Oral tranexamic acid treatment beyond 6 months for melasma patients - A retrospective case series

To the Editor: Melasma is a chronic acquired disorder of primarily facial hyperpigmentation that can cause significant quality of life impairment.[1] Its pathogenesis may involve the induction of various melanogenesis pathways through ultraviolet radiation exposure, keratinocyte and mast cell stimulation, dermal inflammation, hormonal upregulation, and neovascularization.[2,3] Long-term treatment options remain limited yet in demand for patients seeking sustained results. Oral tranexamic acid (TXA), an antifibrinolytic, is an effective off-label treatment for melasma. However, scarce long-term safety data and concern regarding its possible increased thrombotic risk often limits its duration of use to 3 to 6 months; a maximum of 2 years was reported in 1 small ($n = 15$) cohort of patients.[4]

Favorable long-term safety data for oral TXA exists in the gynecologic literature[5] where it is used for heavy menstrual bleeding at cumulative doses per month roughly 30% higher than that used for melasma, with studies of up to 25 months duration. Thus, we sought to evaluate the safety of using oral TXA beyond 6 months for melasma. A retrospective chart review was performed of patients ≥18 years of age who were treated with oral TXA for melasma for ≥ 6 months at a dermatologic center in Vancouver, Canada. Outcome measures included patient characteristics such as age, sex, skin phototype, comorbidities, previous and/or concurrent treatment, TXA treatment duration, dose, response, and adverse events. Treatment response was evaluated using the melasma severity scale on deidentified photographs at baseline, 6 months, 1 year, and 2 years. Mean melasma severity scale scores between different time points were compared using the Wilcoxon signed rank test.

Twenty-six patients were included, all females with a mean age of 44.5 ± 8.8 years, predominantly skin phototype III (42.3%), history of prior treatment (96.1%), and all used concurrent therapy with usual topical agents (Table I). All patients took oral TXA at 250 mg twice daily and after 6 months, 6 patients reduced to 250 mg once daily for maintenance. Mean duration of treatment was 17.42 ± 5.87 months with a range of 7 to 28 months. There was a statistically significant decrease in mean melasma severity scale scores from 1.96 ± 0.72 at baseline to 0.61 ± 0.75 ($P < .001$) at 6 months, 0.23 ± 0.56 ($P < .001$) at 1 year, and 0.43 ± 0.79 ($P = .014$) at 2 years (Table II). Treatment was generally well-tolerated. Two patients developed gastrointestinal upset, causing 1 to discontinue treatment. There were no other adverse events reported.

In this study, oral TXA at usual dosages for melasma was well-tolerated and maintained effect in patients treated for up to 28 months. No thromboembolic events were observed with treatment beyond 6 months. Anecdotally, the authors also noted reduced use of hydroquinone in these patients, thus TXA may indirectly reduce the risk of

Table I. Patient characteristics

Characteristic	Total $n = 26$
Sex	
Female	26 (100%)
Male	0 (0%)
Age (yr)	
Mean ± SD	44.5 ± 8.8
Median [minimum, maximum]	42 [31, 59]
Skin phototype	
I	0 (0%)
II	3 (11.5%)
III	12 (46.2%)
IV	7 (26.9%)
V	4 (15.4%)
VI	0 (0%)
Medical comorbidities	
Endometriosis	1 (3.8%)
Fibroids	1 (3.8%)
Septic shock	1 (3.8%)
Miscarriage	2 (7.7%)
Cardiac risk factors	
Prior smoking	1 (3.8%)
Family history of stroke	1 (3.8%)
Concurrent hormone therapy	
Oral contraception	0 (0%)
Hormone replacement therapy	0 (0%)
Hormonal intrauterine device	5 (19.2%)
History of prior treatment for melasma	25 (96.2%)
Hydroquinone	18 (69.2%)
Nonhydroquinone botanical brighteners	15 (57.7%)
Laser/intense pulsed light	10 (38.5%)
Other (eg peels, retinoids, cosmeceuticals)	16 (61.5%)
Concurrent therapy	
Yes*	26 (100%)
No	0 (0%)

*Concurrent therapy included usual topical agents such as hydroquinone, nonhydroquinone botanical brighteners, exfoliants, antioxidants, and retinols.

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Table II. Mean melasma severity scale score at baseline, 6-months, 1-year, and 2-year follow-up

Time	*n*	MSS (mean ± standard deviation)
Baseline	26	1.96 ± 0.72
6 mo	26	0.61 ± 0.75
1 yr	14	0.23 ± 0.56
2 yr	6	0.43 ± 0.79

Tested MSS score pair	Z	*P* value
Baseline - 6 mo	−4.417*	<.001
Baseline - 12 mo	−3.695*	<.001
Baseline - 24 mo	−2.456*	.014
6 mo - 12 mo	−1.890*	.059
6 mo - 24 mo	−1.000*	.317
12 mo - 24 mo	−1.000†	.317

Mean MSS scores compared with Wilcoxon signed ranks test.
MSS, Melasma severity scale.
*Based on positive ranks.
†Based on negative ranks.

exogenous ochronosis and irritant contact dermatitis. Most importantly, this treatment was so impactful that patients chose to continue long-term off label treatment despite the lack of clinical trial data. The main limitation is small sample size, thus larger studies are needed to validate the safety of long-term oral TXA for melasma.

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Conflicts of interest

None disclosed.

REFERENCES

1. Jiang J, Akinseye O, Tovar-Garza A, Pandya AG. The effect of melasma on self-esteem: a pilot study. *Int J Womens Dermatol*. 2018;4(1):38-42.
2. Kwon SH, Park KC. Clues to the pathogenesis of melasma from its histologic findings. *Pigment Disord*. 2014;1(141):1-4.
3. Rajanala S, Maymone MBC, Vashi NA. Melasma pathogenesis: a review of the latest research, pathological findings, and investigational therapies. *Dermatol Online J*. 2019;25(10):1-6.
4. Zhu CY, Li Y, Sun QN, Takada A, Kawada A. Analysis of the effect of different doses of oral tranexamic acid on melasma: a multicentre prospective study. *Eur J Dermatol*. 2019;29(1):55-58.
5. Meaidi A, Mørch L, Torp-Pedersen C, Lidegaard O. Oral tranexamic acid and thrombosis risk in women. *EClinicalMedicine*. 2021;35:100882.

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