Low-dose oral minoxidil for treating alopecia: A 3-year North American retrospective case series

To the Editor: Alopecia remains a therapeutic challenge to dermatologists. Topical 5% minoxidil is a Food and Drug Administration (FDA)—approved treatment for androgenetic alopecia (AGA), with a variable response rate. Studies suggest that low dose oral minoxidil (LDOM) requires decreased follicular enzymatic activity compared with its topical form.[1] Although reports document its successful use in dermatology, adaptation in North America has been low. It is unclear whether this is due to concern about patient safety or lack of established oral minoxidil dosing for hair loss.

Through electronic medical records search (YES! EMR, Toronto, Canada), all patients first prescribed LDOM at 2 community dermatology clinics from December 1, 2016, through November 30, 2019, were identified. The total number of clinic visits for alopecia, encounters pertaining to LDOM, and each prescription duration was tabulated. Clinic notes were reviewed to determine alopecia diagnoses, prescription compliance, dosage, blood pressure changes, LDOM side-effects, and the effect on hair shedding and hair growth. The University of Toronto research ethics board approved this retrospective study.

Patients were prescribed oral minoxidil 1.25 mg nightly for 3 months (halved Loniten 2.5 mg tablet;

Table I. Patient demographics and alopecia diagnoses of those who received low-dose oral minoxidil

Demographic	Patients		
Initial recruitment	Total (n = 74)	Men (n = 15)	Women (n = 59)
Confirmed LDOM prescription	Total (n = 51)	Men (n = 12)	Women (n = 39)
Mean age, y	42	33	46
Hair textures			
Caucasian-textured (straight)	28	9	19
Afro-textured (curly)	12	1	11
Asian-textured (straight)	11	2	9
South Asian	9	2	7
Far East Asian	2	0	2
Type of alopecia			
AGA	23	9	14
Multiple scalp diagnoses*	15	2	13
LPP or FFA	6	1	5
TA	3	0	3
CCCA	2	0	2
TE	1	0	1
Chemotherapy-induced alopecia	1	0	1
Previous alopecia therapy			
Topical minoxidil	35	6	29
Concurrent or overlapping alopecia therapy			
5α-reductase antagonists or other antiandrogen therapy	8	0	8 (AGA; FFA; AGA and FFA)
Spironolactone	5	0	5 (AGA; AGA and AA; AGA and TE)
Immunomodulators (methotrexate, hydroxychloroquine, pioglitazone)	4	0	4 (FFA; AGA and LPP/FFA)
Platelet-rich plasma	5	0	5 (AGA)
Antibiotics (doxycycline)	2	0	2 (CCCA)
Retinoids (acitretin)	2	0	2 (FFA/LPP)

Abbreviations denote subtypes of alopecia.
AA, Alopecia areata; *AGA*, androgenetic alopecia; *CCCA*, central centrifugal cicatricial alopecia; *FFA*, frontal fibrosing alopecia; *LDOM*, low-dose oral minoxidil; *LPP*, lichen planopilaris; *TA*, traction alopecia; *TE*, telogen effluvium.
*Multiple scalp diagnoses: men (n = 2), AGA and AA, and AGA and pseudofolliculitis barbae. Women (n = 13), AGA and TE, 4; CCCA and TA, 4; AGA and LPP/FFA, 2; AGA and AA, 1; AGA, TE, and psoriasis, 1; and TE and weathering, 1.

Table II. Patient-reported reasons for stoppage of low-dose oral minoxidil and adverse effects during low-dose oral minoxidil treatment

Stoppage reason	Patient frequency
Aversion to pills	2
Forgetfulness	1
Nausea	1
Facial acne	1
Preference for topical minoxidil	1
Perceived lack of efficacy and hair shedding	1
Facial hypertrichosis	1
Side-effects and symptoms	
Cardiac	
Hypotensive symptoms (reported as lightheadedness)	4 (2 men; lasted 1 wk; 1 episode) (2 women; lasted several days; reported with coprescription spironolactone)
Blood pressure self-assessments	
Improved measurement	2
Unchanged measurement	11
Palpitations	2 (1 woman; lasted 3 wk) (1 woman; episodic and preexisted LDOM)
Ankle edema	1 (woman; lasted 2 wk)
Hair	
Hair shedding	2 (1 woman; discontinued therapy) (1 woman; continued therapy and it stabilized)
Hypertrichosis	22 (3 men: temples, cheek) (19 women: skin of lip; eyebrows - deemed beneficial for 2 FFA patients; chin; cheeks; eyelashes)
Skin	
Urticaria	1 (woman; 1 episode)
Other	
Paresthesia (arms/hands)	1 (woman; intermittently during 4 wk, preexisted LDOM, possibly increased in frequency)

FFA, Frontal fibrosing alopecia; *LDOM*, low-dose oral minoxidil.

Pfizer Canada). They understood the drug's on-label indication and most common side-effects, including facial hair.[2] Self-assessment of blood pressure and night ingestion of LDOM to help mitigate hypotensive symptoms were encouraged. No prescription recipients had documented cardiac, hepatic, or renal disease. In-clinic photography with standard poses was used to monitor clinical progression where permitted. All patients prescribed minoxidil during the 3-year period were included in this as-treated analysis.

This cohort completed 346 alopecia appointments from 2016-2019, including 165 pertaining to LDOM. The average duration of LDOM consumption across all patients who continued therapy was 10 months. There was a total of 509.5 months of LDOM treatment, including a maximum duration of 30 months.

Alopecia was diagnosed clinically (n = 64) and with histology (n = 10). These 74 patients received at least one 3-month prescription for 1.25-mg oral minoxidil during the 3-year period (Table I). The follow-up rate was 72% (53/74) and included 2 patients who returned without filling their prescriptions because of concerns about potential adverse effects. Therefore, 51 of 74 patients prescribed LDOM were confirmed to have started their prescription (Table I).

Most patients requested represcription of LDOM at reassessment (43/51; 84%). Patient reasons for LDOM stoppage were recorded for the remainder (Table II).

At follow-up, escalated 2.5-mg dosing was adopted by 9 of 12 men (75%) and 7 of 39 women (18%) despite known risk of facial hypertrichosis. Side-effects in all patients who continued LDOM were

tabulated (Table II). No patient who continued LDOM reported new cardiac diagnoses or morbidity, including pericardial effusions or pericarditis.

Results from this retrospective series indicate increased scalp hair growth (33/51; 65%) and decreased hair shedding (14/51; 27%) with LDOM. Patients with nonscarring alopecia were most likely to acknowledge and exhibit clinical improvement (Supplemental Discussion available via Mendeley at https://data.mendeley.com/datasets/4sccxmrfzm/1).

The 5 Cs of LDOM are convenience, cosmesis, cost savings, cotherapy feasibility, and compliance.[3] The newly proposed sixth C is "crown efficacy," exhibited by increased hair growth at this scalp region (Supplemental Figs 1-6, https://data.mendeley.com/datasets/4sccxmrfzm/1/files/a99ab998-4da1-42d7-926f-e4de7aca4d73, https://data.mendeley.com/datasets/4sccxmrfzm/1/files/b67819a9-3e1a-46a9-9637-e001a434cba9).

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Exposure to terbinafine in pregnancy and risk of preterm birth, small for gestational age, low birth weight, and stillbirth: A nationwide cohort study

To the Editor: Terbinafine is a commonly used antifungal agent. Although it is generally well tolerated in the nonpregnant population, data evaluating the fetal safety are limited. We recently provided data not suggestive of a risk of major birth defects or spontaneous abortion when terbinafine is used in early pregnancy.[1] Here, we investigated whether terbinafine exposure during pregnancy is associated with preterm birth, small for gestational age, low birth weight, and stillbirth.

Through linkage of nationwide registries, we identified all pregnancies in Denmark (January 1997 to December 2016), including individual-level data on exposure, outcomes, and covariates. The study was designed as previously conducted.[1,2] Pregnancy records with overlapping pregnancies, implausible/missing gestational age, and missing information on birth weight (for these analyses) were excluded. Distinct cohorts were constructed for each outcome analysis. Oral terbinafine exposure was defined as filled prescriptions from 2 weeks before and throughout pregnancy. Outcomes were preterm birth (defined as birth before 37 completed gestational weeks), small for gestational age (below the 10th percentile of the gestational-age-specific birth weight), low birth weight (<2500 g), and stillbirth (fetal death after gestational week 22). Terbinafine-exposed pregnancies were compared with unexposed ones to any antifungal drugs from 1 year before through pregnancy, matched (1:10 ratio) on propensity scores (estimated by logistic regression). Associations were assessed by risk ratios (RRs), except for stillbirth, which was assessed by hazard ratio, computed by Cox regression (version 9.4, SAS). Secondary analyses examined the associations by different exposure definitions, as well as in comparison to topical terbinafine–exposed pregnancies. The Danish Data Protection Agency approved the study. Ethical and informed consent was not required.

From a source cohort of 1,650,649 pregnancies, up to 942 oral terbinafine–exposed and 9420 unexposed individuals were included in the matched cohorts (Table I); baseline characteristics were well balanced. In matched analyses, preterm birth occurred in 37 terbinafine-exposed pregnancies (6.2%) and 344 unexposed ones (5.7%) (RR 1.08; 95% confidence interval [CI] 0.77-1.49); small for gestational age in 55 terbinafine-exposed