factor (eFGF), Interleukin-8 which are implicated in pathogenesis of Melasma [7,8]. Interaction between VEGF on epidermal keratinocytes and dermal proangiogenic factors lead to release of mediators such as arachidonic acid metabolites and plasminogen from proliferated vessels which enhances melanogenesis in Melasma [9]. Role of mast cells in the pathogenesis of Melasma is now- a- days highlighted. The mast cell tryptase degrades type IV collagen that might be the cause of weak basement membrane observed in Melasma. Solar elastosis is another histological feature of Melasma. The “Fitzpatrick macule”a confetti like macule of regularly pigmented skin observed in about 89% chemical photographs of large hyper pigmented patch of Melasma compared with 1% cases of poikiloderma of civatte and 6% of solar lentigenosis. Clinically Melasma are Centro facial (55-75%), malar (43-24%) and mandibular types (15-2%) and histologically epidermal (Melanin increased in the epidermis), dermal (many melanophages present in the dermis) and mixed type. Melasma area severity index (MASI) is used to measure severity before and after treatment. MASI score is calculated by dividing the face into four areas and each area is weighted such that the forehead (F)30%, right malar area (MR)30%, left malar area (ML) 30% and the chin (10%). The final formula for MASI score= 0.3 (DF+HF). AF +0.3 (DMR + HMR) AMR + 0.3 (DML+HML) AML + 0.1 (DC+HC) AC. Total MASI score is 0-48. The physician’s global assessment (PGA) is the most commonly used scoring system for outcome of treatment where likert scale is used [10]. A likert scale is a questionnaire based psychometric ordinal scale in which patients satisfaction score is measured by the following: Score-1 strongly disagree, score-2 undecided, score-3, Neither agree nor disagree, Score-4 agree, score-5 strongly agree [11]. Hydroquinone bleaching cream is the gold standard treatment of Melasma. Current treatment modalities are topical preparations of phenol derivatives-hydroquinone (HQ) 2-4%, Retinoids: Tretinoin 0.05%-0.1%, Adapalene, lsotretionin 0.05%. Azelaic acid (10-20%) combinations-1)HQ 2%+ Tretinoin 0.05% + Fuocinolone acetonide 0.01%, 2)HQ 2% + Tretinoin 0.05%+ Dexamethasone(0.01%) modified kligman's formula, 3)Modified KF + glycolic acid (30-40%) 4) kojic acid 4% + glycolic acid 5% 5) HQ 4% + glycolic acid (10%) 6) Azelaic acid (20%) + Retinoic acid (0.05%). Chemical peels with (i) Alpha hydroxy acid, glycolic acid (30%-70%) ii) phytic acid, pyruvic acid iii) Trichloroacetic acid, lactic acid, salicylic acid, Jessner's solution iv) dermabrasion. Laser therapy: i) laser therapy alone or in combination with chemical peels and or topical therapy ii) pulsed CO_2 laser followed by Q-switched alexandrite laser [12]. Mild itching, burning sensation, erythema, irritant and allergic contact dermatitis, transient hypopigmentation, nail discoloration, post inflammatory hyper pigmentation, risk of possible bone marrow toxicity, development of renal adenomas or carcinogenic effect may occur with hydro quinine. Non hydroquinone based therapies are Arbutin (α or β) e.g; (deoxyarbutin, aleosin, Azelaic acid, kojic acid,gentisic acid, mequinol, flavonoids) Glabridin. Liqourice extract, Mulberry extract, N-acetyl glucosamine, These agents causes skin lightening by tyrosinase inhibition, Others are: i) Melanosome transfer inhibitor (Niacinamide), ii) Melanosome maturation inhibition (Arbutin, Deoxyarbutin), iii) Antioxidant (Vit E, Vit-C), iv) Epidermal turnover enhancer (Retinoic acid, α-Hydroxy acids, salicylic acid, Linoleic acid), v) Plasma inhibitor (Tranexamic acid), vi) α-MSH induced melanin reduction (β-Carotene), vii) protease activator receptor-2 inhibitor, viii) Flavonoids (Pycnogenol) [13]. Tranexamic acid is a synthetic derivative of amino acid lysine is plasmin inhibitor and anti-fibrinolytic agent. It also used for herditary angioedema which works by indirect effect by reducing complement activation. By reducing plasmin activity, it reduces the consumption of C1 esterase inhibitor and hence decrease α- MSH which stimulates melamine synthesis [14]. It is temperature stable, not UV sensitive and does not get oxidized easily. Oral tranexamic acid 500mg/day for upto 6 months is efficacious for Melasma. Commonly reported complications are nausea, diarrhoea, abdominal pain, skin rash, orthostatic hypotension, acute cortical necrosis and disturbance of color vision. It is contra indicated in acquired color vision abnormalities, active coagulopathies and known hypersensitivity to tranexamic acid. Pycnogenol, extract of French pine bark represents a concentrate of phenol compounds consisting of phenolic acid, catechin, taxifolin and procyanidins. It has antioxidant and anti-inflammatory properties as it doubles the intracellular synthesis of anti oxidative enzyme and scavenges free radicals due to the aromatic ring bearing one or more hydroxyl groups. It also causes regeneration and protection of vit-C and Vit-E. It has a protective action against ultraviolet radiation. It has ability to inhibit tyrosine kinase and also regulation of bio synthesis of melanin and suppressing super oxides, Nitric oxide and radical hydroxyl. Orally 100mg/day pycnogenol is effective in Melasma. No side effects were observed, more over improvement of several symptoms as fatigue, constipation, body ache and anxiety [15].

Materials and Methods

This was a multicentre (Laser Aesthetics, Dhaka Bangladesh, US-Bangla Medical College & Hospital, Narayangonj, Bangladesh), comparative study performed on 100 patients with Melasma according to inclusion and exclusion criteria.

Inclusion Criteria

- Men and women without co-morbidities between 20 and 60 years old showing Melasma.

Exclusion criteria

- Pregnancy or intention to get pregnant
- Breast feeding
- History of thrombosis, smoking, oral or injectable contraceptive

There were 2 group of patients which were selected randomly. Group-A patients got cap tranexamic acid 250mg twice daily and group-B patients got cap pycnogenol 50mg twice daily. The evaluations were performed before and 3 months after treatment by following methods:

- MASI (Melasma area severity index)
- Patient evaluation with validated questionnaire for satisfaction before and after the end of treatment (MELASQoL) [16].

Statistical evaluation of the results was processed and compelled by window-based computer software program with SPSS-24(Statistical Packages for social sciences)

Table 1 shows total no of patients were 100. Age distribution were 20-30 years 26(26%), 31-40 years (46%), 41-50 years 20 (20%), 51-60 years 8(8%). According to sex distribution male 20-30 years 4(15%), 31-40 years 5(10%) 41-50 years 2(10%) and Female 20-30 years 22(85%), 31-40 years 41(90%), 41-50 years 18(90%), 51-60 years 8(100%) Location of Melasma were frontal 10(10%), central facial 81(81%), Chin 8(8%) and type of Melasma were epidermal 60(60%) dermal 10(10%) and mixed 30(30%) (Figure 1). After 3 Months treatment with oral tranexamic acid (Group-A) and oral pycnogenol (Group-B) we evaluated the patients. In group-A MASI score were before treatment 20.9 (±9.1) and after treatment 10.8 (±4.6) (P value <0.04) and MELASQoL score were 55.4 (±9.8) before treatment and 38.2(±11.1) after treatment (P value <0.365) In group-B MASI score were 19.2 (±7.1) before treatment and 7.2 (±4.1) after treatment (P value <0.001). MELASQoL score were 43.9(±8.2) before treatment and 25.5(±9.1) after treatment (P value <0.001).

Discussion

Melasma is a chronic skin disease that results in facial pigmentaton characterized by brownish spot. It is more common in female which causes embarrassment and distress to patient. But no treatment guarantees satisfactory result as because pathogenesis of Melasma is not still well defined. Use of hydroquinone topical cream is this gold standard but it is associated with some adverse effects. Now- a- days oral tranexanic acid are used widely. It has better outcome than traditional hydroquinone cream. But oral tranexamic acid has some drawbacks. In our study, treatment with oral tranexamic acid MASI score and MELASQoL score were significantly improved (P value <0.04 and <0.36 respectively). But tranexanic acid is not free of adverse effects such as erythema (14%), desquamation (22%) and burning sensation (12%).

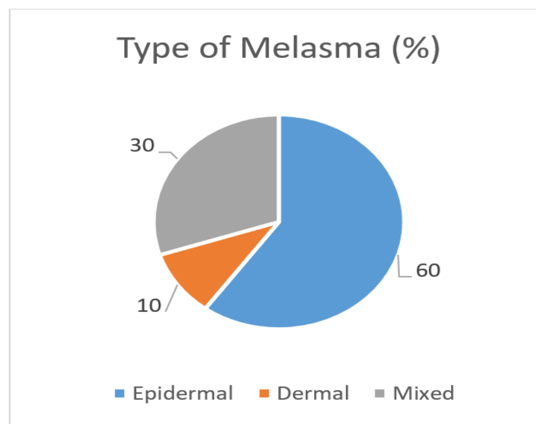

Figure 1: *Types of Melasma (Histological).*

Table1: *Demographic distribution of Patients (n=100).*

Age distribution	Total	Male	Female
20-30	26	4(15%)	22(85%)
31-40	46	5(10%)	41(90%)
41-50	20	2(10%)	18(90%)
51-60	8	0	8(100%)

Table 2: *Types of Melasma.*

location of Melasma	
Frontal	10 (10%)
Central facial	81(81%)
Chin	8(8%)

Table 3: *Evaluation after treatment.*

	Group-A			Group-B		
	Before treatment	After 3 Months treatment	P value	Before treatment	After 3 Months treatment	P value
MASI Score	20.9 (±9.1)	10.8(±4.6)	<0.04	19.2 (±7.1)	7.2 (±4.1)	< 0.001
MELASQoL Score	55.4 (±9.8)	38.2 (±11.1)	<0.365	43.9 (±8.2)	25.5 (±9.1)	<0.001

In our study use of oral pycnogenol had better outcome. Pycnogenol a standardized plant extract, obtained from the bark of the French maritime pine pinus pinaster has evoked great interest in the management of Melasma. About 70% pycnogenol are procyanidins, comprising catechin and epicatechin. Its main advantage is high bioavailability, synergistic action of its ingredients and nearly zero side effects. Pycnogenol is potent antioxidant with anti-inflammatory properties may be also

effective in venous ulcers, climacteric syndrome, arterial hypertension and rheumatological diseases [17]. For instance, a sample of 30 Chinese women with facial Melasma were followed for a month using 25mg pycnogenol orally 3 times daily had improvement in 80% participants with a reduction of 22% in the mean colour intensity and 38% in the affected facial area. A case series performed in venezuela evaluated 48 women and 2 men with high Melasma who took 50mg pycnogenol orally 3 times daily for 12 weeks. After 12 weeks of follow up the mean reductions in mMASI and MELASQoL scores were 31% and 47% respectively. Most participants had pigmented skin (phototype IV) and the author perceived that fairer skin had a greater improvement in Melasma [18]. In our study group B patients receiving oral pycnogenol 50mg 12 hourly we got better outcome than oral tranexamic acid. MASI score were 19.2(±7.1) before treatment and 7.2 (±4.1) after treatment and MELASQoL score were 43.9(±8.2) and 25.5(±9.1) respectively before and after treatment. Both p-value were significant. More over pycnogenol have no side effects but also had some beneficiary effects.

Limitations of the Study

This study had potential limitations due to its short follow up. Specific design for long term efficacy of pycnogenol, as well as its use as maintenance treatment to reduce the risk of relapses after treatment discontinuation are needed to evaluate the best option among these existing strategies for the management of Melasma.

Conclusion

Pycnogenol is well tolerated and more effective orally (50mg 12 hourly for 3 months) than oral tramexamic acid (250mg 12 hourly for 3 months). It can be also used as triple combination cream with tinted sun screen in Melasma.

References

1. Sarkar R, Chugh S, Garg VK. Newer and upcoming therapies for Melasma. Ind j dermatol, venereal leprol. 2012; 78:417.
2. Mahajan VK, Patil A, Blicharz L, Kassir M, Konnikov N, Gold MH, et al. Medical therapies for Melasma. J Cos Dermatol. 2022; 21: 3707-3728.
3. Picardo R, Vallejos Q, Feldman SR, et al. The prevalence of Melasma and its association with quality of life among male migrant Latino workers. Int J Dermatol. 2009; 48: 22-26.
4. Kagha K, Fabi S, Goldman MP. Melasma's impact on quality of life. J Drugs Dermatol. 2020; 19: 184-187.
5. Guinot C, Cheffai S, Latreille J, Dhaoui MA, Youssef S, Jaber K, et al. Aggravating factors for Melasma: a prospective study in 197 Tunisian patients. J Eur Acad Dermatol Venereol. 2010; 24: 1060-1069.
6. Prabha N, Mahajan VK, Mehta KS, Chauhan PS, Gupta M. Cosmetic contact sensitivity in patients with Melasma: results of a pilot study. Dermatol Res Pract. 2014.
7. Maeda K, Naganuma M. Topical trans-4-aminomethylcyclohexanecarboxylic acid prevents ultraviolet radiation-induced pigmentation. J Photochem Photobiol. 1998; 47: 136-141.
8. Maeda K, Tomitab Y. Mechanism of the inhibitory effect of tranexamic acid on melanogenesis in cultured human melanocytes in the presence of keratinocyte-conditioned medium. J Health Sci. 2007; 53: 389-396.
9. Kim EH, Kim YC, Lee ES, Kang HY. The vascular characteristics of Melasma. J Dermatol Sci. 2007; 46: 111-116.
10. Chowdhary B, Mahajan VK, Mehta KS, Chauhan PS, Sharma V, Sharma A, et al. Therapeutic efficacy and safety of oral tranexamic acid 250 mg once a day versus 500 mg twice a day: a comparative study. Arch Dermatol Res. 2021; 313: 109-117.
11. Attawa E, Khater M, Assaf M, Heleem MA. Melasma treatment using an erbium: YAG laser: a clinical, imunohistochemical, and ultrastructural study. Int J Dermatol. 2015; 54: 235-244.
12. Wang CC, Hui CY, Sue YM, Wong WR, Hong HS. Intense pulsed light for treatment of refractory Melasma in Asian persons. Dermatol Surg.2004; 30:1196-1200.
13. Babbush KM, Babbush RA, Khachemoune A. Treatment of Melasma: a review of less commonly used antioxidants. Int J Dermatol. 2021; 60: 166-173.
14. Lee JH, Park JG, Lim SH, Kim JY, Ahn KY, Kim MY, et al. Localized intradermal microinjection of tranexemic acid for treatment of Melasma in Asian patients: A preliminary clinical report. Dermatol Surg 2006; 32: 626-631.
15. Ni Z, Mu Y, Gulati O. Treatment of Melasma with Pycnogenol. Phytother Res. 2002; 16: 567-571.
16. Colferai MM, Miquelin GM, Steiner D. Evaluation of oral tranexamic acid in the treatment of Melasma. J cos dermatol. 2019; 18: 1495-1501.
17. Pourmasoumi M, Hadi A, Mohammadi H, Rouhani MH. Effect of pycnogenol supplementation on blood pressure: A systematic review and meta-analysis of clinical trials. Phytother Res. 2020; 34: 67-76.
18. Alvarez J. Efecto despigmentante del extracto de Pino Marino Francés (Pycnogenol®) en pacientes con hipercromía facial. Arch Venezol Farmacol Terap. 2014; 33: 1-6.